Kirklin/Barratt-Boyes
Cardiac Surgery
Morphology, Diagnostic Criteria, Natural History, Techniques, Results, and Indications
Fourth Edition

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Preface to Fourth Edition

The fourth edition of Cardiac Surgery has been prepared without contributions from two of the authors of the third edition, Drs. Robert B. Karp and Donald B. Doty. Dr. Karp was fatally injured in an automobile accident in 2006. Dr. Doty retired from the practice of cardiothoracic surgery in 2004. We are extremely grateful to both of them for their outstanding contributions, many of which remain in the fourth edition. We are equally pleased to welcome as a contributor to the fourth edition, Dr. James K. Kirklin, son of Dr. John W. Kirklin, co-author with Sir Brian Barratt-Boyes of the first two editions of Cardiac Surgery.

Except for Dr. Frank Hanley, we received our cardiothoracic surgical education at the University of Alabama Medical Center under the tutelage of John Kirklin, and we were privileged to serve as faculty members in the Department of Surgery at the University of Alabama at Birmingham School of Medicine during his tenure as chair of the department and director of the Division of Cardiothoracic Surgery. James Kirklin currently serves as director of that division.

We have all, including Dr. Hanley, been profoundly influenced by the teachings of John Kirklin, and by his intellect, vision, and clinical skills. His commitment to improving the quality of cardiac surgery through rigorous clinical and laboratory investigations and providing superb clinical care and disciplined training of young surgeons was truly exemplary. Although our interactions with Sir Brian Barratt-Boyes were less frequent and less intense, he possessed these same attributes and was an inspiration to us as well. In the last year of his life, he was engaged in updating the echocardiographic and structural valve deterioration data of the entire Green Lane Hospital experience of aortic allografts, with the intent of transmitting these data for analysis by one of us (EHB).

The systematic approach to cardiac surgery developed and promulgated by these two pioneering surgeons, who both died between publication of the third and this fourth edition of Cardiac Surgery, has been a major fixture in our professional careers. The decision to author the third and now fourth editions of Cardiac Surgery was in large part influenced by our desire to perpetuate their philosophical approach to this discipline. Thus, the general format of the three previous editions has been maintained.

All chapters present in the third edition have been revised. They have been rearranged so that every chapter relating to surgical treatment of congenital heart disease (except for Chapter 29, “Congenital Heart Disease in the Adult”) has been placed in Volume 2. Each chapter was rewritten with input from at least two of the four authors. Chapter 4 (“Anesthesia for Cardiovascular Surgery”) was revised by Drs. Colleen G. Koch and Chandra Ramamoorthy. The content, and in some instances the titles, of several chapters have been altered to reflect current knowledge and practice. As an example, the chapter “Heart Failure” in the third edition has been expanded into three chapters in the fourth edition: “Cardiomyopathy,” “Cardiac Transplantation,” and “Mechanical Circulatory Support.” New illustrations and new echocardiographic, computed tomographic, and magnetic resonance images have been added to reflect important advances in the diagnosis and management of congenital and acquired diseases of the heart and great vessels.

We recognize the potential limitation of four authors writing separate portions of this textbook. This challenge was met, in part at least, by dual authorship of each chapter, and by author meetings and correspondence. It was also met by a process of universal review. Specifically, as with the third edition, Dr. Blackstone was designated as the final arbiter. After completion of the revision of each chapter by the primary author, copyedited material was forwarded to Dr. Blackstone in Cleveland, where he and his assistant, Tess Muharsky Parry, reviewed, edited, reorganized, questioned, and adjudicated the entire content of each chapter. It is our hope that this intensive process has improved the accuracy and comprehensiveness of each chapter.

As in the previous editions, Part I of Volume 1 discusses basic concepts of cardiac surgery: anatomy, support techniques, myocardial management, anesthesia, postoperative care, and methodology for generating new knowledge from previous experience. These core chapters are applicable to the broad audience of medical professionals who care for patients with cardiac disease. The remaining chapters of Volume 1 (Parts II to V) discuss specific acquired diseases of the heart and great vessels, and congenital heart disease in adults. This edition has retained, in these later sections and in all of the chapters in Volume 2, presentation of “Indications for Operation” at the end of each chapter, because the indications are the derivatives of comparison of various outcomes (results) of alternative forms of treatments, including no treatment (natural history).

The abbreviation UAB has been retained, and is used to identify data and illustrations from the University of Alabama at Birmingham; similarly, GLH identifies those from Green Lane Hospital in Auckland, New Zealand. The bibliographic references are again designated using the first letter of the surname of the first author and a number (e.g., L4), rather than simply a number. This convention is simple and convenient, and allows the reader to easily locate a given author’s publication among the alphabetically arranged references. The abbreviation CL is used throughout to denote 70% confidence limits around the point estimate. The reasons for presenting 70% rather than 95% or 50% confidence limits are presented in Chapter 6.

The fourth edition is written at a time of great change for the specialty of cardiac surgery. Percutaneous catheter-based interventions are being increasingly used to treat patients with
coronary arteriosclerotic heart disease, aortic valve stenosis, mitral valve regurgitation, hypertrophic obstructive cardiomyopathy, diseases of the thoracic aorta, and congenital cardiac lesions such as patent ductus arteriosus, coarctation of the aorta, atrial and ventricular septal defects, and pulmonary valvar stenosis and regurgitation. Less invasive techniques are rapidly being incorporated into cardiac surgical practice for many conditions that continue to require open surgical repair. These advances must be acknowledged and embraced if cardiac surgery is to thrive in the future.

It is our hope that this textbook will be of value to cardiac surgeons who care for patients with congenital and acquired heart disease and with disorders of major blood vessels in the chest, as well as to cardiologists and interventional cardiologists who treat children and adults with these conditions, anesthesiologists, intensivists, pulmonologists, imaging specialists, cardiovascular nurses, trainees in all of these disciplines, and others.

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This chapter describes normal cardiac and great artery anatomy and dimensions, as well as the terminology usually employed.

**CARDIAC CHAMBERS AND MAJOR VESSELS**

Accurate diagnosis of congenital heart defects depends in part on identifying cardiac chambers and major vessels by their morphology, regardless of their spatial positions (Fig. 1-1).

**Right Atrium**

The right atrium (Fig. 1-2) is the heart chamber that normally receives systemic venous drainage from inferior and superior venae cavae. It also normally receives the major portion of coronary venous drainage from the coronary sinus. Morphologic characteristics important for identifying the right atrium are presence of the limbus of the fossa ovalis, which surrounds the valve of the fossa ovalis (septum primum) superiorly, anteriorly, and posteriorly; a wide-based, blunt-ended, right-sided atrial appendage (auricle); eustachian valve at the orifice of the inferior vena cava and thebesian valve at the orifice of the coronary sinus; and crista terminalis, which separates trabeculated from nontrabeculated (venous) portions of the atrium (Fig. 1-3).

The normal structures are sometimes expressed in an excessive or unusual manner. These are not themselves functionally important abnormalities but are usually associated with cardiac malformations. Thus, the eustachian and thebesian valves may be sufficiently prominent to appear to divide the right atrium into two parts, a common finding in tricuspid atresia. The right atrial appendage may be juxtaposed leftward, and the left atrial appendage is less frequently juxtaposed rightward. Juxtaposition of the atrial appendages is usually associated with cardiac malformations.

Radiologically, the definitive morphologic features of the right atrium may be difficult to recognize. Occasionally, the atrial septum is seen well enough in angiographic profile to delineate the limbus of the fossa ovalis, and sometimes the right atrial appendage is outlined sufficiently to differentiate its shape from that of the left atrial appendage. The fact that the hepatic portion of the inferior vena cava usually drains into the right atrium often makes it possible to determine the location of the right atrium by passage of a catheter from the inferior vena cava to the heart. Cardiovascular magnetic resonance imaging (MRI) and three-dimensional (3D) echocardiographic computed tomography are increasingly able to identify even complex morphologic features of this and other cardiac chambers and their connections.

**Left Atrium**

The left atrium (Fig. 1-4) is the cardiac chamber that normally receives pulmonary venous drainage from the four pulmonary veins. Its septal surface is characterized by the flap valve of the fossa ovalis (septum primum), in contrast to the limbus of the fossa ovalis present on the right atrioseptal surface. The left atrial appendage (auricle) is long and narrow, in contrast to bluntness of the right atrial appendage, and is the best indicator that the atrium is morphologically a left atrium. There is no crista terminalis at the base of the left atrial appendage, the only trabeculated structure in the left atrium.

In general, at cardiac catheterization, the location of the left atrium is determined by exclusion after identifying the position of the right atrium as described earlier. With normal pulmonary venous connection, the left atrium may

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**Figure 1-1** Surface anatomy of heart. Left atrial appendage is long and narrow, whereas right atrial appendage is short and blunt. Aorta originates posterior and to the right of the pulmonary trunk at the base of the heart, but is anterior and to the right by the pericardial reflection (not shown). Right ventricle occupies most of anterior aspect of heart, with left ventricle forming the apex and posterior aspects.
**Figure 1-2** Interior of normal right atrium, viewed from right side at operation. Key: AA, Atrial appendage; AnMV, position of mitral valve anulus on other side of septum, indicated by dotted line; AnTV, anulus of tricuspid valve, indicated by dotted line; ASCTV, anteroseptal commissure of tricuspid valve; CS, coronary sinus orifice; CT, crista terminalis (inside of sulcus terminalis); EuV, eustachian valve; FO, fossa ovalis (sometimes called septum primum); IVC, inferior vena cava orifice; LFO, limbus of fossa ovalis (C-shaped, extending anteriorly and posteriorly to enclose fossa ovalis); SLTV, septal leaflet of tricuspid valve; SVC, superior vena cava orifice; ThV, thebesian valve; TT, tendon of Todaro; X, muscular portion of atrioventricular septum; Z, membranous portion of atrioventricular septum.

**Figure 1-3** Interior of right atrium, oriented as at operation. Right atrium receives superior and inferior venae cavae. Its trabeculated portion is separated from its smooth portion by the crista terminalis. Fossa ovalis is located in center of atrial septum, surrounded on its superior, anterior, and posterior aspects by the limbus. Coronary sinus is positioned inferiorly. Coronary sinus, along with tendon of Todaro and anulus of septal leaflet of tricuspid valve, form the boundaries of triangle of Koch. Atrioventricular node and proximal portions of bundle of His, portions of the specialized conduction system, lie within the triangle of Koch. Right coronary artery lies in atrioventricular groove, the anatomic point of separation of right atrium and right ventricle.
be well opacified after a right ventricular or pulmonary artery injection.

Right Ventricle

Topographically, the right ventricle has a large sinus portion that surrounds and supports a tricuspid atrioventricular (AV) valve (inlet portion) and includes the apex and a smaller infundibulum (outlet portion) that supports a semilunar valve. The inlet and outlet valves of the right ventricle are thus widely separated. The entire sinus portion of the right ventricle and most of the infundibulum (both free wall and septum) are coarsely trabeculated.

The septal surface of the right ventricle is divided into an inlet portion, a trabecular portion (sometimes called the apical trabecular portion), and an outlet portion (Fig. 1-5). Alternatively, the septal surface of the right ventricle may be divided into posterior (basal), middle, apical (anterior), and infundibular (conal) portions (Fig. 1-6). The inlet portion of the ventricular septum surrounds and supports the tricuspid valve. The trabecular portion is that portion with the coarse trabecular pattern typical of the right ventricle (see Fig. 1-6). The outlet portion of the right ventricular aspect of the ventricular septum is smooth but complex and has three components. The largest is the infundibular (conal) septum, which separates the pulmonary from the aortic and tricuspid valves. Only part of the infundibular septum is interventricular (see Fig. 1-5), and in some malformations (e.g., double outlet right ventricle), none of it may be. It must be emphasized that the most distal cephalad portion of the infundibular septum is not, strictly speaking, part of the ventricular septum, because in the normal heart, the pulmonary valve arises from the apex of a cone of muscle and does not have a septal attachment.

A second part of the outlet portion of the septum is the anterior (superior) extension, or division, of the trabecula septomarginalis (septal band). A third small, very anterior portion is a narrow extension superior to the trabecular septum. Laterally to the right, the infundibular septum imperceptibly merges with the free right ventricular wall immediately beyond its attachment to the membranous septum; at that point, it can be called the parietal extension of the infundibular septum (Fig. 1-7). The parietal band lies anterior to the right aortic sinus (see Fig. 1-7), partially overlying that portion of the free wall of the right ventricle termed the ventriculo-infundibular fold. Many surgeons call the infundibular septum and the parietal band the crista supraventricularis. Medially and to the left, the infundibular septum merges with the trabecular portion of the septum between the limbs of the particularly prominent smooth, Y-shaped muscle bundle called the trabecula septomarginalis (Fig. 1-8). The trabecula septomarginalis extends apically to become continuous with the moderator band, a prominent trabeculation running from septum to free wall.

1The phrase inlet septum is in some ways undesirable because the term has developmental implications, and the large inlet septum on the right ventricular side is not duplicated on the left side. Use of the term trabecular to describe a portion of the sinus septum is also undesirable in some ways because part of the infundibular septum is also trabeculated (see Fig. 1-5).
Figure 1-5  Interior of normal right ventricle, particularly trabecular and outlet portions, oriented as at operation. Infundibular (conal) septum separates pulmonary valve from tricuspid valve, and only its rightward portion and inferior part of its central portion form part of the interventricular septum (see also Fig. 1-6). Entire outlet portion of septum of infundibulum is composed of the septal extension of infundibular septum, anterior limb of trabecula septomarginalis (septal band), and in front of that, a heavily trabeculated portion of septum. Key: AL, Anterior (superior) limb of TSM; AP, anterior papillary muscle; InfS, infundibular (conal) septum; MB, moderator band; MS, position of membranous septum; PE, parietal extension of infundibular septum (parietal band); PL, posterior limb of TSM, giving origin to medial papillary muscle; SE, septal extension of infundibular septum; TS, trabeculated portion of septum, part of which lies in infundibulum and remainder in sinus portion of ventricle; TSM, trabecula septomarginalis (septal band); VIF, ventriculoinfundibular fold.

Figure 1-6  Right ventricular side of septum after right atrium, right ventricle, and pulmonary trunk have been exposed by removing their anterior walls and rightward portion of aorta and parietal band (or parietal extension of infundibular septum). Entire right ventricular septum is displayed, together with relationship of infundibular septum to aortic root. In this heart, infundibular septum is less prominent than in some. Dashed line defines atroventricular portion of membranous septum. Dotted lines define arbitrary division of sinus septum into posterior (beneath septal tricuspid leaflet), middle, and apical portions. Specimen corresponds to a right anterior oblique projection in cineangiography. Key: A, Left anterior division septal band; Ao, aorta; CoS, coronary sinus; FO, fossa ovalis; IS, cut end of infundibular septum; NC, noncoronary aortic sinus; P, right posterior division of septal band; PT, pulmonary trunk; R, right coronary aortic sinus; SLTV, septal tricuspid leaflet; TSM, trabecula septomarginalis (septal band).
The junction between outlet and sinus (trabecular) portions of the right ventricle is clearly demarcated only along the lower margin of the outlet portion of the septum. The incomplete muscular ridge formed by the outlet septum (here, specifically, the infundibular septum) and the parietal band, together with the septal and moderator bands, forms a natural line of division between the posteroinferior sinus portion and the anterosuperior outlet portion of the ventricle. \(^2\) It is in this area that ventricular septal defects (VSDs) most commonly occur; the morphology of this area gives the name “junctional,” or “conoventricular,” to these defects.

The papillary muscle arrangement supporting the three leaflets of the tricuspid valve is different from that of the mitral valve in the left ventricle. In the case of the tricuspid valve, in addition to a single large anterior papillary muscle attached to the anterior free wall that fuses with the moderator band, there are multiple smaller posterior papillary muscles attached partly to the posterior (inferior) free wall and partly to the septum, and a group of small septal papillary muscles. The lowermost of these small septal muscles attaches posterior to the trabecula septomarginalis (see Fig. 1-5) and the uppermost, called the *medial (conal) papillary muscle* (muscle of Lancisi or muscle of Luschka), to the posterior limb of the septal band (Fig. 1-9).

**Left Ventricle**

The left ventricle consists of a larger sinus portion, which supports a bicuspid AV valve and includes the apex, and a much smaller outlet (outflow) portion beneath a semilunar...
valve. The inlet and outlet valves of the left ventricle lie juxtaposed within its base, and inflow and outflow portions are separated by the anterior mitral leaflet\textsuperscript{2} (Fig. 1-10).

The entire free wall of the left ventricle and apical half to two thirds of the septum are trabeculated (Fig. 1-11; see also Fig. 1-10), but the trabeculations are characteristically fine compared with those in the right ventricle.\textsuperscript{3}\textsuperscript{1} The septal surface of the left ventricle may be considered to have a sinus portion, most of which is trabeculated, and a smooth outlet (outflow) portion (see Fig. 1-11). The part of the sinus portion of the septum immediately beneath the mitral valve may be termed the \textit{inlet septum}, and the rest of the sinus portion, the \textit{trabecular septum} (Fig. 1-12). The outlet (outflow) portion lies in front and to the right of the anterior mitral leaflet, corresponding to the inlet portion on the right ventricular side of the septum, and includes the AV septum (Fig. 1-13). In contrast to the right ventricular side, where the septal tricuspid leaflet is the only valvar attachment to the septum, on the left ventricular side, the rightward half of the anterior mitral valve leaflet attaches to the septum posteriorly, and the right and part of the noncoronary aortic cusps attach to it anteriorly (see Fig. 1-12). The leftward half of the anterior mitral leaflet is in fibrous continuity with the aortic valve in an area termed the \textit{aortic–mitral anulus} (Fig. 1-14; see also Figs. 1-12 and 1-13). The anteriorly placed right ventricular infundibular (conal) septum lies opposite the aortic valve (Fig. 1-15). It may occasionally be displaced into the left ventricular outflow beneath the aortic valve; occasionally, muscle may also extend between the aortic and mitral valves, forming a true infundibulum to the left ventricle (see Fig. 1-10). The papillary muscles are called \textit{anterolateral} (or simply \textit{anterior}) and \textit{posteromedial} (posterior). No papillary muscles attach to the left side of the ventricular septum.

Myoarchitecture of the Ventricles

The adult ventricular mass is made up of a three-dimensional network of myocardial cells.\textsuperscript{33} This network is highly structured and arranged in layers in which the myocardial cells have a preferred orientation. In all hearts, the ventricular wall is arranged in three layers: superficial (subepicardial), middle, and deep (subendocardial). Superficial and deep layers are present in both right and left ventricles, whereas the middle layer is only present in the left ventricle. The superficial and deep layers are anchored at the ventricular orifices to fibrous structures of the central fibrous skeleton of the heart. This

\[\text{\textsuperscript{1}In this text, cusps of atrioventricular valves are termed leaflets, although current anatomy texts use the term cusp for both semilunar and atrioventricular valves.}\]
Figure 1-10  Interior of left ventricle after anterior ventricular and aortic walls have been excised, leaving obtuse margin, posterior free wall, and septum intact. Specimen is oriented anatomically. Posterior (mural) mitral valve leaflet lies against posterior free wall, whereas anterior mitral leaflet hinges in part from fibrous subaortic curtain and in part from septum and separates outflow portion of ventricle from remaining sinus portion. Arrow indicates direction of left ventricular outflow. Papillary muscles and chordae tendineae support mitral valve. Key: APM, Anterior papillary muscle; ALMV, anterior leaflet of mitral valve; PLMV, posterior leaflet of mitral valve; PPM, posterior papillary muscle; S, septal surface.

Figure 1-11  Interior of left ventricle after the free wall, including mitral valve apparatus, has been displaced to observer’s right and away from the septal surface by a fish-mouth incision into the left ventricle and aorta to demonstrate sinus and outlet portions of the septum. Key: ALMV, Anterior leaflet of mitral valve; MS, membranous septum; NC, noncoronary aortic cusp; O, outlet septum; R, right coronary aortic leaflet; S, sinus septum.
Figure 1-12  Interior of normal left ventricle, viewed from a slightly different perspective than in Fig. 1-11 to demonstrate inlet, outlet, trabecular, and membranous portions of septum. Key: ALPM, Anterolateral papillary muscle; AoM, aortic-mitral anulus (continuity); InS, inlet septum; MS, membranous septum; OS, outlet septum; PMPM, posteroomedial papillary muscle; TS, trabecular septum.

Figure 1-13  Ventricular septum from its left ventricular side, displaying relationship between its outflow portion and aortic and mitral valves. Pins protrude along line of attachment of tricuspid septal leaflet to right ventricular side of septum. Septal tissue inferior to this and dashed line correspond to right ventricular inflow, and septal tissue superior to it corresponds to atrioventricular septum. Arrow indicates a nodulus Arantii. (In this specimen, also shown in Fig. 1-11, right coronary artery ostium is located eccentrically near right noncoronary commissure.) Key: ALMV, Anterior leaflet of mitral valve; AV, atrioventricular septum (muscular portion); L, left aortic cusp; MS, membranous septum, with AV portion superior to dashed line and interventricular portion inferior to it; NC, noncoronary aortic cusp; R, right aortic cusp.
Figure 1-14  Interior of left ventricle, lateral view. Trabecular and outflow portions of ventricular septum are demonstrated. Inflow portion is beneath and behind mitral valve. Anterior leaflet of mitral valve is in fibrous continuity with aortic valve. Passageway below aortic valve, bounded by outflow portion of ventricular septum and anterior leaflet of mitral valve, is called the left ventricular outflow tract. Mitral valve is supported by two papillary muscles, anterior and posterior, arising from free wall of left ventricle.

Figure 1-15  Transverse section of heart at level of medial papillary muscle of tricuspid valve, showing curvature of septum that results in right ventricular infundibulum lying superior and anterior to aortic valve. Curvature of papillary muscles of the mitral valve is also shown. (Specimen is from a 9-month-old infant with a patent ductus arteriosus and pulmonary hypertension.) Key: AV, Aortic valve; LV, left ventricle; MV, mitral valve; P, posterior division of trabecula septomarginalis (septal band) and medial papillary muscle; PB, parietal band (parietal extension of infundibular septum); PV, pulmonary valve; RV, right ventricle; TV, tricuspid valve; VS, ventricular septum.
suggests that myocardial contraction plays an active role in cardiac valve function. The middle layer, unique to the left ventricle, shows a circumferential pattern. No planes of fibrous septation are present between the three layers. Instead, the distinction between one layer and the next is made by a change in muscle fiber direction. This is particularly evident in the ventricular septum, where the superficial layer of the right ventricle invaginates at the interventricular sulcus to form a thin muscular layer that forms the right side of the ventricular septum, covering the circumferentially arranged muscle fibers of the middle layer of the left ventricle. There are age-related changes in direction of the muscle fibers in the superficial layer. With advancing fetal and infant age, muscle fiber arrangement progresses from a horizontal to an oblique orientation. This change is especially evident in the right ventricle and probably reflects the changing pressure gradient between right and left ventricles.

The anatomy of the muscular subpulmonary infundibulum was studied by Merrick and colleagues. They point out a freestanding sleeve of myocardium supporting the pulmonary valve that is separate from the underlying anatomic ventricular septum, and Van Praagh argues that this subsemilunar infundibulum “belongs” to the great arteries, not the ventricles. It may be identified by changing directions of myocardial muscle fibers, referred to by surgeons as “layers” of the septum. This anatomic feature makes possible the safe separation of the pulmonary trunk from the right ventricular outflow tract for use as a valve substitute (autograft).

**Great Arteries**

The aorta is the great artery arising from the base of the heart that normally gives rise to the systemic and coronary arteries. Identity of the aorta is established by recognizing it as the vessel of origin of the brachiocephalic arteries, which never arise from the pulmonary artery. It is not so definitively the vessel of origin of the coronary arteries; occasionally one, or rarely both, coronary arteries may arise from the pulmonary artery. (Appendix 1A).

The pulmonary trunk (main pulmonary artery) is the great artery that normally gives rise to the pulmonary arterial system. The pulmonary trunk characteristically has no brachiocephalic vessels arising from it. At angiography, differentiation between pulmonary trunk and aorta may require careful study, as the brachiocephalic vessels may opacify with the pulmonary trunk by filling through a patent ductus arteriosus. The pulmonary valve is normally anterior, and the aortic valve posterior and to the right, in individuals with visceral and atrial situs solitus.

**ATRIAL SEPTUM**

See “Right Atrium” and “Left Atrium.”

**VENTRICULAR SEPTUM**

The right and left ventricular septal surfaces are asymmetric, related mainly to presence of an infundibulum in the right ventricle only (although Van Praagh and colleagues argue that a small portion of the subsemilunar conus lies just beneath the right aortic valve cusp) [see Appendix 1A]. In addition, higher pressure in the left ventricle makes the sinus septal surface concave on the left side and convex on the right (see Fig. 1-15), a feature accentuated during ventricular systole. The axes of the right and left ventricular outflow tracts differ. That of the right ventricle is almost vertically oriented, whereas that of the left ventricle angles sharply to the right (Fig. 1-16), a feature profiled cineangiographically in the left anterior oblique (LAO) view and in the parasternal long axis view by two-dimensional (2D) echocardiography.

**Muscular Septum**

See “Right Ventricle” and “Left Ventricle.”

**Membranous Septum**

The membranous septum (pars membranacea) is the fibrous part of the cardiac septum separating the left ventricular outflow tract from, in part, the right ventricle and, in part, the right atrium. The line of division between these components is determined by attachment of the tricuspid valve anulus to the septum (see Fig. 1-12). On the right ventricular side of this attachment is the interventricular component. On the right atrial side, it forms the membranous portion of the AV septum.

**Atrioventricular Septum**

The AV septum is the portion of the cardiac septum that lies between the right atrium and left ventricle. It consists of a superior membranous portion and an inferior muscular portion. The AV septum is apparent because the septal attachment of the tricuspid valve is more apical than the septal
attachment of the anterior leaflet of the mitral valve (Fig. 1-17). Viewed from the left ventricular side, the muscular component forms part of the outlet septum (see Fig. 1-13). The AV node lies in the atrial septum adjacent to the junction between membranous and muscular portions of the AV septum, and the bundle of His passes toward the right trigone between these two components (Fig. 1-18).

CONDUCTION SYSTEM

The following description is based on studies of hearts without congenital defects. Abnormalities of the conduction system are associated with certain congenital cardiac malformations and determined primarily by the alignment between atrial and ventricular septal structures and the pattern of ventricular architecture (see Chapters 55 and 56).

Sinus Node

The sinus (sinoatrial) node is located along the anterolateral aspect of the junction between the superior vena cava and the right atrial appendage (Fig. 1-19). In rare cases, it extends medially across the crest of the caval–atrial junction. The node is superficial, lying just beneath the epicardial surface in the sulcus terminalis, and is approximately $15 \times 5 \times 1.5$ mm. It is pierced by the relatively large sinus node artery. (For details of the blood supply, see “Coronary Arteries”.)

Internodal Pathways

The spread of activation between sinus node and AV node occurs preferentially through the muscle bundles delimited by orifices of the right atrium (Fig. 1-19). Considerable histologic and electrophysiologic investigation has been carried out to determine whether pathways of specialized conduction tissue exist within these broad muscle bundles and connect the sinoatrial (SA) and AV nodes. Investigators have not found discrete internodal tracts composed of homogeneous cells or fibers, although some have identified Purkinje-like cells in the major muscle bundles of adult hearts. Controversy continues as to whether these pale cells seen in the atrial myocardium are Purkinje-type cells and whether they form preferential conduction pathways.

Atrioventricular Node

The AV node lies directly on the right atrial side of the central fibrous body (right trigone) in the muscular portion of the AV septum, just anterosuperior to the ostium of the coronary sinus. At times, its posterior margin has been found to lie directly against the coronary sinus ostium. It has a flattened oblong shape and an average dimension in adults of $1 \times 3 \times 6$ mm. Its left surface lies against the mitral anulus. Viewed from the right atrium, the AV node can be localized within a triangle—described by Koch (Fig. 1-20)—formed by the tricuspid anulus, tendon of Todaro (continuation of the...
Figure 1-18  Diagram of right heart, aortic root, and conduction tissue at approximately 65-degree right anterior oblique projection. Plane of mitral valve attachment (dashed line) corresponds to atrial edge of muscular atrioventricular septum and inferior edge of membranous septum, but differs from plane of tricuspid valve (solid line). Muscular portion of atrioventricular septum is frequently smaller than depicted. Key: Ao, Ascending aorta; AVN, atrioventricular node extending into bundle of His and right bundle branch; AVS, muscular atrioventricular septum; CS, coronary sinus; FO, fossa ovalis; IVC, inferior vena cava; M, moderator band; MS, membranous septum, crossed by attachment of tricuspid valve; MV, mitral valve anulus; RC, right coronary artery; S, portion of trabecula septomarginalis (septal band); SVC, superior vena cava; TV, tricuspid valve. (Modified from McAlpine.)

Chapter 1  Anatomy, Dimensions, and Terminology

Bundle of His and Bundle Branches

The common AV bundle (bundle of His) is a direct continuation of the AV node. The bundle passes through the rightward part of the right trigone of the central fibrous body to reach the posteroinferior margin of the membranous ventricular septum. This area is just inferior to the commissure between the tricuspid valve’s septal and anterior leaflets (see Fig. 1-19, B). Its diameter in the region of the central fibrous body is about 1 mm. The bundle courses along the posteroinferior border of the membranous septum and crest of the muscular ventricular septum, giving off fibers that form the left bundle branch. This branching occurs beneath the commissure between the right and noncoronary cusps in close proximity to the aortic valve, over a distance of 6.5 to 20 mm, after which the remaining fibers form the right bundle branch (Fig. 1-21). The bundle of His lies on the left side of the ventricular septal crest in about 75% to 80% of human hearts and on the right side of the crest in the remainder. In the latter situation, the His bundle connects to the left bundle by a relatively narrow stem.

The left bundle branch fans out over the left ventricular septal surface, gradually forming two or three main radiations. It is not uncommon for the anterior and posterior subdivisions to be accompanied by a central, third radiation that originates from the His bundle or from both of the former subdivisions. The anterior radiation travels toward the base of the anterolateral papillary muscle of the left ventricle. The wider posterior subdivision courses toward the base of the posteromedial papillary muscle. Multiple peripheral anastomoses occur among the subdivisions of the left bundle branch system as it distributes to the left ventricle.

The right bundle branch originates from the bundle of His in the region of the anteroinferior margin of the membranous septum and courses along the right ventricular septal surface, passing just below the medial papillary muscle and along the inferior margin of the septal band and the moderator band to the base of the anterior papillary muscle. The fibers then fan out to supply the walls of the right ventricle. Proximally, the right bundle averages about 1 mm in diameter. It is usually subendocardial in its proximal portion, intramyocardial in its middle portion, and again subendocardial near the base of the anterior papillary muscle. VSDs associated with malalignment of portions of the ventricular septum affect these relationships to some extent.

Cardiac Valves

The interrelationships among the heart valves in normally formed hearts are remarkably uniform. The aortic valve occupies a central position, wedged between the mitral and tricuspid valves, whereas the pulmonary valve is situated anterior, superior, and slightly to the left of the aortic valve. The anuli of the mitral and tricuspid valves merge with each other and with the membranous septum to form the fibrous skeleton of the heart. The core of the skeleton is the central fibrous body, with its two extensions, the right
Cardiac conduction system. **A**, Sinus node is located on anterolateral aspect of junction between superior vena cava and right atrial appendage. Internodal pathways are not well defined anatomically and are presented here as proposed pathways. Atrioventricular (AV) node lies in triangle of Koch. Right and left bundle branches spread out on subendocardial surfaces of right and left aspects of ventricular septum. **B**, This section of the heart, taken more posterior than that shown in **A**, demonstrates location of AV node in triangle of Koch, bounded by coronary sinus, anulus of tricuspid valve septal leaflet, and tendon of Todaro. The common AV bundle (bundle of His) continues from AV node to penetrate central fibrous body and reach posteroinferior margin of membranous septum. Left bundle branch spreads over left ventricular aspect of ventricular septum. Right bundle branch continues on right ventricular surface of ventricular septum into moderator band.
and left fibrous trigones. The right fibrous trigone forms a dense junction between the mitral and tricuspid anuli, the left ventricular-aortic junction below the noncoronary cusp, and the membranous septum. The trigone is pierced by the bundle of His. The left fibrous trigone, situated more anteriorly and to the left, lies between the left ventricular-aortic junction and the mitral anulus. The tendon of the infundibulum is a fibrous band joining the more superiorly placed pulmonary valve to the central cardiac skeleton. The tendon of Todaro also joins the central fibrous body (see “Atrioventricular Node”).

By virtue of similarities in morphology and function, the heart valves naturally fall into two groups: AV (mitral and tricuspid) valves and semilunar (aortic and pulmonary) valves.
Mitral Valve

The AV valve of the left ventricle, the mitral valve, is bicuspid, with an anterior (aortic, or septal) leaflet and a posterior (mural, or ventricular) leaflet (Fig. 1-23). Tissue that could be called commissural leaflets is usually present at the commissures between these two leaflets. The combined area of the two mitral leaflets is twice that of the mitral orifice, resulting in a large area of coaptation.\(^{3,4,17}\) When this large area is lost because of malalignment of the leaflets, undue stress is placed on the chordae tendineae, and they may rupture. Although there has been some controversy as to the definition of commissural areas, particularly in regard to clefts in the posterior leaflet, Silver and colleagues describe chordae tendineae that define the limits of the septal (anterior) and posterior leaflets.\(^{1,2}\)

Rusted and colleagues found the depth of commissures in the normal mitral valve averaged 0.7 to 0.8 cm and never exceeded 1.3 cm in the 50 hearts they studied.\(^5\)

The larger anterior (septal, aortic, anteromedial) leaflet is roughly triangular in shape, with the base of the triangle inserting on about one third of the anulus. It has a relatively smooth free margin with few or no indentations. A distinct ridge separates the region of closure (rough zone) from the remaining leaflet (clear zone).\(^1\) The clear zone is devoid of direct chordal insertions. The anterior leaflet is in fibrous continuity with the aortic valve through the aortic–mitral anulus and forms a boundary of the left ventricular outflow tract.\(^{11}\) This region of continuity occupies about one fourth of the mitral anulus and corresponds to the region beneath half the left coronary cusp and half the noncoronary cusp of the aortic valve. The limits of this attachment are demarcated by the right and left fibrous trigones (Fig. 1-24). The commissure between the left and noncoronary sinuses of the aortic valve is located directly over the middle of the anterior leaflet of the mitral valve (Fig. 1-25; see also Fig. 1-24). These points do not correspond to the commissures of the mitral valve (see Fig. 1-4). The AV node and bundle of His are at risk of surgical damage adjacent to the right trigone.

The smaller posterior (mural, ventricular, posterolateral) leaflet inserts into about two thirds of the anulus and typically has a scalloped appearance. Ranganathan and colleagues found the posterior leaflet to be divided into three segments in 46 of the 50 normal mitral valves they studied.\(^1\) The posterior leaflet has rough and clear zones corresponding to those of the anterior leaflet, as well as a basal zone close to the anulus, which receives chordae directly from left ventricular trabeculae.\(^1,2,11\)

The mitral valve leaflets may be described using a segmental classification. The valve leaflets are segmented into six sections, A1 to A3 for the anterior and P1 to P3 for the posterior (see Fig. 1-25, C). Sections A1 and P1 represent the anterolateral sections, A2 and P2 the middle sections, and A3 and P3 the posteromedial sections. This segmental classification has been useful in describing morphology observed at operation,\(^4,10\) multiplane 2D transesophageal echocardiography,\(^9,14\) and 3D echocardiography.\(^5,4\)

The majority of chordae tendineae to the mitral valve originate from the two large papillary muscles of the left ventricle: anterolateral and posteromedial. Each leaflet receives chordae from both papillary muscles, and the majority insert on the free leaflet edge.\(^5\) Papillary muscles are often thought of as fingerlike structures protruding into the left ventricular cavity from the ventricular wall, possibly because these muscles are frequently visualized in two dimensions by angiography or echocardiography. Actually, the papillary muscles have a
somewhat crescent shape that conforms to the curvature of the free wall of the left ventricle. This is reasonable because the papillary muscles and chordae tendineae are derived embryologically by undermining of the left ventricular myocardium.

Victor and Nayak examined 100 normal human hearts at autopsy, evaluating and characterizing the papillary muscles and arrangement of the chordae. The anterolateral papillary muscle is attached by chordae tendineae to the left half of the anterior and posterior mitral leaflets (as viewed by a surgeon through the usual right-side approach to the mitral valve), whereas the postero-medial papillary muscle is attached by chordae tendineae to the right-sided half of both anterior and posterior leaflets. Papillary muscles are considered an anterolateral “group” and a postero-medial “group” because there is often more than a single papillary muscle “belly.” There are patterns of mostly single or two muscle bellies, but occasionally three, four, or even five bellies are observed. When there are three muscle bellies, the papillary muscle supporting the chordae to the commissure arises separately from the ventricular wall. Commisural chordae are shorter than the others and usually originate from the highest tip of the papillary muscle. Victor and Nayak also described variations of the chordal attachments. There are usually 4 to 12 chordae originating from each papillary muscle group (range, 2 to 22). Chordal branching results in a number of chordae inserting to the mitral valve leaflet, ranging from 12 to 80.

Acar and colleagues proposed a clinical morphologic classification of the papillary muscles. A single undivided papillary muscle is referred to as type I. Type II refers to papillary muscles cleaved in a sagittal plane into two heads that separately support the anterior and posterior leaflets of the mitral valve. Type III papillary muscles are cleaved in a coronal plane, forming an individual head that supports the commissural chordae. Type IV refers to papillary muscles divided into multiple heads, with a separate papillary muscle originating as a separate muscular band close to the mitral anulus, which supports short chordae to the commissure.

Tandler defined three orders of chordae. Those of the first order insert on the free margin of the leaflet, those of the second order insert a few to several millimeters back from the free edge, and those of the third order insert at the base of the leaflet (applicable only to the posterior leaflet).
region. The leaflets and chordae tendineae are thinner than those of the mitral valve. Its orientation is nearly vertical. The anterior (anterosuperior) leaflet is the largest of the three leaflets and may have notches creating subdivisions. Silver and colleagues found a notch close to the anteroseptal commissure in 47 of the 50 anterior leaflets they examined. This notch was occasionally as deep as a commissure, but could be differentiated from a true commissure by the type of chordal attachments. The chordae attaching to this leaflet arise from anterior and medial papillary muscles. The anterior papillary muscle is the larger of the two, its base arising from the right ventricular free wall and trabecula septomarginalis.

The posterior (inferior) leaflet is usually the smallest and is commonly scalloped. Its chordae originate from the posterior and anterior papillary muscles. It is attached wholly to the ventricular free wall. The septal leaflet is usually slightly larger than the posterior leaflet. Its chordae arise from the posterior and septal papillary muscles. Most of this leaflet and its chordae attach to the membranous and muscular portions of the ventricular septum, although part may attach to the posterior wall or the right ventricle. The transition between the attachments to the posterior wall and septum is associated with a fold in the leaflet.

Lam and colleagues reclassified chordae into rough zone (including strut chordae), cleft, basal, and commissural chordae. These investigators suggest that this classification provides a clear definition of mitral valve leaflets and should be useful in studying mitral valve function.

The design of the mitral valve offers the largest possible orifice during the diastolic phase of ventricular filling and limits the slightest obstruction to flow at low pressures in the left atrium and left ventricle. The valve opens as the anterior leaflet swings anteriorly from the posterior leaflet. Orifice dimensions are enhanced by flexion of the anterior leaflet (see Fig. 1-25, B). During systole, the mitral valve closes under the full load of left ventricular contraction. The anterior leaflet straightens and extends toward the posterior leaflet. The posterior leaflet functions like a shelf to stop the movement of the anterior leaflet as the leaflets appose.

Tricuspid Valve

The tricuspid valve, the AV valve of the right ventricle, has three leaflets: anterior, posterior, and septal (Fig. 1-26). Its orifice is roughly triangular and larger than the mitral orifice. The anulus is relatively indistinct, especially in the septal region. The leaflets and chordae tendineae are thinner than those of the mitral valve. Its orientation is nearly vertical.

The anterior (anterosuperior) leaflet is the largest of the three leaflets and may have notches creating subdivisions. Silver and colleagues found a notch close to the anteroseptal commissure in 47 of the 50 anterior leaflets they examined. This notch was occasionally as deep as a commissure, but could be differentiated from a true commissure by the type of chordal attachments. The chordae attaching to this leaflet arise from anterior and medial papillary muscles. The anterior papillary muscle is the larger of the two, its base arising from the right ventricular free wall and trabecula septomarginalis.

The posterior (inferior) leaflet is usually the smallest and is commonly scalloped. Its chordae originate from the posterior and anterior papillary muscles. It is attached wholly to the ventricular free wall.

The septal leaflet is usually slightly larger than the posterior leaflet. Its chordae arise from the posterior and septal papillary muscles. Most of this leaflet and its chordae attach to the membranous and muscular portions of the ventricular septum, although part may attach to the posterior wall of the right ventricle. The transition between the attachments to the posterior wall and septum is associated with a fold in the leaflet.
The walls of the sinuses are considerably thinner than the wall of the aorta proper, an important consideration when designing proximal aortotomies.

The crown-shaped anulus, fibrous trigones, aortic cusps, aortic sinuses, and sinutubular junction share a dynamic coordinated action to provide unidirectional transmission of large volumes of blood pumped intermittently through the channel while maintaining laminar flow, minimal resistance, optimal coronary artery flow, and least damage to blood elements during widely variable and frequently changing conditions.

The origins of the coronary arteries are the basis of a nomenclature for the sinuses and cusps. The ostia of the right and left coronary arteries identify the right and left sinuses and cusps. The sinus and cusp without an associated coronary artery are termed noncoronary. Several other nomenclatures for the cusps and sinuses have been described (see Morphology in Chapter 52).

Aortic Valve

The aortic valve is normally tricuspid and composed of delicate cusps and sinuses of Valsalva. These components form three cuplike structures that constitute the entire valve mechanism; the valve is in fibrous continuity with the anterior leaflet of the mitral valve and the membranous septum (see Fig. 1-25).

The free edge of each cusp is of tougher consistency than the remainder of the cusp. At the midpoint of each free edge is a fibrous nodulus Arantii. On either side of each nodulus is an extremely thin, crescent-shaped portion of the cusp termed the lunula (see Fig. 1-13). The lunulae are occasionally fenestrated near the commissures. These regions form the area of coaptation during valve closure.

The aortic sinuses (sinuses of Valsalva) are dilated pockets of the aortic root that form the outer component of the three cuplike closing structures of the aortic valve (see Fig. 1-25). The coronary arteries arise from two of the aortic sinuses. The walls of the sinuses are considerably thinner than the wall of the aorta proper, an important consideration when designing proximal aortotomies.

The pulmonary valve structure is similar to that of the aortic valve. The pulmonary valve normally has three cusps, with a nodule at the midpoint of each free edge, and lunulae and thin, crescent-shaped coaptive surfaces on both sides of the nodules. The pocket behind each cusp is the sinus. Major differences from the aortic valve are (1) lighter construction of pulmonary valve cusps, (2) normal absence of coronary artery origins, and (3) normal lack of fibrous continuity with the anterior tricuspid valve leaflet. Pulmonary valve cusps are supported entirely by freestanding musculature, having no direct relationship with the ventricular septum. The pulmonary valve is lifted away from the ventricular septum by the subpulmonary infundibulum. The first septal branch of the left anterior descending coronary artery pierces the
ventricular septum below the shortest part of the subpulmonary infundibulum. The artery is protected by the subpulmonary infundibulum.

Pulmonary valve cusps have been described by several terminologies, usually named by their relationships to the aortic valve: right, left, and anterior (nonseptal). Kerr and Goss found that a commissure of the pulmonary valve was adjacent to a commissure of the aortic valve in 199 of 200 specimens they studied. These investigators suggested that the cusps of each arterial valve should be termed right adjacent, left adjacent, and opposite (or, as suggested by Anderson, right facing, left facing, and nonfacing) in relationship to the adjacent commissure of each valve.

CORONARY ARTERIES

From an anatomic point of view, the coronary artery system divides naturally into two distributions, left and right. From the standpoint of the surgeon, the coronary artery system is divided into four parts: the left main coronary artery, the left anterior descending coronary artery and its branches, the left circumflex coronary artery and its branches, and the right coronary artery and its branches. The branches of each of the last three vessels must also be familiar to the surgeon.

The major coronary arteries form a circle and a loop about the heart (Fig. 1-27). The circle is formed by the right coronary and left circumflex arteries and is displayed in the left anterior oblique (LAO) projection. The loop is formed by the left anterior descending and posterior descending arteries and is demonstrated in the right anterior oblique (RAO) projection. Circulation is right dominant. Right coronary artery, which forms the right component of circle, is visualized. B, Left coronary injection in LAO projection. Note that this is a left dominant circulation. Left circumflex artery, which forms the left component of circle, is visualized. C, Left coronary injection in RAO projection. Left dominant circulation allows demonstration of both components of the loop: left anterior descending and posterior descending arteries. Key: AV, Atrioventricular node artery; CX, left circumflex artery; LAD, left anterior descending artery; LM, left marginal artery; PD, posterior descending artery; RC, right coronary artery; RPL, right posterolateral artery.
serves the left side of the heart to a greater extent than it does the right side in terms of the number and volume of vessel segments involved.\textsuperscript{21} A right dominant artery does not necessarily supply branches to the inferior surface of the left ventricle, however, because it may terminate only as the posterior descending artery. Blood supply to the anterior portion of the left ventricle comes from the diagonal branches of this portion of the loop, the left anterior descending coronary artery. That to the lateral part of the anterior portion comes from the first branches of both the left anterior descending and circumflex arteries. The ventricular septum receives its blood supply from the loop that encircles it, formed by the left anterior descending coronary artery in front and the posterior descending artery behind.

Variability in the origin of the posterior descending artery is expressed by the term dominance. A right dominant coronary circulation is one in which the posterior descending coronary artery is a terminal branch of the right coronary artery. A left dominant circulation, which occurs in about 10\% to 15\% of hearts, is one in which the posterior descending coronary artery is a branch, usually the last one, of the left circumflex coronary artery. Left dominance occurs more frequently in males than in females. This distinction as to whether the right or left coronary supplies the posterior descending artery is important in evaluating patients with coronary artery disease and in planning coronary artery bypass grafting.

The following is a general description of coronary artery anatomy in normal hearts.\textsuperscript{81,86,87,88,92,93,95,108} As with the conduction system, some congenital cardiac malformations are associated with abnormalities of the coronary arteries. The nomenclature is based on the U.S. National Heart, Lung, and Blood Institute’s Proposal and Manual of Operations for Collaborative Studies in Coronary Artery Surgery\textsuperscript{109} (Fig. 1-28) and the American Heart Association’s coronary artery disease reporting system.\textsuperscript{110} Both systems include rules for defining the various segments of the major coronary arteries. Fig. 1-29 is also supplied to provide a more dimensional representation of the coronary arteries on the surface of the heart and should be studied along with the brief descriptions that follow.

Left Main Coronary Artery

The left main coronary artery extends from the ostium in the left sinus of Valsalva to its bifurcation into the left anterior descending and left circumflex branches. Its usual length is 10 to 20 mm, with a range of 0 to 40 mm. It normally courses between the pulmonary trunk and the left atrial appendage to reach the left AV groove. Occasionally, additional vessels originate from the left main coronary artery and course parallel to the diagonal branches of the left anterior descending branch.\textsuperscript{111} Such an additional artery (formerly called a ramus intermedius) is termed the first diagonal branch of the left anterior descending artery. Rarely (in 1\% of persons), the left main coronary artery is absent, the left anterior descending and left circumflex coronary arteries originating directly from the aorta via separate ostia.

Left Anterior Descending Coronary Artery

Beginning as a continuation of the left main coronary artery, the left anterior descending coronary artery courses along the anterior interventricular sulcus to the apex of the heart. Part of it may be buried in muscle. In most cases, this artery extends around the apex into the posterior interventricular sulcus, supplying the apical portion of both right and left ventricles.\textsuperscript{112} This vessel supplies branches to the right ventricular free wall (usually small), septum, and left ventricular free wall. One or more branches to the right ventricle connect with infundibular branches from the proximal right coronary artery. This important route for collateral flow is the loop of Vieussens. The septal arteries arise almost perpendicularly
Figure 1-29  Coronary arteries. A, Left coronary artery. Left main coronary artery originates from aorta and divides to form left anterior descending and left circumflex coronary arteries. Branches of left anterior descending artery on surface of heart are termed diagonal arteries, whereas those coursing into the ventricular septum are called septal arteries. Branches of left circumflex artery on posterior wall of left ventricular surface are termed obtuse marginal arteries. A large artery originating near the left main coronary bifurcation and supplying the obtuse margin between the diagonal branches of left anterior descending and circumflex marginal branches was formerly called an intermediate branch or ramus intermedius. B, Right coronary artery, right dominant pattern. Right coronary artery originates from aorta and courses in the atrioventricular (AV) groove. Branches of right coronary artery supplying blood to right ventricle are called right ventricular branches, except for the nearly constant and often large branch at the acute margin of the heart, termed the acute marginal artery. Right coronary artery divides at the crux of the heart into right posterior descending branch, which courses over posterior aspect of ventricular septum, and right posterolateral segment artery, which continues in the AV groove, providing branches to posterior wall of left ventricle. Arterial branches to the specialized conduction system frequently arise from right coronary artery. Sinoatrial node branch originates from proximal portion of right coronary artery. AV node branch originates from the U-bend in posterior lateral segment of right coronary artery.
from the left anterior descending coronary artery, a characteristic sometimes helpful in angiographic identification of the anterior descending artery. A variable number of diagonal arteries course obliquely between the anterior descending and left circumflex arteries and supply the left ventricular free wall anteriorly and laterally.

Variations in the left anterior descending artery are infrequent, although in about 4% of hearts, it exists as two parallel vessels of about equal size. It may terminate before the apex or extend as far as the posterior AV groove.

**Left Circumflex Coronary Artery**

The left circumflex coronary artery originates at about a 90-degree angle, with its initial few centimeters lying medial to the base of the left atrial appendage. The sinus node artery occasionally originates from the first few millimeters of the left circumflex artery. Rarely, the circumflex artery terminates before the obtuse margin. A large branch originating from the proximal left circumflex artery and coursing around the left atrium near the AV groove is termed the atrial circumflex artery. The ventricular branches of the circumflex artery, the obtuse marginal arteries, supply the obtuse margin of the heart and may be embedded in muscle. Often their position can then be identified at operation by the altered color (reddish or light tan) of the overlying thin muscle layer compared with that of the remainder of the ventricular wall. Those branches supplying the inferior surface of the left ventricle in a heart with a left dominant system (or in one with a co-dominant system in which the right coronary artery gives rise only to a posterior descending artery) are termed left posterolateral (marginal) arteries. In hearts with a left dominant system, the left circumflex coronary artery gives rise to the posterior descending artery at or usually before the crux. Variations in the origin and length of the left circumflex artery, and in the number and size of its marginal branches, are common.

**Right Coronary Artery**

The right coronary artery is usually a single large artery and courses down the right AV groove. Branches supplying the anterior right ventricular free wall exit from the AV sulcus in a looping fashion because of the depth of the right coronary artery in the sulcus. In this same area, the anterior right atrial artery arises, and this branch often gives origin to the sinus node artery. More distally, a lateral right atrial artery usually arises (this artery is frequently severed when an oblique atriotomy is made). In the region of the acute margin of the heart, a relatively constant long branch of the right coronary artery arises, the acute marginal artery, which courses most of the way to the apex of the heart. The right coronary artery in most hearts crosses the crux, where it takes a characteristic deep U-turn, giving off the atrioventricular node artery at the apex of the turn. The right coronary artery then terminates by bifurcating into the right posterior descending coronary artery and the right posterolateral segment artery. The posterior descending coronary artery descends in the posterior interventricular sulcus for a variable distance, giving rise to septal, right ventricular, and left ventricular branches. Variations in its anatomy are numerous, and it frequently arises before the crux. The right posterolateral segment of the right coronary artery gives origin to marginal branches to the inferior surface of the left ventricle in most hearts with a right dominant system.

Variations in the right coronary artery are common. It may have a dual origin from the right sinus of Valsalva. In about 10% of hearts, it bifurcates within a few millimeters of the aortic ostium, forming two diverging trunks of equal size. In half the cases, the artery supplying the right ventricular infundibulum arises separately from the aortic sinus and is then termed the conus artery. The sinoatrial node (sinus node) artery originates from the second or third centimeter of the right coronary artery in many hearts (see “Coronary Arterial Supply to Specialized Areas of the Heart”). The acute marginal artery crosses the diaphragmatic surface of the right ventricle in 10% to 20% of hearts and reaches the anterior aspect of the diaphragmatic portion of the ventricular septum, to which it gives branches.

**Coronary Arterial Supply to Specialized Areas of the Heart**

The predominant blood supply to the ventricular septum is from the left anterior descending coronary artery via four to six large septal arteries 70 to 80 mm in length. In contrast, the septal arteries from the posterior descending coronary artery (except for the AV node artery) are rarely more than 15 mm in length (Fig. 1-30). They supply only a small zone of the ventricular septum near the posterior interventricular sulcus and in the region of the AV node. The septal arteries from the posterior descending artery may, however, serve as an important source of collateral circulation. Until their final terminations, the septal arteries from both anterior and posterior descending arteries course along the right ventricular side of the septum, where pressure is lower than on the left side. In 10% of hearts with a left dominant circulation, the entire blood supply is from the left coronary artery.

The sinus node artery is a single artery in 89% and double in 11% of hearts. Its origin is from the right coronary artery in 55% to 65% of cases and from the left circumflex or left main coronary artery in the remainder. When it arises from the right coronary artery, it courses posteriorly and superiorly over the anterior wall of the right atrium beneath the right atrial appendage and courses obliquely between the anterior descending and left circumflex arteries and supplies the right atrial appendage. The sinus node artery occasionally originates from the proximal left circumflex artery, it courses over the left atrial appendage. The Kugel artery anastomoses with branches of the sinus node artery. The AV node artery courses superiorly and anteriorly from the left circumflex artery, it courses posteriorly and superiorly from the first few millimeters of the left circumflex artery. The AV node artery (except for the AV node artery) is rarely more than 15 mm in length (Fig. 1-30). They supply only a small zone of the ventricular septum near the posterior interventricular sulcus and in the region of the AV node. The AV node artery may penetrate the interatrial septum in its course to the superior vena cava. It then encircles the cava clockwise or counterclockwise, or bifurcates and encircles it in both directions. If the sinus node artery arises from the left circumflex artery, it courses over the left atrial wall, variably penetrates the interatrial septum, and ascends to the base of the superior vena cava, encircling that vessel as when it originates from the right coronary artery.

The AV node artery arises from the characteristic U-turn of the right coronary artery as it crosses the crux of the heart. The AV node is usually supplied by the dominant coronary artery. The AV node artery courses superiorly and anteriorly and terminates with a distinctive angulation. An important accessory blood supply to the AV node is the Kugel artery, which originates from the proximal segment of either the right coronary artery or the left circumflex artery and courses through the interatrial septum to the crux of the heart to anastomose with the AV node artery. In the atrial septum, Kugel artery anastomoses with branches of the sinus node artery. Kugel artery is the source of blood supply to the AV node in 40% of normal hearts.
Figure 1-30  Blood supply of ventricular septum. Most of the septum is supplied by left anterior descending coronary artery via large septal arteries. Septal arteries from posterior descending artery are relatively small. In this right dominant circulation, note origin of the atrioventricular (AV) node artery from the characteristic U-turn of right coronary artery. (Modified from James and Burch.)

Figure 1-31  Origin and distribution of sinus node artery. Sinus node artery may arise from right coronary artery and encircle base of superior vena cava in (A) a clockwise direction or (B) a counterclockwise direction, or it may (C) bifurcate and encircle it in both directions. It may also arise from (D) the left circumflex artery and encircle the base of the superior vena cava as in A, B, or C. (Modified from Lewis and colleagues.)
**Dimensions of Normal Cardiac and Great Artery Pathways**

Cardiac and great artery pathways with normal dimensions accommodate blood flow at rest and during exercise and stress, with little or no pressure drop across the pathway. Sluysmans and Colan have hypothesized that optimal size of cardiovascular structures is such as to mimic hemodynamic cost of providing blood flow across the physiologic range of cardiac output. The body does this by optimizing the relationship between vessel radius and flow rate. To achieve minimum work requires minimizing viscous energy (shear stress related to inverse radius) and inertial energy related to pulsatile flow, which is directly related to radius (Fig. 1-32). Sluysmans and Colan show that this optimization of energy is related to body surface area (BSA) over a wide range of sizes of mammals, including humans. For valve and blood vessel area, this relationship is linear with BSA; for diameter of vessels, this relationship is to the square root of BSA (BSA^{0.5}).

Although the theoretical relationship tolerates vessel dimensions over a substantial range, in some patients being considered for cardiac surgery, dimensions are so small as to preclude a satisfactory outcome. Therefore, prediction of outcome based on dimensions of a pathway becomes important. A major problem in predicting outcome in a patient simply from subjective evaluation of the size of a structure is that this evaluation may be grossly inaccurate because of unconscious comparison of the size of the structure in question with that of a neighboring unusually large structure. Prediction of outcome simply from subjective evaluation is also affected by the preformed bias of the observer, as well as by inexperience. Therefore, measurements and their relationship to outcome are required for reproducible, accurate predictions, and decisions must be made regarding the methods for expressing the dimensions.

**Dimensions of the Pathway**

The measured dimension is usually expressed as diameter of the pathway. Occasionally a circular shape is assumed, and the dimension is transformed to cross-sectional area. Under some circumstances, cross-sectional area can be measured directly. In other circumstances, an elliptical shape is assumed, and major and minor axes are measured and area calculated with an equation that applies to ellipses. Use of observed (measured) dimensions generally requires their being related to normal dimensions, which vary with body size and age (allometric growth). Normal dimensions may also vary according to imaging modality, image...
projection (e.g., anteroposterior vs. lateral), phase of the cardiac cycle, method of fixation in the case of specimens, and other factors. These must be specifically controlled in making the measurements.

Dimensions have been measured in autopsy specimens and by cineangiography (in which dimensions must be corrected for magnification), echocardiography (M-mode, 2D, 3D, cineangiography), and in a few instances MRI. However, normal values are not available in each of these modalities, so dimensions have to be related to available normal values, even if from another modality.

Echocardiography has evolved as the most commonly used modality for measuring these dimensions. Pathway dimensions have been determined by echocardiography at nearly all ages of life, from fetal to age 90. Hornberger and colleagues established dimensions by high-resolution 2D echocardiography for the fetal aortic arch in 92 fetuses aged 16 to 38 weeks gestation to facilitate diagnosis of left heart and aortic abnormalities, particularly coarctation. Skelton and colleagues followed changes in cardiac dimensions of preterm infants during the first month of life, suggesting there are differences from term infants, with preterm babies showing mild left ventricular dysfunction.

Pathway dimensions for hearts from birth to about 20 years have been determined by M-mode and 2D echocardiography. Daubeney and colleagues prospective study aimed at developing equations relating cardiac dimensions to body area over the range of 0.1 to 2.0 m² is particularly useful. A number of studies in adults use 2D echocardiography (transthoracic or transesophageal) with pathway dimensions measured directly or derived from Doppler ultrasound measurements and the continuity equation. The age range is often wide, but there are populations studied at mean age 23, 28, 33, 45, and 53 years. Swinne and colleagues called attention to age-associated changes in left ventricular outflow tract geometry observed in normal subjects, mostly after age 70. These changes consist of a more acute septo-aortic angle or septal bulge that is not associated with left ventricular outflow tract obstruction. These may represent degenerative changes associated with aging.

Normalization of Pathway Dimensions

Pathway dimensions may be used without any normalization to body size or age. Some cardiologists who work exclusively with adult patients express aortic size simply in centimeters. This method is not recommended, not only for the obvious reason that it is unacceptable when the population being considered consists of patients who range from very young to very old, but also because it takes no account of differences between adults of differing size.

Normalization may be based on age, height, weight, or BSA. Normalization to body size generally is termed indexing. Normalization may also be to another structure, such as the size of the descending aorta at the diaphragm. Normalization to another body structure generally is termed a ratio. The preference is for normalization to BSA of the patient, but this is often done by dividing the value of the dimension by the BSA, expressing it as “per square meter BSA.” This preference presumes a strictly linear relation between the dimension and BSA, which may be inaccurate. If a structure’s area is measured, the relationship to BSA is probably accurate. If instead a diameter of a structure is normalized this way, it will be inaccurate. What must be achieved is normalization that is constant across body size from smallest neonate to adult.

Indexed cross-sectional area and diameter of mitral and tricuspid valves, left ventricular–aortic junction (aortic valve “anulus”), right ventricular infundibulum, and right ventricular–pulmonary trunk junction (pulmonary valve “anulus”) in normal individuals are summarized in Table 1-1 according to the modality in which the dimension was measured. Those for the pulmonary trunk, right and left pulmonary arteries, and descending thoracic aorta at the diaphragm are summarized in Table 1-2. Values for the diameter of the upper descending thoracic aorta on both sides of the ductus arteriosus are also available. These tables are not intended as a source of normalized dimensions in patients, but rather as a reference and guide to the appendixes to this chapter, which contain specific regression equations and nomograms for calculating mean normal values and their standard deviations for use in patients.

Standardization of Dimensions

Values of dimensions are made useful by standardizing them to body size. They are expressed as deviation from their mean normal value for body size in terms of number of standard deviations from the mean. Standardization takes into account the fact that values in normal individuals of the same size vary. The mathematical framework for standardization of dimensions is the normal distribution domain because of its mathematical flexibility and tractability. This framework may require transformation of the dimension scale of the variable under consideration to comply with assumptions of the normal distribution.

A less desirable alternative is standardization according to percentiles (the 50th percentile is the median). This method is commonly used in relating body weight or height to age. Although percentiles are easily expressed, the method has the major disadvantage that the relationships cannot be reduced to equations. This increases the difficulty of relating dimensional data to outcome.

Once in the normal distribution domain, any given value for a dimension can be expressed in terms of the number of standard deviations of the given value from the mean value of that dimension in normal individuals. This is the z value, or z score (Fig. 1-33). The transformation to a dimensionless z value is as follows:

\[
z = \frac{\text{Observed dimension} - \text{Mean normal dimension}}{\text{Standard deviation around mean normal dimension}}
\]

where (1) is the observed dimension or its appropriate transformation in scale in the patient who is of a known size (BSA), and (2) and (3) refer to corresponding values in normal individuals of the same BSA as the patient, obtained from regression analysis and equations.

Appendix 1B includes dimensions (obtained at autopsy) of various cardiac and pulmonary artery pathways in normal individuals. In Appendix 1C, the dimensions were obtained at in vivo cineangiography, and in Appendix 1D at in vivo 2D echocardiography. Appendix 1E compares pathway dimensions in normal individuals from different measurement modalities. Additional reliable information is contained in other sources (e.g., Roman et al. R3).
<table>
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<tr>
<th>Structure, Modality, and Source</th>
<th>Cross-Sectional Area (mm^2 · m^-2 BSA)</th>
<th>Diameter (mm · m^-2 BSA)</th>
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<td>Ormiston et al.</td>
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<td>Hanséus et al. (short axis)</td>
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*aNormalization is in terms of BSA.

Key: 2D, Two-dimensional; BSA, body surface area; LV, left ventricle; RV, right ventricle.
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*Normalization is in terms of BSA.
Key: 2D, Two-dimensional; BSA, body surface area; RPA, right pulmonary artery.
dimensions to the percentage of a population of normal individuals
with that specific dimension or a smaller one. Exact percentage on
vertical axis, related by dashed lines to the patient’s z value, is the
percentile of normal individuals with the corresponding z value. A
patient with a specific z value has the dimension of the correspond-
ing percentile of the normal population.

Dimensions of the Pulmonary Arteries

Indexing and standardizing the dimensions of the pulmonary
arteries present special problems because of the multiplicity of
methods that have been used. They have been important in
considering treatment for patients with tetralogy of Fallot and
pulmonary stenosis, tetralogy of Fallot with pulmonary
atresia, and conditions for which the Fontan operation is
performed.

Among the different methods for expressing dimensions of the
pulmonary arteries are the McGoon ratio, the sum of the diameters of the prebranching portions of the right and left pulmonary arteries, pulmonary artery area index (PAAI), cross-sectional area index (Nakata index), and z value. The z value is the preferred method. It should be applied to more distal portions of the pulmonary arteries as well.

To facilitate transformation of already published dimensions of the pulmonary arteries in patients with congenital heart disease to a different normalization, relationships between the values obtained by these various methods are shown in Appendix 1F.

Relating Dimensions to Outcome

The goal is an equation expressing the continuously variable
relationship between normalized dimensions of the patient and
some outcome event (e.g., death, freedom from reoperation, postrepair $P_{RV/LV}$, cardiac index). Obtaining the equation may require detailed studies and complex analyses, but once obtained, the equation is made easy to use by expressing it in a nomogram. This process is the basis of many of the depictions in the subsequent chapters.

As is already evident from Appendix 1B, 1C, and 1D, the normalization used in relating dimensions to outcome can be to measurements made at autopsy or at cineangiography, 2D echocardiography, MRI, or other imaging method. Although in theory it may seem proper to normalize

measurements made on cineangiography, for example, using
normalizing equations based on cineangiographic measurements, this is in fact unnecessary. If the same method of normalizing the patient’s dimensions is used in predicting outcome as was used in previous studies that determined the relationship between dimensions and outcome, this suffices. For example, in normalizing measurements of the dimensions of the tricuspid valve made at cineangiography, one might like to use equations based on cineangiographic measurements. Unfortunately, an insufficient number of measurements is made at cineangiography in normal individuals to generate equations for indexing or standardizing tricuspid measurements by this modality.

Equations for standardization of tricuspid measurements using measurements obtained by 2D echocardiography are available, as are measurements made at autopsy. Based on these practical considerations, normalization to autopsy or echocardiographic measurements may be used for standardizing tricuspid dimensions to a z value, even though these measurements are made by cineangiography (see Appendix 1E). Thus the nomograms shown in Appendix 1D or the actual equations described in tables in Appendixes 1B through 1D may be used. However, once a disparate standardization of a dimension is related to outcome, the user of that relationship must make that identical standardization. This is analogous to the use of a ruler. Rulers may be subdivided into inches or centimeters, but once a scale is chosen, it must be used consistently.

DIMENSIONS OF NORMAL VENTRICLES

Normal ventricular volumes, masses, and dimensions—assuming normal myocardial contractility and loading conditions—can accommodate normal blood flow at rest and during exercise. Sometimes the dimensions of the left or right ventricle are smaller or larger than those of the other, leading to problems in simply judging the normality of the size and its relationship to outcome, for the same reasons as in the case of pathway dimensions.

Accurate and precise ventricular diameters, volumes, and masses are difficult to obtain, because ventricles may have unusual shapes. Nevertheless, a number of useful studies have been done that use M-mode and 2D directed M-mode echocardiography to determine left ventricular volume and mass and to relate these dimensions to body size over the life course of humans. Particularly interesting is de Simone and colleagues’ study of left ventricular mass in overweight children and adults. They found that height is the best means of normalizing left ventricular mass. Normalization of ventricles to body size has also been challenged for obese subjects by Whalley and colleagues. BSA is highly sensitive to weight, less so to height. Whalley and colleagues support normalizing to fat-free mass, but requirement of specialized equipment is a barrier to its widespread use. Their view is not shared by all. Vasan and colleagues provide “cut” limits for range of normal values (90th and 95th percentiles) for ventricular mass and thickness and atrial and ventricular dimensions derived from nearly 5000 subjects in the Framingham Heart Study. Bull and colleagues proposed making surgical decisions based on the size (in terms of $z$ values) of the AV valve guarding the entrance to the ventricle, rather than on the size of the ventricle itself.
The \( z \) value method (standardization) can be used to describe patients’ ventricular volumes and masses, although this general body of knowledge is not yet well developed, in part because of methodological problems. The \( z \) value method can also be used for diameters. Table 1-3 gives the mean values for normal individuals of various body sizes, as an approximation and for guidance rather than for use in calculating patient-specific \( z \) values. Appendix Fig. 1G-1 presents the information in a form from which patient-specific \( z \) values can be calculated.

**TERMINOLOGY AND CLASSIFICATION OF HEART DISEASE**

Understanding the morphology of heart disease is fundamental to its surgical treatment. Morphology could be described fully using any one of a number of systems of terminology and classification. However, appropriate and accurate terminology and classification are important because they greatly facilitate understanding and teaching of cardiac morphology, diagnosis, and surgical treatment. Also, they determine the method of categorization of cases, a procedure essential to the study of groups of patients.

The system of terminology and classification used here evolved over many years, to a considerable extent in response to clinical, and particularly surgical, needs. It was based originally on the teaching of Edwards and his pupil, Becu. It has been profoundly influenced and modified on numerous occasions by the work of Van Praagh, has benefited through the years from the work of Van Mierop and of Lev and Bharati, and has embraced many of the concepts of Anderson and Becker.\(^{A12,B6}\)

Following the ideas of Lev, terminology based on the somewhat shifting sands of embryology has been avoided as much as possible. Any terms that have embryologic implications are used only because they have become conventional. This is not to deny the importance of the science of embryology, but rather to emphasize the importance of precise description of morphology (see Appendix 1A). Complete description of a cardiac anomaly includes the anatomic variables listed in Box 1-1.\(^{B6,R11,R6,E7,S14,V10}\)

Nomenclature and classification schemes are essential for accurate data reporting and establishment of databases. A continuing worldwide effort of surgeons, cardiologists, morphologists, perfusionists, pathologists, and government officials has resulted in the International Pediatric and Congenital Cardiac Code (IPCCC).\(^{S5}\) The framework of this effort will serve as a guideline for future efforts at classification of cardiac morphology. These efforts have not as yet embraced a true ontology of congenital heart disease that, at least in theory, could integrate with a cardiovascular Gene Ontology to couple phenotype with genotype.

### Situs of the Thoracic Viscera and Atria

The possible situs of the thoracic viscera and atria are (1) situs solitus, or usual situs, (2) situs inversus, and (3) situs ambiguous. **Situs solitus** means that the right/left relationships of the asymmetric viscera and the atria are usual. That is, the right (eparterial) and left (hyparterial) mainstem bronchi are normally positioned, the right atrium is to the right of the left atrium, and the left atrium is to the left. **Situs inversus** indicates that the right/left relationships are the opposite of usual. In chemical language, these are isomers. With rare exceptions, atrial and thoracic visceral situs are the same (concordant). **Situs ambiguous** is the absence of lateralization in the thoracic organs and atrial chambers.\(^{V3,V4}\) in the latter case, this condition is termed atrial isomerism (see Chapter

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<tr>
<th>Structure</th>
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<td>Lange et al.(^{T3})</td>
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<td>Nakazawa et al.(^{N2})</td>
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<td>Thilenius and Arcilla(^{T4})</td>
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</tr>
<tr>
<td>WALL THICKNESS (mm)</td>
<td></td>
</tr>
<tr>
<td>Autopsy:</td>
<td></td>
</tr>
<tr>
<td>Rowlatt et al.(^{R4})</td>
<td>13</td>
</tr>
<tr>
<td>2D echocardiography:</td>
<td></td>
</tr>
<tr>
<td>Henry et al. (diastolic)(^{H5})</td>
<td>9.9</td>
</tr>
<tr>
<td>Henry et al. (systolic)(^{H5})</td>
<td>15</td>
</tr>
<tr>
<td>SEPTUM (mm)</td>
<td></td>
</tr>
<tr>
<td>2D echocardiography:</td>
<td></td>
</tr>
<tr>
<td>Henry et al. (diastolic)(^{H5})</td>
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<tr>
<td>Henry et al. (systolic)(^{H5})</td>
<td>13</td>
</tr>
<tr>
<td>MASS (g)</td>
<td></td>
</tr>
<tr>
<td>Autopsy:</td>
<td></td>
</tr>
<tr>
<td>Graham et al.(^{G3})</td>
<td>88</td>
</tr>
<tr>
<td>2D echocardiography:</td>
<td></td>
</tr>
<tr>
<td>Henry et al. (^{H5})</td>
<td>95</td>
</tr>
<tr>
<td><strong>Right Ventricle</strong></td>
<td></td>
</tr>
<tr>
<td>VOLUME (mL)</td>
<td></td>
</tr>
<tr>
<td>Angiography, end-diastolic:</td>
<td></td>
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<tr>
<td>Graham et al.(^{G3})</td>
<td>58</td>
</tr>
<tr>
<td>Lange et al.(^{T3})</td>
<td>68</td>
</tr>
<tr>
<td>Nakazawa et al.(^{N2})</td>
<td>67</td>
</tr>
<tr>
<td>Thilenius and Arcilla(^{T4})</td>
<td>74</td>
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<td>Angiography, end-systolic:</td>
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<tr>
<td>Lange et al.(^{T3})</td>
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<td>Thilenius and Arcilla(^{T4})</td>
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<td>WALL THICKNESS (mm)</td>
<td></td>
</tr>
<tr>
<td>Autopsy:</td>
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<tr>
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<tr>
<td>Rowlatt et al. (inlet)(^{R4})</td>
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<tr>
<td><strong>Heart Weight (g)</strong></td>
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<tr>
<td>Autopsy:</td>
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<tr>
<td>Kitzman et al. (adult females)(^{K8})</td>
<td>186</td>
</tr>
<tr>
<td>Kitzman et al. (adult males)(^{K8})</td>
<td>187</td>
</tr>
<tr>
<td>Rowlatt et al. (children)(^{R9})</td>
<td>112</td>
</tr>
<tr>
<td>Scholz et al. (female infants and children)(^{S9})</td>
<td>110</td>
</tr>
<tr>
<td>Scholz et al. (male infants and children)(^{S9})</td>
<td>114</td>
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</tbody>
</table>

\(^{a}\)Normalization is in terms of BSA.

Key: 2D, Two-dimensional; BSA, body surface area.
In asplenia and polysplenia, the usually asymmetric structures tend to be symmetric. In both, in contrast to normal, the length of the right and left mainstem bronchi is the same, as is the relation of each bronchus to its pulmonary artery and the configuration of the artery. Persons with asplenia tend to have bilateral right-sidedness and right atrial isomerism, a condition identified by finding the right-type configuration of mainstem bronchi and its pulmonary artery on both left and right sides (the bronchus is relatively short and posterior and superior to the pulmonary artery, which bifurcates into an upper and lower trunk). Patients with polysplenia tend to have bilateral left-sidedness and left atrial isomerism, with the left-type configuration of the mainstem bronchi and its pulmonary artery on both sides (the bronchus is anterior and inferior to the pulmonary artery, which gives off individual branches rather than a discrete trunk to the upper lobe).

A determination of situs can sometimes be made by study of the plain chest radiograph. When there is situs ambiguous, a common atrium is often present, and only the morphology of the atrial appendages indicates whether there is right or left atrial isomerism (see Chapter 58). Complex forms of congenital heart disease tend to occur in patients with atrial isomerism, although in rare cases the heart is normal.

Situs of the Ventricles

In situs solitus, ventricles are said to have normal (usual, concordant) situs when the morphologically right ventricle is anterior and to the right of the morphologically left ventricle, which is posterior and to the left. Van Praagh’s term, D-loop, may be used to describe this ventricular situs or isomer, as may his term right-handedness, also used by Anderson. D-loop indicates that the sinus portion of the morphologically right ventricle is to the right vis-à-vis that of the left. In hearts with D-loop (as described by Van Praagh), direction of blood flow in the right ventricle is from right to left through the right-sided tricuspid valve and inflow (sinus) portion to the usually left-sided outflow portion (infundibulum). D-loop or right-handedness can also be defined as existing when the palmar surface of the right hand can be placed on the septal surface of the right ventricle such that the thumb is in the inlet (tricuspid valve), the wrist is in the apical trabecular component, and the fingers are in the outlet (pulmonary valve).

In situs solitus, ventricles are said to be inverted when the morphologically right ventricle is more or less posterior and to the left of the morphologically left ventricle; Van Praagh’s term, L-loop, applies here, as does the term left-handedness. In L-loop, the sinus (inlet) portion of the morphologically right ventricle is to the left vis-à-vis that of left ventricle; that is, internal organization is opposite of that in D-loop, and direction of blood flow is from the left-sided tricuspid valve to the right-sided infundibulum. L-loop, or left-handedness, can also be defined as existing when the palmar surface of the left hand can be placed on the septal surface of the right ventricle such that the thumb is in the inlet, the wrist is in the apical trabecular component, and the fingers are in the outlet. L.M. Barger (UAB; personal communication) suggested that looking through the right ventricle’s AV valve toward its apex, in D-loop the septal structures are to the left, and in L-loop they are to the right.

In atrial situs inversus, L-loop is the normal (usual, concordant) situs and D-loop is the inverted situs. The definitions of loop, or handedness, are independent of atrial or visceral situs and are thus the same as just described. Because there are two possible ventricular situses (D-loop and L-loop) in both atrial situs solitus and atrial situs inversus, there are four basic hearts, an idea expressed many years ago by Stanger, Edwards, and colleagues (see Appendix 1H). When thoracic and atrial situs are ambiguous, only ventricular situs can be described, and its relationship to thoracic and atrial situs is “ambiguous.”

Completeness of the Ventricles

Both the right and left ventricle may be considered to have inlet, sinus, and outlet portions when complete. Either ventricle may be incomplete (or rudimentary). For example, the inlet portion of the right ventricle is absent in hearts with tricuspid atresia.

Dominance of the Ventricles

Normally, the size of the two ventricles is similar and can be said to be balanced. In many kinds of cardiac conditions, one ventricle is larger, or dominant, and the smaller one can be severely hypoplastic. The dominance may be mild, moderate, or severe. Generally, a ventricle is said to be dominant only when the other ventricle is too small to maintain adequate pulmonary or systemic blood flow.

Cardiac Connections

Information about cardiac connections is fundamental in describing any malformed heart and requires elucidation at both AV and ventriculoarterial levels. The AV connection may be concordant (right atrium connects to right ventricle;
left atrium connects to left ventricle), discordant (right atrium connects to left ventricle; left atrium connects to right ventricle), univentricular (atria connect to only one ventricle; see Chapter 56 for more details of this subset), or ambiguous (situs ambiguous of atria). When an AV valve is straddling, it is considered to be connected to the ventricle into which more than 50% of the valve orifice faces. As Bharati and colleagues have pointed out, it is pertinent to distinguish between straddling of the valve anulus across the septum and of the chordal attachments into an inappropriate ventricle.88 Milo and colleagues suggested that the term overriding be used when referring to the anulus, and straddling when referring to chordal attachments.56

The ventriculoarterial connection may be discordant (left ventricle connects wholly or nearly so to aorta; right ventricle to pulmonary artery) or discordant (right ventricle connects to aorta, left ventricle to pulmonary artery, commonly called transposition of the great arteries). As with AV connections, when a semilunar valve is overriding a VSD, it is considered to be connected to the ventricle from which more than 50% of the valve area arises. The connection may also be double outlet (great arteries arise wholly or for the most part from one ventricle).

The ventriculoarterial connection may be considered single outlet when there is a common arterial trunk (truncus arteriosus communis) or only a single artery, usually the aorta, connected to a ventricle. In the latter case, there is usually pulmonary atresia, and categorization as single outlet ventriculoarterial connection, although morphologically precise, considerably complicates the presentation of information in many types of congenital heart disease. Alternatively, the ventriculoarterial connections can be termed concordant, discordant, or double outlet by identifying the connection, although atretic, of the pulmonary artery to a ventricle. Even when there is a ventriculopulmonary artery discontinuity, this is often possible. For example, when the morphology is typical for tetralogy of Fallot, except that there is only a single ventricular outlet because of pulmonary atresia, the condition is called tetralogy of Fallot with pulmonary atresia (see Chapter 38).

Cardiac and Arterial Positions

Normally, the cardiac apex points to the left, a situation called levocardia. The term dextrocardia applies when the cardiac apex points to the right, and mesocardia when it is in the midline. There is merit to using the term dextroversion to denote dextrocardia with situs solitus of the viscera and atria, and levoversion to denote levocardia with situs inversus. Dextroversion and levoversion alter the geometry and position of all cardiac chambers. Thus, the position of the heart is important surgically, but it is not a basic abnormality, as is D- or L-loop. The left atrium is generally to the left and the right atrium to the right in situs solitus, and vice versa in situs inversus.

Position of the ventricles is determined primarily but not exclusively by the ventricular situs (loop or handedness). The morphologically right ventricle is usually anterior and to the right in D-loop, and the left ventricle posterior and to the left. Generally, with L-loop (inverted ventricles), the morphologically left ventricle is anterior and to the right, and the morphologically right ventricle is posterior and to the left. However, the ventricles may be side by side or directly anteroposterior to each other, with either ventricle in either position. Ventricles may also be in a superoinferior (over and under) position; this occurs most commonly with L-loop but can occur with D-loop. This and probably other positional anomalies are most clearly seen by echocardiographic and angiographic study and may be entirely overlooked by autopsy studies. Positional interrelations are not basic pathologic entities, but rotational anomalies producing variations of the four basic hearts.

The possible positions of the origins of the great arteries are nearly infinite around the 360 degrees of a circle but may be simplified as (1) normal, with aorta to the right (in visceroatrial situs solitus) or left (in inversus) and somewhat posterior to the pulmonary artery; (2) aorta anterior to the pulmonary artery, either directly or somewhat to the right (D-malposition); (3) aorta to the left of the pulmonary artery (L-malposition); and (4) aorta posterior to the pulmonary artery. Normally, the great arteries tend to cross rather than run parallel. In contrast, when the great arteries are malposed, their first portions are usually parallel.

As indicated, these are all positional arterial abnormalities and are not basic parts of a malformation. However, certain probabilities exist. For example, the inflow portion of the right ventricle is usually on the side of the aortic origin.

Atrioventricular Flow Pathways

In normal hearts, AV flow pathways are more or less parallel. In cases of crisscross AV flow pathways, they cross over each other. The term crisscross hearts was introduced by Ando and colleagues416 and Anderson and colleagues418 in 1974, but the condition had been described earlier by Lev and Rowlatt in 1961.57

The word crisscross has led to confusion and controversy. One point of view is that in some abnormal hearts, the pathways cross when viewed on cineangiography. Another point of view is that this is an illusion.414 In any event, crisscross has no implications with regard to internal ventricular architecture or AV connections. The crisscross of the flow pathways is produced by positional abnormalities of the ventricles (often a superior/inferior position). Hypoplasia of the inflow or sinus of the right ventricle often contributes to crisscross. In most cases of crisscross, there is ventriculoarterial discordant connections and either discordant ventriculoarterial connections or double outlet right ventricle.

Defects and Abnormalities

Defects involving cardiac septa, chambers, and valves occur as more or less isolated anomalies, but are more common when connection and rotational anomalies exist. Such defects must be described separately for each heart, along with segmental situs, connections, and positions of the heart. Possible defects include VSD, atrial septal defect, AV septal defect, anomalous systemic and pulmonary venous connections, congenital valvar and subvalvar lesions, straddling AV valves, and abnormalities of septal morphology, including infundibular (conal) development.

Conventional Diagnoses

As a summarizing convenience, certain old and widely used phrases that are in themselves not anatomically specific but well understood by surgeons continue to be useful. In each
instance, morphology denoted by a given phrase must be defined, in part because others may use the same phrase (e.g., transposition of the great arteries) differently. Such phrases include AV canal (see Chapter 34), tetralogy of Fallot (see Chapter 38), Taussig-Bing heart (see Chapter 53), complete transposition of the great arteries (see Chapter 53), double outlet ventricle (see Chapters 53 and 54), corrected transposition of the great arteries (see Chapter 55), isolated ventricular inversion (see Chapter 55), and anatomically corrected malposition of the great arteries (see Chapter 57). In the interest of readability, the text does not use quotation marks for these phrases; once defined they are used primarily for convenience.

Symbolic Convention of Van Praagh

Van Praagh’s symbolic convention for the heart—for example, S,D,D heart—is widely used and a convenient and concise way of expressing certain anatomic features and relations. The first symbol refers to situs (isomerism) of thoracic viscera and atria (S for solitus, I for inversus). The second symbol indicates situs (isomerism) of the ventricles in terms of D-loop and L-loop (see “Situs of the Ventrices”). When taken with the first symbol, it is of fundamental significance in designating which of the four basic hearts, or isomeric combinations, is present. The third symbol refers to position of the aortic origin (D for right-sided, L for left-sided).

1A Morphogenesis

Kirklin and Barratt-Boyes were reluctant to use terms with developmental implications, but our understanding of developmental events that lead on the one hand to normal anatomy and on the other to morphologic abnormalities has greatly expanded in recent years. It is now well understood that certain anomalies of the aorta can be traced to abnormalities of fetal remodeling of the embryonic aortic arches. Abnormalities of the aorta in bicuspid aortic valve appear traceable to neural crest cells that migrate late in heart development. Van Praagh and colleagues present a unifying developmental theory for a large number of congenital heart anomalies, including transposition of the great arteries, double outlet ventricles, tetralogy of Fallot, and VSD. These anomalies have in common variable remodeling (resorption) of the embryonic subarterial conus, particularly that under the developing aortic valve. Insights such as this give rise to the idea, for example, that tetralogy of Fallot is fundamentally a monolesion from a developmental perspective.

Discoveries about the genetic basis for a number of cardiac abnormalities are also on the rise. How this knowledge will be instrumental in advancing cardiac surgery in particular and cardiothoracic medicine in general is uncertain at this time.

1B Normal Pathway Dimensions from Autopsy Specimens

Rowlatt and colleagues provided extensive information about the dimensions (measured as circumference) of cardiac valves in formalin-fixed autopsy specimens from apparently normal children. Because usually it is the diameter that is measured by echocardiography, angiography, and in the operating room, circumferences have been transformed to diameter, assuming that valve orifices are perfectly circular and using the equation:

\[
\text{Diameter} = \frac{\text{Circumference}}{\pi}
\]

These dimensions can also be expressed in terms of cross-sectional area, using for the transformation the equation:

\[
\text{Area} = \pi \left(\frac{\text{Diameter}}{2}\right)^2
\]

Krovetz and Westaby and colleagues also made measurements from adult autopsy specimens that are compatible with those of Rowlatt and colleagues. These investigators added the information that as adults age, the aortic orifice gradually enlarges. Eckner and colleagues measured
pressure-fixed autopsy specimens and found dimensions similar to but slightly larger than those of Rowlett and colleagues.\(^{31}\) Scholz and colleagues also present extensive information on cardiac dimensions obtained in autopsy specimens.\(^{30}\) Their findings and equations are generally similar to those of Rowlett and colleagues, except they find that valve dimensions are best normalized to age and gender of the individual (rather than to body surface area [BSA]). These investigators believe that the predicted values from their regression equations are applicable to either fresh or fixed specimens and compare well with systolic anular dimensions obtained by imaging techniques in living subjects.

Most of the information in this book relating dimensions in patients to those obtained at autopsy uses equations derived from the work of Rowlett and colleagues\(^{34}\) to compute the mean normal value and standard deviation based on the patient’s BSA. This group expressed dimensions as circumference and BSA as cm\(^2\). For use in this text, these have been transformed into diameter (assuming the cross-section was a perfect circle) and m\(^2\). Diameters of cardiac valves for normal individuals are summarized in Table 1B-1.

Capps and colleagues\(^{52}\) analyzed 6801 fresh autopsied hearts for valve cryopreservation over the range of 0.18 to 3.55 m\(^2\) BSA. Mean indexed aortic valve area \((n = 4636)\) was 2.02 ± 0.52 cm\(^2\) · m\(^{-2}\). Mean diameters of each valve within ranges of BSA are given in Table 1B-2. Regression equations useful for predicting mean normal aortic and pulmonary valve diameters are given for males, females, and overall in Table 1B-3. This analysis ignores increase in valve size due to aging, which, though normal, may be considered a degenerative process.

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### Table 1B-1 Diameters (mm) of Normal Cardiac Valves\(^{5}\)

<table>
<thead>
<tr>
<th>BSA (m(^2))</th>
<th><strong>BSA</strong> (m(^2))</th>
<th><strong>Mitral</strong></th>
<th><strong>Tricuspid</strong></th>
<th><strong>Aortic</strong></th>
<th><strong>Pulmonary</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Mean ± SD</strong></td>
<td><strong>Mean ± SD</strong></td>
<td><strong>Mean ± SD</strong></td>
<td><strong>Mean ± SD</strong></td>
<td><strong>Mean ± SD</strong></td>
</tr>
<tr>
<td>0.25</td>
<td>11.4 ± 9.8-13.0</td>
<td>13.4 ± 11.8-15.0</td>
<td>7.2 ± 6.2-8.2</td>
<td>8.4 ± 7.3-9.6</td>
<td></td>
</tr>
<tr>
<td>0.30</td>
<td>12.5 ± 10.9-14.2</td>
<td>14.9 ± 13.3-16.5</td>
<td>8.1 ± 7.1-9.1</td>
<td>9.3 ± 8.2-10.5</td>
<td></td>
</tr>
<tr>
<td>0.35</td>
<td>13.5 ± 11.9-15.2</td>
<td>16.2 ± 14.5-17.8</td>
<td>8.8 ± 7.8-9.8</td>
<td>10.1 ± 8.9-11.2</td>
<td></td>
</tr>
<tr>
<td>0.40</td>
<td>14.4 ± 12.7-16.0</td>
<td>17.3 ± 15.6-18.9</td>
<td>9.5 ± 8.5-10.5</td>
<td>10.7 ± 9.6-11.9</td>
<td></td>
</tr>
<tr>
<td>0.45</td>
<td>15.1 ± 13.5-16.7</td>
<td>18.2 ± 16.6-19.9</td>
<td>10.1 ± 9.1-11.1</td>
<td>11.3 ± 10.2-12.5</td>
<td></td>
</tr>
<tr>
<td>0.50</td>
<td>15.8 ± 14.1-17.4</td>
<td>19.1 ± 17.5-20.7</td>
<td>10.6 ± 9.6-11.6</td>
<td>11.9 ± 10.7-13.0</td>
<td></td>
</tr>
<tr>
<td>0.60</td>
<td>16.9 ± 15.3-18.6</td>
<td>20.6 ± 19.0-22.2</td>
<td>11.4 ± 10.4-12.5</td>
<td>12.8 ± 11.6-13.9</td>
<td></td>
</tr>
<tr>
<td>0.70</td>
<td>17.9 ± 16.3-19.5</td>
<td>21.9 ± 20.3-23.5</td>
<td>12.2 ± 11.2-13.2</td>
<td>13.5 ± 12.4-14.7</td>
<td></td>
</tr>
<tr>
<td>0.80</td>
<td>18.7 ± 17.1-20.4</td>
<td>23.0 ± 21.4-24.6</td>
<td>12.8 ± 11.8-13.8</td>
<td>14.2 ± 13.0-15.3</td>
<td></td>
</tr>
<tr>
<td>0.90</td>
<td>19.5 ± 17.8-21.1</td>
<td>24.0 ± 22.3-25.6</td>
<td>13.4 ± 12.4-14.4</td>
<td>14.8 ± 13.6-15.9</td>
<td></td>
</tr>
<tr>
<td>1.00</td>
<td>20.1 ± 18.5-21.8</td>
<td>24.8 ± 23.2-26.5</td>
<td>13.9 ± 12.9-14.9</td>
<td>15.3 ± 14.1-164</td>
<td></td>
</tr>
<tr>
<td>1.20</td>
<td>21.3 ± 19.7-22.9</td>
<td>26.3 ± 24.7-28.0</td>
<td>14.8 ± 13.8-15.8</td>
<td>16.2 ± 15.0-17.4</td>
<td></td>
</tr>
<tr>
<td>1.40</td>
<td>22.3 ± 20.6-23.9</td>
<td>27.6 ± 26.0-29.2</td>
<td>15.6 ± 14.6-16.6</td>
<td>17.0 ± 15.8-18.1</td>
<td></td>
</tr>
<tr>
<td>1.60</td>
<td>23.1 ± 21.5-24.8</td>
<td>28.7 ± 27.1-30.3</td>
<td>16.2 ± 15.2-17.2</td>
<td>17.6 ± 16.5-18.8</td>
<td></td>
</tr>
<tr>
<td>1.80</td>
<td>23.9 ± 22.2-25.5</td>
<td>29.7 ± 28.1-31.3</td>
<td>16.8 ± 15.8-17.8</td>
<td>18.2 ± 17.1-194</td>
<td></td>
</tr>
<tr>
<td>2.00</td>
<td>24.5 ± 22.9-26.2</td>
<td>30.6 ± 28.9-32.3</td>
<td>17.3 ± 16.3-18.3</td>
<td>18.7 ± 17.6-19.9</td>
<td></td>
</tr>
</tbody>
</table>

*Values are based on measurements made in hearts obtained at autopsy from apparently normal children (the oldest was 15 years of age). The relationship of these measurements to those obtained in other modalities is shown in Appendix Figs. 1E-1 to 1E-4.*

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### Table 1B-2 Left Ventricular–Aortic Junction (Aortic Valve) and Right Ventricular–Pulmonic Junction (Pulmonary Valve) Diameters in Males and Females According to Body Surface Area Range

<table>
<thead>
<tr>
<th>BSA Range</th>
<th><strong>Males</strong></th>
<th><strong>Females</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Aortic Valve</strong></td>
<td><strong>Pulmonary Valve</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Diameter (mm)</strong></td>
<td><strong>Diameter (mm)</strong></td>
</tr>
<tr>
<td>0.21-0.30</td>
<td>19</td>
<td>8.8 ± 1.0</td>
</tr>
<tr>
<td>0.31-0.40</td>
<td>34</td>
<td>10.0 ± 1.6</td>
</tr>
<tr>
<td>0.41-0.50</td>
<td>57</td>
<td>11.2 ± 0.9</td>
</tr>
<tr>
<td>0.51-0.60</td>
<td>64</td>
<td>12.3 ± 1.2</td>
</tr>
<tr>
<td>0.61-0.70</td>
<td>70</td>
<td>13.5 ± 1.3</td>
</tr>
<tr>
<td>0.71-0.80</td>
<td>57</td>
<td>14.1 ± 1.1</td>
</tr>
</tbody>
</table>
### Table 18-2  Left Ventricular–Aortic Junction (Aortic Valve) and Right Ventricular–Pulmonic Junction (Pulmonary Valve) Diameters in Males and Females According to Body Surface Area Range—cont’d

<table>
<thead>
<tr>
<th>BSA Range (m²)</th>
<th>Aortic Valve</th>
<th>Pulmonary Valve</th>
<th>Aortic Valve</th>
<th>Pulmonary Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Diameter (mm)</td>
<td>n</td>
<td>Diameter (mm)</td>
</tr>
<tr>
<td>0.81-0.90</td>
<td>37</td>
<td>14.6 ± 1.5</td>
<td>39</td>
<td>17.6 ± 2.0</td>
</tr>
<tr>
<td>0.91-1.00</td>
<td>48</td>
<td>15.6 ± 1.3</td>
<td>61</td>
<td>18.7 ± 1.9</td>
</tr>
<tr>
<td>1.01-1.10</td>
<td>42</td>
<td>16.3 ± 1.5</td>
<td>51</td>
<td>19.5 ± 1.8</td>
</tr>
<tr>
<td>1.11-1.20</td>
<td>42</td>
<td>17.2 ± 1.9</td>
<td>45</td>
<td>20.4 ± 1.9</td>
</tr>
<tr>
<td>1.21-1.30</td>
<td>25</td>
<td>17.1 ± 1.6</td>
<td>39</td>
<td>20.6 ± 1.8</td>
</tr>
<tr>
<td>1.31-1.40</td>
<td>38</td>
<td>18.7 ± 1.7</td>
<td>55</td>
<td>21.6 ± 2.1</td>
</tr>
<tr>
<td>1.41-1.50</td>
<td>39</td>
<td>19.1 ± 2.3</td>
<td>44</td>
<td>22.3 ± 2.5</td>
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<tr>
<td>1.51-1.60</td>
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<td>20.7 ± 2.4</td>
<td>69</td>
<td>23.5 ± 2.3</td>
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<tr>
<td>1.61-1.70</td>
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<td>20.8 ± 2.1</td>
<td>135</td>
<td>23.7 ± 2.4</td>
</tr>
<tr>
<td>1.71-1.80</td>
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<td>21.5 ± 2.0</td>
<td>230</td>
<td>24.5 ± 2.4</td>
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<tr>
<td>1.81-1.90</td>
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<td>25.2 ± 2.2</td>
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<td>25.7 ± 2.1</td>
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<tr>
<td>2.01-2.10</td>
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<td>23.0 ± 1.8</td>
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<td>26.2 ± 2.1</td>
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<tr>
<td>2.11-2.20</td>
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<td>23.6 ± 1.9</td>
<td>309</td>
<td>26.8 ± 2.0</td>
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<tr>
<td>2.21-2.30</td>
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<td>23.8 ± 1.8</td>
<td>210</td>
<td>26.8 ± 2.0</td>
</tr>
<tr>
<td>2.31-2.40</td>
<td>115</td>
<td>24.1 ± 1.9</td>
<td>134</td>
<td>27.3 ± 1.9</td>
</tr>
<tr>
<td>2.41-2.50</td>
<td>85</td>
<td>24.4 ± 1.9</td>
<td>133</td>
<td>27.5 ± 1.7</td>
</tr>
<tr>
<td>2.51-2.60</td>
<td>43</td>
<td>24.8 ± 1.8</td>
<td>45</td>
<td>27.8 ± 1.8</td>
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<tr>
<td>2.61-2.70</td>
<td>33</td>
<td>25.2 ± 2.3</td>
<td>47</td>
<td>28.1 ± 1.9</td>
</tr>
<tr>
<td>2.71-2.80</td>
<td>8</td>
<td>24.3 ± 2.4</td>
<td>15</td>
<td>27.5 ± 2.5</td>
</tr>
<tr>
<td>2.81-2.90</td>
<td>8</td>
<td>25.8 ± 1.8</td>
<td>21</td>
<td>28.2 ± 1.3</td>
</tr>
</tbody>
</table>

Data modified from CryoLife Inc., 1999.

Key: BSA, Body surface area. BSA (m²) = 0.024265 · weight (kg)\(^{0.6378}\) · height (cm)\(^{0.3364}\) (from Haycock and colleagues\(^{16}\)).

### Table 18-3  Regression Coefficients of Valve Anulus Diameter (mm) on Body Surface Area (m²)

<table>
<thead>
<tr>
<th>Structure</th>
<th>n</th>
<th>Intercept (b₀)</th>
<th>Slope (b₁)</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVD</td>
<td>2993</td>
<td>2.785 ± 0.0025</td>
<td>0.4777 ± 0.0037</td>
<td>0.08927</td>
</tr>
<tr>
<td>PVD</td>
<td>3508</td>
<td>2.936 ± 0.0022</td>
<td>0.4455 ± 0.0032</td>
<td>0.08835</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVD</td>
<td>1643</td>
<td>2.769 ± 0.0029</td>
<td>0.4517 ± 0.0050</td>
<td>0.09293</td>
</tr>
<tr>
<td>PVD</td>
<td>1972</td>
<td>2.913 ± 0.0028</td>
<td>0.4425 ± 0.0047</td>
<td>0.09563</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AVD</td>
<td>4636</td>
<td>2.778 ± 0.0019</td>
<td>0.4727 ± 0.0030</td>
<td>0.09167</td>
</tr>
<tr>
<td>PVD</td>
<td>5480</td>
<td>2.926 ± 0.0018</td>
<td>0.4483 ± 0.0027</td>
<td>0.09179</td>
</tr>
</tbody>
</table>

Modified from Capps and colleagues.\(^{21}\)

\(^{1}\)General form of equation: predicted diameter = exp(intercept + slope · Ln(BSA)), where exp is the base of the natural logarithms (Ln).

Key: AVD, Aortic valve anulus diameter; BSA, body surface area; PVD, pulmonary valve anulus diameter; SD, standard deviation.
Normal Pathway Dimensions from Cineangiography

Using cineangiograms made in both anteroposterior and lateral projections in 42 normal children, Bini and colleagues measured cardiac and great artery dimensions at peak systole and in diastole (Bini M, Naftel DC, Blackstone EM: unpublished study, 1984). Median patient age was 12 months, range 2 days to 16 years; 25% were 2 months of age or younger, and 25% were 67 months of age or older; 24 were males and 18 were females. Consideration of adoption was usually the indication for study. Structures measured included midportion of the right ventricular infundibulum and junction of the right ventricle and pulmonary artery (“anulus”); distal end of the pulmonary trunk; origin, midportion, and immediately prebranching portion of the right pulmonary artery; origin and immediately prebranching portion of the left pulmonary artery; and aorta immediately downstream to the aortic valve, immediately before the takeoff of the brachiocephalic artery, and immediately above the diaphragm. By dividing the measured internal diameter of the cardiac catheter in the same frame by the known internal diameter of the catheter, a correction factor was calculated and used to correct the measured value for magnification.

To account for increased scatter of dimension data as body surface area (BSA) increased, logarithmic transformations were made of both dimension and body size. Individual regression equations (derived only when the number of observations was >10) were developed for each location and individually for systole and diastole in the anteroposterior and lateral projections. Mean normal diameter and standard deviation according to BSA were derived from these equations. A similar analysis of cineangiographic measurements was made earlier by Sievers and colleagues. Both groups, working without knowledge of the other, found logarithmic transformation to best express the relations. Information for the equations is presented in Tables 1C-1 and 1C-2. The equations may be used to calculate the mean normal dimensions and standard deviations of the right ventricular outflow tract and pulmonary arteries for a specific BSA, for use in determining the z value of the dimension of a structure in a patient.

Dimensions of a part of the left ventricular tract and aorta were also determined by the Bini and Sievers groups (Bini M, Naftel DC, Blackstone EH: unpublished study, 1984) (see Tables 1C-1 and 1C-2). Clarkson and Brandt made measurements of the aorta in cineangiograms of normal infants and young children, similar to those of Bini and colleagues.

Most of the information in this book relating patient dimensions to z values based on cineangiographic measurements uses regression equations derived from measurements made by Bini and colleagues, which are similar to those made by Sievers and colleagues (see Tables 1C-1 and 1C-2). Unfortunately, they did not measure the tricuspid valve. These equations are used to calculate normal mean values and standard deviations according to the patient’s BSA; then the equation given in “Standardization of Dimensions” (see text) is used to calculate the z value. These equations and nomograms are for diameter. Some prefer to express the dimensions of the pulmonary arteries as cross-sectional area. Because of the logarithmic transformation used in the Bini and Sievers analyses, the z value for cross-sectional area is the same as that for diameter.
### Table 1C-1 Coefficients of Linear Regression Equation Relating Diameter in Anteroposterior Projection to Body Surface Area in Normal Subjectsa

<table>
<thead>
<tr>
<th>Structure</th>
<th>Systole</th>
<th>Diastole</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n Scale Factor (Intercept)</td>
<td>Exponent (Slope)</td>
<td>SD (Logarithmic Domain)</td>
</tr>
<tr>
<td>RV infundibulum</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Pulmonary trunk:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right ventricular-PA junction</td>
<td>29</td>
<td>2.897</td>
<td>0.6033</td>
</tr>
<tr>
<td>Midportion</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Right pulmonary artery:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Origin</td>
<td>34</td>
<td>2.787</td>
<td>0.6768</td>
</tr>
<tr>
<td>Midportion</td>
<td>32</td>
<td>2.671</td>
<td>0.6886</td>
</tr>
<tr>
<td>Prebranching</td>
<td>34</td>
<td>2.784</td>
<td>0.6340</td>
</tr>
<tr>
<td>Left pulmonary artery:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Origin</td>
<td>17</td>
<td>2.692</td>
<td>0.7079</td>
</tr>
<tr>
<td>Prebranching</td>
<td>27</td>
<td>2.694</td>
<td>0.7075</td>
</tr>
<tr>
<td>RPA + LPA diameters</td>
<td>27</td>
<td>3.450</td>
<td>0.6727</td>
</tr>
<tr>
<td>Aorta:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular-aortic junction</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Commissural level</td>
<td>31</td>
<td>2.960</td>
<td>0.5057</td>
</tr>
<tr>
<td>Pre-brachiocephalic</td>
<td>28</td>
<td>2.899</td>
<td>0.5183</td>
</tr>
<tr>
<td>Descending thoracic at diaphragm</td>
<td>35</td>
<td>2.506</td>
<td>0.4694</td>
</tr>
</tbody>
</table>


aNormal structure size (diameter or cross-sectional area) is calculated as $\text{Ln(size[diameter or cross-sectional area])} = \text{scale factor} + \text{exponent} \cdot \text{Ln(BSA)}$, where body surface area (BSA) is expressed as square meters. Size can then be obtained by exponential transformation (e taken to the power of the logarithm). If diameter is used, coefficients are as shown in the table. If cross-sectional area is used, a circular lumen is assumed and the coefficients modified by multiplying the scale factor by 2 and subtracting 0.2415645 from the value obtained [Ln($\pi$) − 2Ln(2)], by multiplying the exponent by 2, and by multiplying the standard deviation by 2. In all instances, $P < .0001$.

The z value (number of standard deviations a structure is above or below normal size) is calculated from the observed size as the logarithm of the observed size minus the calculated logarithm of normal size, divided by the standard deviation. Because the analysis uses the logarithmic transformation, z obtained using diameters is identical to one using cross-sectional area. All logarithms are natural logarithms.

b(Systolic + diastolic diameters)/2.

Key: LPA, left pulmonary artery; PA, pulmonary artery; $\tau$, correlation coefficient; RPA, right pulmonary artery; RV, right ventricular; SD, standard deviation.
Table 1C-2  Coefficients of Linear Regression Equation Relating Diameter in Lateral Projection to Body Surface Area in Normal Subjects<sup>a</sup>

<table>
<thead>
<tr>
<th>Structure</th>
<th>Systole</th>
<th></th>
<th></th>
<th></th>
<th>Diastole</th>
<th></th>
<th></th>
<th></th>
<th>Average</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scale Factor</td>
<td>Exponent</td>
<td>SD</td>
<td></td>
<td>Scale Factor</td>
<td>Exponent</td>
<td>SD</td>
<td></td>
<td>Scale Factor</td>
<td>Exponent</td>
<td>SD</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>(Intercept)</td>
<td>(Slope)</td>
<td>(Logarithmic Domain)</td>
<td></td>
<td>(Intercept)</td>
<td>(Slope)</td>
<td>(Logarithmic Domain)</td>
<td></td>
<td>(Intercept)</td>
<td>(Slope)</td>
<td>(Logarithmic Domain)</td>
<td></td>
</tr>
<tr>
<td>RV infundibulum</td>
<td>23</td>
<td>2549</td>
<td>0.4080</td>
<td>0.1337</td>
<td>0.89</td>
<td>23</td>
<td>2.929</td>
<td>0.3450</td>
<td>0.1133</td>
<td>0.89</td>
<td>23</td>
<td>2.7600</td>
<td>0.3720</td>
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<tr>
<td>Pulmonary trunk:</td>
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<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Right ventricular-PA junction</td>
<td>29</td>
<td>2.863</td>
<td>0.4664</td>
<td>0.1326</td>
<td>0.92</td>
<td>29</td>
<td>2.898</td>
<td>0.4602</td>
<td>0.1120</td>
<td>0.94</td>
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<td>0.1327</td>
<td>0.95</td>
<td>23</td>
<td>2.965</td>
<td>0.5725</td>
<td>0.1350</td>
<td>0.94</td>
<td>22</td>
<td>3.052</td>
<td>0.6037</td>
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<tr>
<td>Origin</td>
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<tr>
<td>Midportion</td>
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</tr>
<tr>
<td>Prebranching</td>
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<td></td>
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</tr>
<tr>
<td>Left pulmonary artery:</td>
<td></td>
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<td>Origin</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Prebranching</td>
<td>19</td>
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<td>0.1922</td>
<td>0.90</td>
<td>19</td>
<td>2.500</td>
<td>0.7146</td>
<td>0.2447</td>
<td>0.85</td>
<td>19</td>
<td>2.573</td>
<td>0.7178</td>
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<td></td>
<td></td>
<td></td>
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<td>Aorta:</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular-aortic junction</td>
<td>24</td>
<td>2.929</td>
<td>0.4220</td>
<td>0.1249</td>
<td>0.90</td>
<td>24</td>
<td>2.833</td>
<td>0.4440</td>
<td>0.1406</td>
<td>0.89</td>
<td>24</td>
<td>2.879</td>
<td>0.4320</td>
</tr>
<tr>
<td>Commissural level</td>
<td>29</td>
<td>2.985</td>
<td>0.5310</td>
<td>0.1896</td>
<td>0.87</td>
<td>29</td>
<td>2.896</td>
<td>0.5174</td>
<td>0.1987</td>
<td>0.85</td>
<td>29</td>
<td>2.942</td>
<td>0.5247</td>
</tr>
<tr>
<td>Pre-brachiocephalic</td>
<td>27</td>
<td>2.864</td>
<td>0.5098</td>
<td>0.1609</td>
<td>0.87</td>
<td>27</td>
<td>2.811</td>
<td>0.5209</td>
<td>0.1625</td>
<td>0.87</td>
<td>27</td>
<td>2.838</td>
<td>0.5151</td>
</tr>
<tr>
<td>Descending thoracic at diaphragm</td>
<td>27</td>
<td>2.462</td>
<td>0.4576</td>
<td>0.1817</td>
<td>0.82</td>
<td>27</td>
<td>2.389</td>
<td>0.4546</td>
<td>0.1751</td>
<td>0.83</td>
<td>27</td>
<td>2.427</td>
<td>0.4564</td>
</tr>
</tbody>
</table>

*From Bini M, Naftel DC, Blackstone EH: Unpublished study, 1984, except for values for RV infundibulum, which are from Sievers and colleagues.\(^{15}\)*

*Key and footnotes \(a\) and \(b\) are identical to those for Table 1C-1.*
Normal Pathway Dimensions from Two-Dimensional Echocardiography

Dimensions obtained by two-dimensional (2D) echocardiography are sometimes measured and expressed as length of anulus (without a commitment as to the shape of the orifice), sometimes as the shortest axis (anteroposterior) and the longest axis (lateral), and sometimes as cross-sectional area measured directly on the 2D echocardiographic image, without an assumption as to shape. Sometimes both the smallest and largest dimensions in a cardiac cycle are measured and expressed.

Daubeney and colleagues\textsuperscript{1,2} have provided a comprehensive catalog of cardiac structural dimensions by 2D echocardiography in normal infants and children. Definition of each dimension and the 2D echocardiographic view in which it was measured are given in Table 1D-1. For the most part, a regression equation was developed using BSA in the logarithmic transformation domain. The regression equation is:

$$\text{Ln}[\text{Mean normal diameter (mm)}] = \text{Intercept} + \text{Slope} \cdot \text{Ln}(\text{BSA})$$

where \textit{mean normal diameter} is specific for BSA, BSA is expressed in square meters, and \text{Ln} is the natural logarithm. Values for the intercept and slope, as well as for the standard deviations (root mean square error), are presented in Table 1D-2. Values are the largest ones during the cardiac cycle, nearly always at end-diastole. The \text{z} value equation (see “Standardization of Dimensions” in text) can then be used to calculate the \text{z} value. More simply, a nomogram (Fig. 1D-1) may be used.

King and colleagues measured dimensions of mitral and tricuspid valves by 2D echocardiography.\textsuperscript{5} Based on these data, regression equations were developed for mean normal diameter (logarithmic transformation) and BSA (logarithmic transformation) as shown in Table 1D-3. A digital nomogram is presented in Table 1D-4.

Habbal and Somerville measured dimensions of the left ventricular–aortic junction (aortic “anulus”) in normal children by 2D echocardiography.\textsuperscript{1,1} Their regression equation relating mean normal value to BSA is:

### Table 1D-1  Cardiac Dimensions Measured, Echocardiographic Views Used, and Definitions of Each Measurement

<table>
<thead>
<tr>
<th>Cardiac Dimension</th>
<th>Echocardiographic View</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tricuspid valve</td>
<td>Apical four chamber</td>
<td>Distance between “hinge points” of leaflets at level of anulus</td>
</tr>
<tr>
<td>RV–pulmonic junction</td>
<td>Parasternal short axis</td>
<td>Distance between “hinge points” of attachment of the valve</td>
</tr>
<tr>
<td>Pulmonary trunk</td>
<td>Parasternal short axis</td>
<td>Diameter of pulmonary trunk halfway between RV–pulmonic junction and bifurcation</td>
</tr>
<tr>
<td>Right pulmonary artery</td>
<td>Parasternal short axis</td>
<td>Diameter immediately beyond bifurcation</td>
</tr>
<tr>
<td>Left pulmonary artery</td>
<td>Parasternal short axis</td>
<td>Diameter immediately beyond bifurcation</td>
</tr>
<tr>
<td>Mitral valve (anteroposterior)</td>
<td>Parasternal long axis</td>
<td>Distance between “hinge points” of leaflets at level of anulus</td>
</tr>
<tr>
<td>Mitral valve (lateral)</td>
<td>Apical four chamber</td>
<td>Distance between “hinge points” of leaflets at level of anulus</td>
</tr>
<tr>
<td>LV–aortic junction</td>
<td>Parasternal long axis</td>
<td>Distance between “hinge points” of attachment of the valve</td>
</tr>
<tr>
<td>Sinuses of Valsalva</td>
<td>Parasternal long axis</td>
<td>Maximum anteroposterior diameter of aortic root at level of sinuses of Valsalva</td>
</tr>
<tr>
<td>Sinutubular junction</td>
<td>Parasternal long axis</td>
<td>Maximum anteroposterior diameter of aortic root at level of sinutubular junction</td>
</tr>
</tbody>
</table>

Key: LV, Left ventricular; RV, right ventricular.
PART I General Considerations

Table 1D-2  Regression Equations Relating Cardiac Dimension and Body Surface Area

<table>
<thead>
<tr>
<th>Structure and View (in Diastole)</th>
<th>Intercept</th>
<th>Slope</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve anteroposterior</td>
<td>23.9</td>
<td>8.56</td>
<td>1.8</td>
</tr>
<tr>
<td>Lateral</td>
<td>32.3</td>
<td>12.47</td>
<td>3.2</td>
</tr>
<tr>
<td>Tricuspid valve</td>
<td>34.4</td>
<td>12.29</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Based on data from King and colleagues. From Daubeney and colleagues.

The form of the equation is Ln(mean normal value of structure) = intercept + slope · Ln[BSA], where Ln is the natural logarithm and BSA is body surface area (m²). The structures are expressed in cm or cm². Value of z can be calculated as z = [Ln(measured structure) − Ln(mean normal value)]/SD. Key: A-P, Anteroposterior; Lat, lateral; SD, standard deviation (root mean square error).

Table 1D-3  Values for the Intercept, Slope, and Standard Deviation Describing Normal Echocardiographic Diameters

<table>
<thead>
<tr>
<th>Structure and Axis</th>
<th>Intercept</th>
<th>Slope</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve anteroposterior</td>
<td>23.9</td>
<td>8.56</td>
<td>1.8</td>
</tr>
<tr>
<td>Lateral</td>
<td>32.3</td>
<td>12.47</td>
<td>3.2</td>
</tr>
<tr>
<td>Tricuspid valve</td>
<td>34.4</td>
<td>12.29</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Based on data from King and colleagues. Measured in parasternal long-axis projection. Measured in four-chamber view. Key: SD, Standard deviation.

Mean normal value = 17.20[1 − exp(−2.486 · BSA)] + 0.4663 · BSA

where Ln is the natural logarithm and exp is e, the base of the natural logarithms. The standard deviation is 0.09717 and was obtained in the log-log domain to stabilize variability. Therefore, as in the case of Bini and colleagues' analysis of cineangiographic data and Daubeney and colleagues' analysis of 2D echocardiography, the z value for cross-sectional area in a given patient is the same as for diameter, because of the logarithmic transformations used.

Using 2D echocardiography in children, Snider and colleagues measured cross-sectional dimensions of the right pulmonary artery and pulmonary trunk. The regression equation is:

\[ \text{Mean normal diameter (mm) = Intercept + Slope} \cdot \sqrt{\text{BSA}} \]

where BSA is expressed in square meters. Values for the intercept and slope are given in Table 1D-5. Because insufficient numeric data are presented to permit derivation of the standard deviation for the mean normal diameter, z values cannot be derived from this analysis.
Figure 1D-1 Nomograms expressing measured diameter of the indicated structure (isobars) in an individual of a given body surface area (horizontal axis) as a z value (vertical axis). Mean normal values and standard deviations used in equations to calculate z values were obtained from Daubeney and colleagues (see Table 1D-2). A, Tricuspid valve. B, Right ventricular–pulmonic junction (pulmonary valve).

Continued
Figure 1D-1, cont’d  
C, Pulmonary trunk. D, Right pulmonary artery.
Figure 1D-1, cont’d  

E, Left pulmonary artery. F, Mitral valve (anteroposterior, parasternal long-axis view).
Figure 1D-1, cont’d  **G**, Mitral valve (lateral, apical four-chamber view).  **H**, Left ventricular–aortic junction (aortic valve).
Figure 1D-1, cont’d  1, Sinuses of Valsalva. J, Sinutubular junction. Key: LV, Left ventricular.
Comparison of Pathway Dimensions from Different Measurement Modalities

Comparisons between Cineangiographic Dimensions and Those Obtained at Autopsy

The relationship of measurements obtained by imaging techniques to those obtained from autopsy specimens is arguable, but as was expressed earlier, this is not critical in studies relating dimensions to outcome when the $z$ value is used. Differences relating to measurement modalities are nonetheless interesting.

Dimensions obtained from autopsy data are probably the most complete and reliable dimensions available. Even among postmortem direct measurements of dimensions, however, differences exist. As stated earlier, Scholz and colleagues found that dimensions are similar in both fresh and fixed specimens (except that when pressure fixation is used, the tricuspid valve and right heart dimensions are somewhat larger) and that dimensions in autopsy specimens from normal children are similar to those obtained by imaging techniques. However, Alboliras and colleagues obtained data indicating that autopsy measurements should be multiplied by 1.04 to be comparable to cineangiographic measurements. Bull and colleagues derived a multiplication factor of 1.4 for this purpose.

A comparison of the carefully performed cineangiographic measurements of Sievers and colleagues with those of Rowlatt and colleagues indicates that normal dimensions for the left ventricular–aortic junction were about 40% larger cineangiographically than at autopsy (Fig. 1E-1). A similar comparison of the dimensions of the right ventricular–pulmonary artery junction indicated that in subjects of less than about 1 m² body surface area (BSA), cineangiographic measurements were about 17% larger, and that in larger subjects, cineangiographic measurements were 33% larger (Fig. 1E-2).

Sepehri and colleagues found that in diseased states in children, dimensions of the left ventricular–aortic junction obtained at autopsy were similar to those obtained from cineangiography, whereas those of the mitral valve obtained by cineangiography were approximately 16% larger than those obtained at autopsy. These same investigators, using a perfusion fixation technique, found the tricuspid valve to be about 50% larger by cineangiography and the pulmonary valve about 14% larger, thereby confirming the statements of Scholz and colleagues.

Comparisons between Two-Dimensional Echocardiographic Dimensions and Those Obtained at Autopsy

An informal comparison between the echocardiographic measurements of the mitral valve by King and colleagues and those obtained at autopsy by Rowlatt and colleagues suggests that in subjects who have less than about 0.5 m² BSA, the echocardiographic dimensions are about 33% larger (Fig. 1E-3). A similar comparison between the echocardiographic dimensions obtained by Riggs and colleagues and those obtained in autopsy specimens by the Rowlatt group indicates that dimensions were similar in small subjects, but the echocardiographically determined dimensions were about 20% larger in patients with BSAs greater than 1 m².

Other Comparisons

Formal comparisons of dimensions of cardiac structures in normal subjects obtained by angiography and echocardiography are missing. However, N.C. Nanda (personal communication, 1989) believes that in diseased states, echocardiographic dimensions are slightly larger than angiographic ones, probably because different bordering structures are used to define the dimension in these two different imaging techniques.

It is particularly difficult to compare dimensions derived from all three modalities. However, a comparison made for the tricuspid valve suggests that there is considerable difference in dimensions obtained using different measurement modalities (Fig. 1E-4).
**Figure 1E-1** Relation between diameter of left ventricular–aortic junction (aortic “anulus”) and body surface area, according to whether measurements were made in fixed autopsy specimens (Rowlatt and colleagues\(^\text{R4}\)) or by cineangiography (Sievers and colleagues\(^\text{S15}\)). Solid lines represent continuous point estimates of the relations, and dashed lines enclose 70% confidence interval.

**Figure 1E-2** Relation between diameter of right ventricular–pulmonary artery junction (pulmonary “anulus”) and body surface area, according to whether measurements were made on fixed autopsy specimens (Rowlatt and colleagues\(^\text{R4}\)) or by cineangiography (Sievers and colleagues\(^\text{S15}\) and Bini M, Naftel DC, Blackstone EH: Unpublished study, 1984). Meanings of depictions are as described for Fig. 1E-1.

**Figure 1E-3** Relation between diameter of mitral valve orifice and body surface area, according to whether measurements were made in fixed autopsy specimens (Rowlatt and colleagues\(^\text{R4}\)) measuring circumference or by echocardiography (King and colleagues\(^\text{K5}\) measuring major and minor axes; Riggs and colleagues\(^\text{R2}\) measuring area directly). Meanings of depictions are as described for Fig. 1E-1. Key: AP, Anteroposterior.

**Figure 1E-4** Relation between diameter of tricuspid valve and body surface area, according to whether measurements were made in fixed autopsy specimens (Rowlatt and colleagues\(^\text{R4}\)), by cineangio- graphy (Alboliras and colleagues,\(^\text{A6}\) Bull and colleagues\(^\text{B13}\)), or by echocardiography (King and colleagues\(^\text{K5}\)). Meanings of depictions are as described for Fig. 1E-1.
Four data sets were used to derive the interrelationships among three methods of expressing the dimensions of the right and left pulmonary arteries: (1) 35 normal children among the 42 studied by Bini and colleagues (see Appendix 1C), (2) 168 patients who had undergone repair of tetralogy of Fallot with pulmonary stenosis, whose cineangiograms were made before any surgical procedure, \(^{31}\) (3) 215 patients with tetralogy of Fallot and pulmonary atresia, \(^{31}\) and (4) 106 patients who had undergone the Fontan operation. \(^{33}\)

Comparisons are expressed in Figs. 1F-1, 1F-2, and 1F-3.

**Figure 1F-1** Relation between McGoon ratio and \(z\) value for summed diameters of right and left pulmonary arteries just before the takeoff of their first branch. **A**, Analysis of all patients as a single group. Symbols represent an individual patient’s values, solid line represents the continuous point estimate of the relation, and dashed lines enclose 70% confidence interval. The regression equation is:

\[
\text{McGoon ratio} = 2.355 \cdot \exp(0.1356 \cdot z)
\]

where \(\exp\) is \(e\), the base of the natural logarithms. **B**, Individual analysis of each of the four groups. No confidence limits are displayed. Key: \(P\), Pulmonary; \(PS\), pulmonary stenosis; TF, tetralogy of Fallot.

**Figure 1F-2** Relation between cross-sectional area index (mm\(^2\) \(\cdot\) m\(^{-2}\)), the so-called Nakata index, and \(z\) value for summed diameters of the right and left pulmonary arteries just before takeoff of their first branch. **A**, Analysis of all patients as a single group. Meanings of depictions are as described for Fig. 1F-1. The regression equation is:

\[
\text{CSA index} = 288.6 \cdot \exp(0.1856 \cdot z)
\]

where \(\exp\) is \(e\), the base of the natural logarithms. **B**, Individual analysis of each of the four groups. No confidence limits are displayed.
Figure 1F-3 Relation between McGoon ratio and cross-sectional area index (mm$^2 \cdot$ m$^{-2}$). A, Analysis of all patients as a single group. Meanings of depictions are as described for Fig. 1F-1. The regression equation is:

McGoon ratio = 0.07332 \cdot CSA index + 0.599

B, Individual analysis of each of the four groups. No confidence limits are displayed. Key: CSA, Cross-sectional area; P, pulmonary; PS, pulmonary stenosis; TF, tetralogy of Fallot.

1G Normal Ventricular Volume, Masses, and Dimensions from Different Measurement Modalities

Right and left ventricular dimensions and area, left ventricular wall thickness and mass, and septal thickness were measured by echocardiography (Table 1G-1). Regression equations are presented in Table 1G-2. Fig. 1G-1 shows the information presented in pairs of figures.

In addition to the measurements of Daubeney and colleagues, the relation between right ventricular end-diastolic volume (RVEDV) and body surface area (BSA) was presented by Graham and colleagues, Thilenius and Arcilla, Nakazawa and colleagues, and Lange and colleagues. Graham’s equation and its use for $z$ values is:

$$\ln(\text{mean normal RVEDV, mL}) = 4.162 + 1.340 \cdot \ln(\text{BSA, m}^2)$$

and:

$$z = \frac{\ln(\text{observed RVEDV}) - \ln(\text{normal RVEDV})}{0.2710}$$

where 0.2710 is the standard deviation and $\ln$ is the natural logarithm.

The relation between right ventricular end-systolic volume (RVESV) and BSA was presented by Graham and colleagues, Thilenius and Arcilla, and Lange and colleagues. Graham’s equation and its use for $z$ values is:

$$\ln(\text{mean normal RVESV, mL}) = 3.692 + 1.284 \cdot \ln(\text{BSA, m}^2)$$

and:

$$z = \frac{\ln(\text{observed RVESV}) - \ln(\text{normal RVESV})}{0.3211}$$

Mean normal value for right ventricular infundibular wall thickness from Rowlatt and colleagues is 2.962 ± 0.779 mm and:

$$z = \frac{\text{Observed wall thickness} - 2.962}{0.779}$$

Mean normal value for right ventricular wall thickness in the area of the tricuspid valve is 3.117 ± 1.55 mm and:

$$z = \frac{\text{Observed wall thickness} - 3.117}{1.55}$$

The relation between heart weight and BSA was studied by Kitzman and colleagues, Scholz and colleagues, and Rowlatt and colleagues (Table 1G-3). The regression equation in all cases is:
Table 1G-1  Cardiac Dimensions Measured, Echocardiographic Views Used, and Definitions of Each Measurement

<table>
<thead>
<tr>
<th>Cardiac Dimension</th>
<th>Echocardiographic View</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV inflow</td>
<td>Apical four chamber</td>
<td>Ventricular length from midpoint of plane of tricuspid valve anulus to apex of RV</td>
</tr>
<tr>
<td>RV outflow</td>
<td>Subcostal parasagittal</td>
<td>Perpendicular from RV free wall to midpoint of RV pulmonic junction</td>
</tr>
<tr>
<td>RV area</td>
<td>Apical four chamber</td>
<td>Maximal area bordered by RV endocardium (excludes area of papillary muscles)</td>
</tr>
<tr>
<td>LV inflow</td>
<td>Apical four chamber</td>
<td>Ventricular length from midpoint of plane of mitral valve anulus to apex of LV</td>
</tr>
<tr>
<td>LV end-diastolic dimension</td>
<td>M-mode, parasternal long axis</td>
<td>M-mode measurement of a line of inquiry of 2D echocardiogram at level of tips of mitral leaflet at onset of QRS</td>
</tr>
<tr>
<td>LV end-systolic dimension</td>
<td>M-mode, parasternal long axis</td>
<td>M-mode measurement of a line of inquiry of 2D echocardiogram at level of tips of the mitral leaflet, narrowest dimension</td>
</tr>
<tr>
<td>LV area</td>
<td>Apical four chamber</td>
<td>Maximal area bordered by LV endocardium (excludes area of papillary muscles)</td>
</tr>
<tr>
<td>Interventricular septum</td>
<td>M-mode, parasternal long axis</td>
<td>M-mode measurement of a line of inquiry of 2D echocardiogram at level of tips of mitral leaflet at onset of QRS</td>
</tr>
<tr>
<td>LV posterior wall</td>
<td>M-mode, parasternal long axis</td>
<td>M-mode measurement of a line of inquiry of 2D echocardiogram at level of tips of mitral leaflet at onset of QRS</td>
</tr>
<tr>
<td>LV mass</td>
<td>M-mode, parasternal long axis</td>
<td>M-mode measurement of a line of inquiry of 2D echocardiogram at level of tips of mitral leaflet at onset of QRS</td>
</tr>
</tbody>
</table>

Modified from Daubeney and colleagues.52

“Derived from LV end-diastolic dimension (LVEDd), diastolic LV posterior wall thickness (PW), and diastolic septal thickness (S) as: LV mass (g) = 1.04 [(LVEDd + PW + S)^3 − LVEDd^3] − 13.6.52

Key: 2D, Two-dimensional; LV, left ventricular; RV, right ventricular.

Table 1G-2  Regression Equations Relating Cardiac Dimension and Body Surface Areaa

<table>
<thead>
<tr>
<th>Structure</th>
<th>π</th>
<th>Intercept</th>
<th>Slope</th>
<th>SD</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV inflow</td>
<td>119</td>
<td>1.823</td>
<td>0.4962</td>
<td>0.1086</td>
<td>0.95</td>
</tr>
<tr>
<td>RV outflow</td>
<td>101</td>
<td>1.943</td>
<td>0.6185</td>
<td>0.1009</td>
<td>0.97</td>
</tr>
<tr>
<td>RV area</td>
<td>116</td>
<td>2.795</td>
<td>0.9566</td>
<td>0.1753</td>
<td>0.97</td>
</tr>
<tr>
<td>LV inflow</td>
<td>121</td>
<td>1.893</td>
<td>0.4936</td>
<td>0.09847</td>
<td>0.96</td>
</tr>
<tr>
<td>LV end-diastolic dimension</td>
<td>110</td>
<td>1.392</td>
<td>0.4853</td>
<td>0.08230</td>
<td>0.97</td>
</tr>
<tr>
<td>LV end-systolic dimension</td>
<td>110</td>
<td>0.9209</td>
<td>0.4661</td>
<td>0.1205</td>
<td>0.93</td>
</tr>
<tr>
<td>LV area</td>
<td>120</td>
<td>3.141</td>
<td>1.020</td>
<td>0.1806</td>
<td>0.97</td>
</tr>
<tr>
<td>Interventricular septum</td>
<td>86</td>
<td>0.1978</td>
<td>0.003832</td>
<td>0.1257</td>
<td>0.73</td>
</tr>
<tr>
<td>LV posterior wall</td>
<td>102</td>
<td>0.3131</td>
<td>0.007282</td>
<td>0.1067</td>
<td>0.74</td>
</tr>
<tr>
<td>LV mass</td>
<td>103</td>
<td>4.211</td>
<td>1.288</td>
<td>0.4209</td>
<td>0.89</td>
</tr>
</tbody>
</table>

Modified from Daubeney and colleagues.52

The form of this equation is mean normal value of structure = intercept + slope · height (cm).

The form of this equation is mean normal value of structure = intercept + slope · weight (kg).

Key and footnote a are identical to those for Table 1D-2.

Table 1G-3  Regression Coefficients for Use in Estimating Mean Normal Heart Weight from Body Surface Areaa

<table>
<thead>
<tr>
<th>Source</th>
<th>Intercept</th>
<th>Slope</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kitzman et al. (adults)</td>
<td>5.162</td>
<td>0.8167</td>
<td>0.237</td>
</tr>
<tr>
<td>Females</td>
<td>5.204</td>
<td>0.9471</td>
<td>0.144</td>
</tr>
<tr>
<td>Males</td>
<td>4.748</td>
<td>1.127</td>
<td>0.202</td>
</tr>
<tr>
<td>Scholz et al. (children)</td>
<td>4.806</td>
<td>1.210</td>
<td>0.197</td>
</tr>
<tr>
<td>Females</td>
<td>4.785</td>
<td>1.201</td>
<td>0.1844</td>
</tr>
<tr>
<td>Males</td>
<td>4.806</td>
<td>1.210</td>
<td>0.197</td>
</tr>
</tbody>
</table>

Key: SD, Standard deviation.

\[
\text{Ln(mean normal heart weight, g)} = \text{Intercept} + \text{Slope} \cdot \text{Ln(BSA, m}^2\text{)}
\]

The values are for intercept and slope. The z value equation for heart weight is:

\[
\text{z} = \frac{\text{Ln(observed weight)} - \text{Ln(normal weight)}}{\text{SD}}
\]

where SD is standard deviation.

A study by Chirinos and colleagues reviews the various approaches for allometric scaling of left ventricular mass, with particular attention to the effect of obesity-associated increased heart mass.56
Figure 1G-1  Relation between body size and right and left ventricular dimensions and area, and left ventricular (LV) wall thickness and mass. The expression of body size, height, weight, or body surface area that best correlated with the cardiac measurement is used. Presentation of the figures is in pairs, with the raw data points in the first panel, on which is superimposed the line of regression and confidence limits equivalent to 1 and 2 standard deviations, and z value and body size in the second panel as in Fig. 1D-1. A, Right ventricular (RV) inflow length and body surface area (BSA). B, RV inflow length, relating measured value and BSA to z value.

Continued
Figure 1G-1, cont’d  C, RV outflow length and BSA. D, RV outflow length, relating measured value and BSA to z value.
Figure 1G-1, cont’d  
E, RV area and BSA. F, RV area, relating measured value and BSA to z value.

Continued
Figure 1G-1, cont’d  G, LV inflow length and BSA. H, LV inflow length, relating measured value and BSA to z value.
Figure 1G-1, cont’d  I, LV area and BSA.  J, LV area, relating measured value and BSA to z value.
Figure 1G-1, cont’d  
K, LV end-diastolic dimension and BSA. L, LV end-diastolic dimension, relating measured value and BSA to z value.
Figure 1G-1, cont’d  M, LV end-systolic dimension and BSA. N, LV end-systolic dimension, relating measured value and BSA to z value.

Continued
Figure 1G-1, cont’d  
O, Posterior wall thickness and weight.  
P, Posterior wall thickness, relating measured value and weight to z value.
Figure 1G-1, cont'd  **Q.** Interventricular septum thickness and height.  **R.** Interventricular septum thickness, relating measured value and height to z value.
Figure 1G-1, cont’d  S, LV mass and BSA.  T, LV mass, relating measured value and BSA to z value.
Van Praagh’s symbolic representation may be combined with those of atrioventricular and ventricular arterial connections as shown in Figures 1H-1 through 1H-3. In Van Praagh’s convention, the first letter (S or I) refers to atrial position (solitus or inversus), the second letter (D or L) to ventricular loop, and the third letter to position of the origin of the aorta (recognized by its two coronary ostia) in relation to origin of the pulmonary trunk. Arrangement of boxes and abbreviations is identical in all similar models presented.

**REFERENCES**


B


C


D


E

F


G


H


K


Cardiac arrhythmias in the neonate, infant, and child. East Norwalk, Conn: Appleton & Lange, 1977, p. 29.


M


N


O


P


Y

Z
Hypothermia, Circulatory Arrest, and Cardiopulmonary Bypass

Section I: Hypothermic Circulatory Arrest

Historical Note

Hypotheses

Oxygen Consumption during Hypothermia

Relationship between oxygen consumption and body temperature

Total body oxygen consumption after surface cooling

Oxygen consumption during hypothermia in tissue slices and isolated organs

Other Phenomena during Hypothermia and Circulatory Arrest

No-reflow phenomenon

Changes in plasma volume

Damaging Effects of Circulatory Arrest during Hypothermia

Brain function and structure: risk factors

For damage

Temperature and duration

Characteristics of the cooling process

Cerebral blood flow during cooling and rewarming

Biochemical milieu

Electroencephalogram before arrest

Patient age

Effects of brain damage

Evidence of gross neurologic damage

Postoperative intellectual capacity

Spinal cord function

Renal function and structure

Experimental studies

Studies in humans

Liver function

Safe Duration of Circulatory Arrest

Section II: Whole-Body Perfusion during Cardiopulmonary Bypass

Historical Note

Uniqueness of Cardiopulmonary Bypass

Controlled Variables

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Venous input from the patient

Vacuum-assisted venous return

Siphon (gravity) drainage

Venous pumping

Gas exchange

Arterial oxygen levels

Arterial carbon dioxide pressure

Heparin levels

PERFUSATE

Diluent

Hemoglobin concentration

Albumin concentration

Other additives

Changes during cardiopulmonary bypass

Total systemic blood flow

Arterial pressure waveform

Systemic venous pressure

Pulmonary venous pressure

Temperature

Response variables

Whole-body (non-specific) inflammatory response

Response to use of a pump-oxygenator

Humoral response

Cellular response

Metabolic response

Details of the whole-body inflammatory response

Neutrophil activation

Platelet response

Complement activation

Kallikrein-bradykinin activation

Coagulation cascade

Fibrinolytic cascade

Arachidonic acid cascade

Cytokines

Other mediators of inflammation

Protein denaturation

Oxygen consumption

Total body oxygen consumption

Cerebral oxygen consumption

Mixed venous oxygen levels

Metabolic acid-base status

Hemolysis

Systemic vascular resistance and arterial blood pressure

Distribution of blood flow

Cerebral blood flow

Cutaneous blood flow

Venous tone

Catecholamine response

Adrenal cortical hormones

Vasopressin

Body composition

Thermal balance

Agents of damage

Foreign surfaces

Shear stresses
Section I  Hypothermic Circulatory Arrest

HISTORICAL NOTE

In 1950, Bigelow and colleagues, in their publications on experimental hypothermia produced by surface cooling, introduced the concept that whole-body hypothermia might be useful in cardiac surgery. They subsequently reported cooling dogs to 20°C by surface cooling, with recovery after 15 minutes of circulatory arrest. In 1951, Boerema and colleagues reported experimental studies indicating that when animals were cooled by a femoral-femoral shunt through a cooling coil, up to 15 minutes of circulatory arrest (produced by inflow stasis) were tolerated without apparent ill effect. Using surface cooling, Lewis and Taufic reported successful repair of an atrial septal defect in a 5-year-old girl in 1953, and in the same year, Swan and colleagues reported successful results in a series of patients treated using the same technique. In 1958, Sealy and colleagues reported successful clinical cases in which hypothermia was combined with cardiopulmonary bypass (CPB). In 1959, Drew and colleagues reported experimental studies in which CPB (using the subject’s own lungs as the oxygenator) was used to cool and rewarm the subject, and operations were done during circulatory arrest at 15°C. In 1960, Guiot and colleagues and Weiss and colleagues reported use of hypothermia and circulatory arrest for cardiac surgery in humans. In 1961, Kirklin and colleagues at Mayo Clinic reported results of operation with hypothermic
tem perature is substantially lower than nasopharyngeal hypothermia is produced by surface cooling, internal tem perature of the organism during the arrest period. Conveniently, according to this equation, the reaction rate increases by two to three times for an increase in temperature of 10°C. Chemists use the symbol Q10 for this multiple.

At physiologic temperatures, biochemical systems operate only on the upswing of the curve. Thus—particularly when the range of temperatures is relatively small—this relationship finds numeric expression in the van’t Hoff law, which relates the logarithm of a chemical reaction rate directly to temperature. Conveniently, according to this equation, the reaction rate increases by two to three times for an increase in temperature of 10°C. Chemists use the symbol $Q_{10}$ for this multiple.

Because oxygen uptake is the expression of all oxidative reactions, both direct and indirect, the logarithm of $V_{O_2}$ might be expected to be directly proportional to temperature. In general, this appears to be so. Whether the observed decline in $V_{O_2}$ during clinical hypothermia can be accounted for entirely on this physicochemical basis is doubtful, however (see “Oxygen Consumption during Hypothermia in Tissue Slices and Isolated Organs” later in this section).
Box 2-1  Kinetics of Oxygen Consumption

The relationship of oxygen consumption \( (V_{O_2}) \) to perfusion flow rate \( (Q) \) and temperature \( (T) \) is not linear; that is, a unit increase in \( Q \) or \( T \) does not increment \( V_{O_2} \) a constant amount. A number of formal mathematical models (see Box 6-5 in Chapter 6) have been proposed that relate, in particular, metabolic activity and \( T \) based on fundamental thermodynamics. These models provide a good starting point for examining \( V_{O_2} \) data for other empirical relations, such as with blood flow.

**Arrhenius Equation**
The Arrhenius equation relates reaction rate \( k \) to temperature \( T \), the universal gas constant \( R \), activation energy \( E_a \), and a constant related to molecular collision as:

\[
k = A e^{\frac{E_a}{RT}}
\]

where \( e \) is the base of the natural logarithms. If logarithms are taken of both sides of this equation, one obtains the following:

\[
\ln[k] = \ln[A] - \frac{E_a}{RT}
\]

Constants \( A \), \( R \), and \( E_a \) are coalesced \((a, b)\) to obtain a log-inverse equation:

\[
\ln[k] = a - \frac{b}{T}
\]

Therefore, one can examine the correlation of the logarithm of oxygen consumption and inverse temperature to see if the data are consistent with this relation.

**van’t Hoff Law \((Q_{10})\)**
Another relation is expressed in the van’t Hoff law, which is generally formulated in terms of change in metabolic rate \( (k) \) per 10°C change in temperature \( (Q_{10}) \):

\[
Q_{10} = \left( \frac{k_1}{k_2} \right)^{\frac{10}{T_1 - T_2}}
\]

If \( T_1 - T_2 = 10^\circ \), then \( Q_{10} \) is simply the ratio of \( k_1 \) to \( k_2 \) (metabolic rates at each temperature). This relation can be derived from the parameter \( b \) in the Arrhenius equation.

**Hyperbolic Equation**
Metabolic rate (reflected in \( V_{O_2} \)) and \( Q \) should be independent until blood flow becomes limiting. This suggests a hyperbolic relation between the two variables:

\[
\frac{1}{V_{O_2}} = \frac{1}{c + \frac{d}{Q}}
\]

where \( c \) is the asymptotic (limit of \( V_{O_2} \) value of \( V_{O_2} \) as \( Q \) becomes large (metabolic rate independent of flow).

**Empirical Relations**
Actual data may be better characterized by (1) a linear relation (rare), (2) a log-linear (exponential) relation, (3) a log-log relation, (4) an inverse-log relation, or a more complex relation. Many of these models can be fitted to data using linear regression (see Box 6-5 in Chapter 6) by logarithmic or inverse transformations of scale. Others require iterative nonlinear optimization methods to obtain parametric estimates (see Box 6-14 in Chapter 6).

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**Total Body Oxygen Consumption after Surface Cooling**

When hypothermia is induced by cooling the surface of anesthetized humans or experimental animals, cooling is rather uniform throughout the body, and temperatures of internal organs and regions differ by less than 2°C.\(^{C18}\) Therefore, values for whole-body \( V_{O_2} \) at various body temperatures are probably useful, and the relative magnitude of reduction can be assumed to be similar throughout the body.

Good data in this area are available from the animal experiments of Bigelow and colleagues, Ross, and Penrod.\(^{R31,R12,R22}\) Data for surface cooling in humans are sparse, although Harris estimated \( Q_{10} \) to lie between 1.9 and 4.2 in 10 surface-cooled infants.\(^{H17}\) The experimental data were reanalyzed using (1) a linear equation, (2) the Arrhenius equation, and (3) the van’t Hoff law. The van’t Hoff law best fits this combined set of data (Fig. 2-1) and is considered the most appropriate model for this purpose.\(^{R31,R12,R22}\) This model also best fits the relation between temperature and cerebral oxygen consumption during CPB in humans.\(^{C37}\)

Kent and Peirce studied \( V_{O_2} \) in experimental animals during hypothermia produced by combined surface and core cooling.\(^{K4}\) Their data are similar to those obtained from surface cooling alone.

**Oxygen Consumption during Hypothermia in Tissue Slices and Isolated Organs**

Data from the studies described could lead to an underestimation of true oxygen demand, because only areas in which perfusion of the microcirculation continues can participate in oxygen consumption (tissue and cellular stores of oxygen being trivial). In theory at least, a considerable part of the reduction in oxygen consumption from surface cooling could be from shutting down the microcirculation of portions of the body or from arteriovenous shunting. New technologies, particularly magnetic resonance imaging (MRI), may resolve some of these questions.\(^{N14,S7}\)

Studies of tissue slices at various temperatures show that oxygen consumption is in fact reduced by hypothermia.\(^{F12,F29,F31}\) These studies and those of isolated organs suggest that \( Q_{10} \), although differing from tissue to tissue, is on average about 2 (for references and a table of \( Q_{10} \) values, see Harris and colleagues).\(^{H18}\) Measurement of human whole-body \( V_{O_2} \) before and after heating, rather than cooling, indicates a \( Q_{10} \) in this range (=1.9).\(^{S11}\) Vasodilatation caused by heating presumably ensures access of oxygen to the tissues, and this \( Q_{10} \) probably represents true tissue oxygen requirement. A \( Q_{10} \) greater than 1.9 associated with cooling may therefore indicate that oxygen delivery has been compromised by inadequate flow rate. Fuhrman and colleagues have spent many years investigating this possibility. They showed that, in general, there was a close agreement between resting \( V_{O_2} \) at 37°C and tissue slice respiration.\(^{F31,M9}\) However, rats cooled by immersion to 18°C exhibited a 33% lower \( V_{O_2} \) than would be expected from studies of tissue slice respiration at this temperature.\(^{F12}\) The discrepancy was not accounted for either by inhomogeneities in whole-body temperature or by known changes in \( Q_{10} \) exhibited by some tissues (in part related to altered function at reduced temperatures). The precise mechanism remains unknown. It could be due to arteriovenous shunting or to shutting down of perfusion to
species differences in tissue respiration, suboptimal conditions for tissue respiration in the studies with tissue slices, or increased \( \text{VO}_2 \) during whole-body perfusion caused, for example, by catecholamine release.

A striking and important fact from whole-body, tissue, and organ studies is that \( \text{VO}_2 \) is not reduced to near zero at temperatures close to 0°C. Metabolic activity is therefore continuing, and the time limits of safe circulatory arrest must be finite. Furthermore, this continuing metabolic activity causes a tendency for organs and systems to rewarm during some areas of the body. Microvascular physiologists have referred to the latter as a decrease in effective capillary density. This may result not only from reduced cardiac output and vasoconstriction but also from changes in blood viscosity, geometry, and compliance of red blood cells, plasma “skimming,” and clumping of formed blood elements.

Some studies of tissue slices and isolated perfused organs show a relative reduction of oxygen consumption at any degree of hypothermia that is greater than in those of the body as a whole (Table 2-1). This may be related to known

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**Figure 2-1** Temperature and oxygen consumption. (Note reversal of temperature scale from normothermia on the left to hypothermia on the right.) A, Figure contains two depictions. One is a group of symbols representing data points relating measured whole-body oxygen consumption (\( \text{VO}_2 \)) to body temperature in dogs made hypothermic by surface cooling. (Crosses are data points from Ross; circles from Bigelow and colleagues; squares from Penrod.) From these, a regression equation, the second depiction, was derived, showing the van’t Hoff relation between \( \text{VO}_2 \) and temperature (Appendix Equation 2A-1). Solid line (representing the point estimates) and dashed lines (70% confidence band) are nomograms of the equation. Slope indicates a \( Q_{10} \) of 2.7. B, Nomogram of the same equation, with oxygen consumption expressed as percentage of control value at 37°C.
the arrest period. Donald and Kerr showed in dog brains cooled to 1°C to 2°C that an increase in temperature occurred during a 30-minute period of circulatory arrest and that this was in part related to the gradient between brain and room temperature and in part to continuing metabolic activity in the brain.

**OTHER PHENOMENA DURING HYPOTERMIA AND CIRCULATORY ARREST**

**No-Reflow Phenomenon**

It is only a hypothesis that a numeric relationship exists between V\textsubscript{O\textsubscript{2}} and safe circulatory arrest time at any given temperature. In fact, existence of a necessary and close relationship between the two over a wide range of temperatures would be surprising in view of other phenomena that occur during circulatory arrest. One of these is regional vascular occlusion in the brain and probably in all organs and tissues, leading to the no-reflow phenomenon. This is an obstructive lesion of the microcirculation that prevents local reperfusion and leads to additional damage after the general circulation of blood has been reestablished.

The no-reflow phenomenon could theoretically damage the brain after hypothermic circulatory arrest. However, Norwood and colleagues have shown experimentally that this phenomenon develops as a result of severe hypoxia or anoxia, not because of circulatory arrest per se. They have also shown that hypothermia to 20°C prevents the no-reflow phenomenon from 90 minutes of anoxia produced by continuing perfusion at an arterial Pa\textsubscript{O\textsubscript{2}} of about 10 mmHg. Thus, this phenomenon may represent, at least in part, hypoxic endothelial cell injury, with altered expression of endothelial relaxing and constricting factors. In experimental studies, hypoxia followed by reoxygenation results in an almost twofold increase in release by endothelial cells of endothelin-1, the most powerful vasoconstrictor yet identified. Other experimental studies have shown that this response can be blunted when ischemia is induced under hypothermic conditions, so hypoxia may promote a procoagulant response in endothelial cells that can result in intravascular microthrombosis. Edema, as well as neutrophil and platelet plugging, may also contribute to the impaired perfusion that occurs following ischemia, despite what appears to be adequate restoration of blood flow.

**Changes in Plasma Volume**

Chen and colleagues demonstrated progressive hemoconcentration and decrease in plasma volume during surface cooling of infants to 25°C, an observation supporting their own and previous experimental studies. This may represent sequestration of plasma in portions of the vascular bed and plasma leakage into the interstitial fluid compartment.

**DAMAGING EFFECTS OF CIRCULATORY ARREST DURING HYPOTERMIA**

It is generally agreed that the brain has the shortest safe circulatory arrest time of any organ or region of the body, although occasionally the kidney seems to be damaged by a period of circulatory arrest when the brain is not. Although other organs and regions can be severely damaged by long periods of circulatory arrest, their safe arrest times are generally longer than that of the brain.

**Brain Function and Structure: Risk Factors for Damage**

The possibly damaging effects of circulatory arrest on the brain, as well as the risk factors related to it in patients undergoing cardiac operations during hypothermic circulatory arrest, are incompletely understood. The conduct of cooling and rewarming by CPB and the damaging effects of CPB itself likely contribute to or interact with the injury produced by circulatory arrest per se.

Duration of total arrest of cerebral blood flow is clearly a determinant of the amount of brain damage, but the safe duration of circulatory arrest to the brain (the duration within which irreversible structural or functional damage does not occur) is affected by a few known risk factors and no doubt by other risk factors that are as yet poorly understood. Furthermore, in patients undergoing cardiac surgery, brain damage that occurs in the setting of hypothermic circulatory arrest is rarely diffuse. In adults, it is usually manifested by specific intellectual or motor deficits, whereas in neonates, infants, and small children it is more likely to be manifested by seizures or choreoathetoid movements. This may be related to the phenomenon of selective neuronal vulnerability, a heightened sensitivity of specific neuron groups to ischemic injury. This sensitivity has been correlated with the concentration of specific membrane receptors whose density in

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**Table 2-1 Oxygen Consumption (V\textsubscript{O\textsubscript{2}})**

<table>
<thead>
<tr>
<th>Tissue Slices (Rats)(^a)</th>
<th>Isolated In Situ Organs (Dogs)(^b) (Cooling Coil Shunt)</th>
<th>Isolated In Situ Organs (Dogs)(^c) (Surface Cooling)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organ</td>
<td>(37^\circ\mathrm{C})</td>
<td>(25^\circ\mathrm{C})</td>
</tr>
<tr>
<td>Brain</td>
<td>1.98 ± 0.31</td>
<td>0.73 ± 0.139</td>
</tr>
<tr>
<td>Kidney</td>
<td>3.87(^a)</td>
<td>1.63(^a)</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.76</td>
<td>0.36</td>
</tr>
</tbody>
</table>

\(^a\)Expressed as mL · h\(^{-1}\) · g\(^{-1}\) wet weight ± SD. Data have been rearranged and recalculated to allow comparisons.

\(^b\)Data from Fuhrman.\(^20\)

\(^c\)Data from Rosomoff and Holaday.\(^21\)

\(^d\)Kidney cortex.

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\(\overline{\text{V}}\text{O}_2\)
specific areas varies with age. Concentration of these receptors is transiently high in the basal ganglia in the neonatal period, which may relate to the appearance of choreoathetosis as a result of ischemic injury in the very young.

Risk factors for irreversible structural and functional brain damage from circulatory arrest, in addition to duration of the arrest, include mean and regional brain temperature during circulatory arrest, rate of cooling and rewarmin, cerebral blood flow and distribution during cooling, arterial blood pressure during cooling and reperfusion, electrical activity before arrest, biochemical milieu and catecholamine levels during cooling and circulatory arrest, absence of pharmacologic interventions before and after cessation of cerebral blood flow, and total management of reperfusion.

Temperature and Duration
Most clinical studies of the relationship of temperature to safety of a given circulatory arrest time are flawed by lack of information about the temperature of the brain itself and by the variety of sites of measurement of temperature ( tympanic membrane, nasopharynx, rectum, midesophagus, bladder, extremity skin) used to estimate safety. There is little consistent correlation between some of these sites, although temperature of the tympanic membrane and nasopharynx most closely resembles mean temperature of the brain. For this reason, these sites should be used whenever possible.

Animal experiments and clinical experiences indicate that when the brain is cooled to 15°C to 20°C, circulatory arrest of 30 minutes or less is tolerated without development of evident structural or functional damage. During such a period, adenosine triphosphate (ATP) concentrations decline to 35% of initial values but return rapidly to normal during reperfusion. Evidence that circulatory arrest of 45 minutes at these temperatures is safe is less secure.

Considerable information supports the inference that circulatory arrest of 60 minutes or more at temperatures of 15°C to 18°C is associated with irreversible structural or functional damage, although it may be tolerated without evident damage by some subjects under some circumstances. In experimental studies by Folkerth and colleagues and Fisk and colleagues, histologic evidence of anoxic brain damage was found in all animals subjected to hypothermic circulatory arrest for 45 to 60 minutes, although some animals survived without evident functional abnormality. Half (2 of 4) of the animals studied by Kramer and colleagues showed no recovery of ATP when subjected to 60 minutes of hypothermic circulatory arrest.

Some clinical studies have found few problems associated with 60 minutes or more of hypothermic circulatory arrest. Particularly striking is the experience of Coselli and colleagues, who found no clinical evidence of brain damage attributed to hypothermic circulatory arrest (mean nasopharyngeal temperature 16.9°C; range, 10.1°C-24.1°C) in 56 patients with arrest times ranging from 14 to 109 minutes (median 36 minutes). Comprehensive neuropsychometric studies were not undertaken. Hemiparesis or hemiplegia attributed to cerebral edema developed in 3 of 51 surviving patients (6%; CL 3%-11%). In contrast, Gega and colleagues, in a subsequent study of 394 patients undergoing aortic arch replacement, reported 8 strokes (13%; CL 8.6%-18%) among 61 patients in whom the duration of hypothermic circulatory arrest exceeded 40 minutes. Only 10 strokes (3.3%; CL 2.3%-4.3%) occurred among the remaining 333 patients with shorter intervals of circulatory arrest.

Temporary neurologic dysfunction (postoperative confusion, agitation, delirium, obtundation, or transient parkinsonism without localizing signs) can occur in up to 20% of survivors of operations on the thoracic aorta in which hypothermic circulatory arrest is used. Incremental risk factors associated with developing this complication are duration of hypothermic circulatory arrest and increasing patient age. Prevalence of temporary neurologic dysfunction increases substantially among patients in whom duration of circulatory arrest exceeds 60 minutes (Fig. 2-2). Although postoperative delirium is not permanent, it can be an important complication. Among a group of patients undergoing pulmonary thromboendarterectomy, circulatory arrest times of greater than 50 minutes were a powerful risk factor for its occurrence.

Some evidence supports the concept that continuous perfusion of the brain for 60 or more minutes at low temperature also produces neurolologic sequelae in a few patients (see “Evidence of Gross Neurologic Damage”). However, cold (10°C-15°C) continuous perfusion of brains already at 15°C resulted in no intellectual or other deficit in trained rhesus monkeys.

Characteristics of the Cooling Process
Uneven cooling of the brain is probably a risk factor for brain damage, although evidence is largely indirect. Almond and colleagues conducted experiments in dogs undergoing hypothermic circulatory arrest for 30 minutes. Results were interpreted to indicate structural and functional brain damage when cooling by CPB was done with the perfusate 20°C colder than the patient. These investigators believed that this did not occur when the blood was only 4°C to 6°C cooler than the subject. However, the damage might have been related to the short period of cooling required with the very cold blood, producing uneven brain cooling, as suggested by the work of Zingg and Kantor. The longer period of cooling required with the blood only 4°C to 6°C colder than the subject probably produced more uniform cooling. In their patients, Stewart and colleagues noted a considerably higher
prevalence of major neurologic events after circulatory arrest when core cooling by CPB alone was used, compared with surface cooling first to 28°C, followed by core cooling (Table 2-2). A reasonable presumption is that the more rapid core cooling resulted in uneven cooling of the brain. In another study in neonates and infants, rapid core cooling was associated with more evidence of neurologic deficits after hypothermic circulatory arrest than more prolonged core cooling. Again, a reasonable presumption is that prolonged core cooling results in more uniform cooling of the brain.

Cerebral Blood Flow during Cooling and Rewarming

The relationship of cerebral blood flow during cooling (before establishing hypothermic circulatory arrest) to safety of the arrest period has received little investigation. The earlier literature suggested that reduced arterial blood pressure during CPB without circulatory arrest contributes to postoperative neurologic dysfunction, presumably because the hypotension resulted in reduced cerebral blood flow but this possibility now appears less certain (see “Cerebral Blood Flow” under Distribution of Blood Flow in Section II).

More recently, when cerebral blood flow was measured during operations involving hypothermic circulatory arrest in children, Grecley and colleagues observed that patients with increased oxygen extraction before circulatory arrest may be particularly vulnerable to cerebral injury. In a subsequent study, they demonstrated that during cooling, a parallel reduction in cerebral oxygen consumption and cerebral blood flow occurred. However, in three of four patients who were subsequently found to have sustained neurologic injury, oxygen extraction before the period of circulatory arrest was increased, suggesting that cerebral blood flow during this period was inadequate to sustain metabolic requirements. Other studies in children have confirmed the observation that cerebral blood flow generally decreases with temperature during cooling, and that coupling with cerebral metabolism is maintained even at low temperatures when ventilation is managed according to the alpha-stat strategy.

Information is available about the magnitude and effect of cerebral blood flow during rewarming. Experimental studies have found that cerebral blood flow is reduced during rewarming after circulatory arrest (Fig. 2-3). With or without circulatory arrest, this phenomenon occurs in humans during cardiac surgery and may affect outcome. In infants, cerebral blood flow is reduced during rewarming immediately after hypothermic circulatory arrest and after achieving normothermia. Based on measurements of jugular venous oxygen saturation, oxygen delivery appears to be adequate during this period of reduced flow. In a study of 255 adult patients undergoing elective coronary artery bypass grafting (CABG) with or without associated cardiac valve replacement, Croughwell and colleagues observed a decline in postoperative cognitive function in 38%. The severity of decline was related to greater arteriovenous oxygen content difference between radial artery and jugular venous blood (CavO2) during rewarming. This increase in oxygen extraction was associated with a low jugular venous oxygen saturation and low cerebral blood flow.

Biochemical Milieu

Only incomplete information is available in the area of biochemical milieu. It is uncertain whether some variables are actual risk factors or surrogates for the real risk factor. Arterial blood pH and PCO2 during cooling may have important direct effects on brain tissue at the beginning of the period of circulatory arrest, and thereby on outcome, but they also influence cerebral blood flow, and perhaps its distribution, during cooling (see Controlled Variables in Section II). Any effect they may have on neurologic outcome, which is uncertain, could be through either mechanism.

Brunberg and colleagues and Anderson and colleagues suggested that increased tissue glucose, such as is usually present at the beginning of the arrest period, may lead to excessive glycolysis and acidosis during the arrest period, possibly resulting in tissue damage from lactic acid accumulation. This possibility makes it imprudent to

### Table 2-2 Major Neurologic Events after Hypothermic Circulatory Arrest

<table>
<thead>
<tr>
<th>Method</th>
<th>No. of Patients</th>
<th>Circulatory Arrest (min)</th>
<th>No.</th>
<th>%</th>
<th>CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface cooling to 28°C, then core cooling</td>
<td>80</td>
<td>42.5 ± 13.6</td>
<td>0</td>
<td>0</td>
<td>0-2</td>
</tr>
<tr>
<td>Core cooling only</td>
<td>138</td>
<td>42.8 ± 15.4</td>
<td>8</td>
<td>6</td>
<td>4-9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>218</strong></td>
<td></td>
<td><strong>8</strong></td>
<td><strong>6</strong></td>
<td><strong>4-9</strong></td>
</tr>
</tbody>
</table>

Data from Stewart and colleagues.511

*Excludes seizures followed by uneventful convalescence.

*Repair of ventricular septal defect, tetralogy of Fallot, transposition of the great arteries, and atrioventricular septal defects. Mean temperature ± standard deviation during arrest for both groups was 19.7 ± 1.7°C.

![Figure 2-3 Cerebral blood flow (mL · 100 g⁻¹ · min⁻¹) in gerbils after induction of and recovery from hypothermia by surface cooling. Along the horizontal axis is rectal temperature. Break between 37°C and 18°C represents 48 minutes of circulatory arrest (total bilateral carotid artery occlusion) at 18°C (arrest group) or continuing hypothermic perfusion (no arrest group). Note that cerebral blood flow was lower during rewarming in those animals that had total cessation of cerebral blood flow for 48 minutes. (From Kirklin.110)*
use glucose solutions for priming the pump-oxygenator and for intravenous infusion when a period of circulatory arrest is contemplated.

Based on the work of Choi and of Olney and colleagues, evidence has accumulated indicating that the neuroexcitatory amino acids—particularly glutamate, the major transmitter mediating synaptic excitation in the mammalian central nervous system—have potent neurotoxic activity during conditions of depleted cellular energy (e.g., hypoxia, ischemia) when the synaptic reuptake of these amino acids, a highly energy-dependent process, is compromised.\textsuperscript{17,66} Resulting overaccumulation of glutamate leads to excessive excitation of the glutamate receptors, leading to an increase in intracellular calcium and eventual neuronal cell injury and death. This process has been observed in experimental animals after 2 hours of circulatory arrest.\textsuperscript{85} Neuronal necrosis is selective and corresponds closely to distribution of excitatory amino acid receptors.\textsuperscript{84} The hippocampus, cerebellum, and basal ganglia, which have high concentrations of glutamate receptors, are characteristically most vulnerable to this injury, implying excitation as an underlying mechanism.\textsuperscript{84,85}

Apoptosis, or programmed cell death, has been demonstrated experimentally in the neocortex of piglets following hypothermic circulatory arrest for 90 minutes at 19°C.\textsuperscript{13,14} Damaged neurons were observed between 8 and 72 hours after reperfusion. Caspase 3 and caspase 8, the principal cysteine proteases involved in apoptosis, were substantially elevated in these animals compared to control animals (no CPB or CPB without circulatory arrest). ATP levels were similar to those of control animals. Glutamate excitotoxicity secondary to hypothermic circulatory arrest has been shown to mediate neuronal apoptosis as well as necrosis.\textsuperscript{79}

Fessatidis and colleagues' experimental studies using histopathologic techniques demonstrated that the cerebellum is the most vulnerable area of the brain to prolonged periods (>70 minutes) of hypothermic (15°C) circulatory arrest.\textsuperscript{10,11}

Electroencephalogram Before Arrest

Electroencephalographic (EEG) criteria for safe circulatory arrest are conflicting. In a study by Coselli and colleagues, the longest recorded durations of safe circulatory arrest in adults were in situations in which a full formal EEG had recorded \textit{electrocerebral silence} (no electrical activity of cerebral origin at maximal gain, 2 \textmu V \cdot mm\textsuperscript{-1}) for 3 minutes before the arrest.\textsuperscript{30} Mean nasopharyngeal temperature at this point was 16.9°C (range, 10.1°C-23.1°C).

In a subsequent study by Stecker and colleagues of 109 adult patients undergoing hypothermic circulatory arrest, electrocerebral silence was achieved at a mean nasopharyngeal temperature of 17.8°C (range, 12.5°C-27.2°C).\textsuperscript{28} Using a standardized protocol, this required cooling for a mean of 27.5 minutes (range, 12-50 minutes). Distinctions of times to cool to various EEG events are shown in Fig. 2-4. The time to cool to electrocerebral silence was prolonged by high hemoglobin concentration, low arterial partial pressure of carbon dioxide, and slow cooling rates. Only 60% of patients demonstrated electrocerebral silence by either a nasopharyngeal temperature of 18°C or a cooling time of 30 minutes. Although cooling to an end point such as electrocerebral silence provides a more reproducible effect of hypothermia on the nervous system than cooling to a specific temperature (e.g., 12.5°C, which was sufficient to produce electrocerebral silence in all patients in this study), the optimal temperature for circulatory arrest could not be determined.\textsuperscript{28}

Others have found that in infants and children cooled to a nasopharyngeal temperature of 18.5°C, the EEG was characterized by continuous phasic activity.\textsuperscript{28,13,10,11} During cooling, however, there was a gradual disappearance of fast components and an increase in slow components. Occasionally, repetitive rapid discharges occurred. Such reports indicate that when circulatory arrest is established, electrocerebral silence develops after an interval that is inversely related to nasopharyngeal temperature at the beginning of the arrest period.\textsuperscript{10,11} However, Reilly and colleagues reported persistent EEG activity during circulatory arrest, perhaps reflecting activity in the white matter and cerebellum.\textsuperscript{11} This is of interest because of the occasional postoperative occurrence of choreoathetoid movements in humans and high-stepping gaits in experimental animals. These abnormalities may be due in part to uneven brain cooling secondary to regional differences in flow.

When CPB is resumed after circulatory arrest in infants, EEG activity is absent initially and then gradually returns as rewarming proceeds.\textsuperscript{25} In general, after 20 to 30 minutes of rewarming, the EEG has returned approximately to its control condition.\textsuperscript{25} This latent period between resumption of whole-body perfusion for rewarming and time of return of reasonably normal EEG activity is believed by Weiss and colleagues to be related to the important metabolic (oxygen) debt that develops during the arrest period.\textsuperscript{11} This in turn is influenced by brain temperature during arrest and by duration of the arrest. They observed that when circulatory arrest lasted less than 40 minutes, EEG activity always reappeared within less than 20 minutes, whereas longer periods of circulatory arrest were followed by longer and more varied latent periods.\textsuperscript{11}

In adults, Stecker and colleagues observed that lower nasopharyngeal temperatures at the time of circulatory arrest resulted in a slower return to continuous activity.\textsuperscript{29} Prolonged time to recovery of continuous EEG activity and higher temperature at which the EEG first became continuous were associated with increased risk of neurologic injury. Patients who sustained postoperative neurologic injury also had a longer period of circulatory arrest (52 ± 21 minutes) than patients who did not (37 ± 12 minutes) (\textit{P} = .006).

\textbf{Patient Age}

Although it has been stated that very young patients suffer less brain damage than older patients from hypothermic circulatory arrest, there is little factual support for this concept. Relative to the general population, cognitive, language, and motor performances are importantly reduced at age 4 years in infants younger than 3 months in whom circulatory arrest has been used.\textsuperscript{14} In a randomized trial of 171 neonates with D-transposition of the great arteries who had open repair using either hypothermic circulatory arrest or low-flow CPB, the circulatory arrest group at age 4 years had lower motor scores and more speech abnormalities (\textit{P} = .03). They also performed worse on tests of fine motor and visuospatial skills.\textsuperscript{14} At 8 years, the circulatory arrest group performed worse on tests of motor function (\textit{P} = .003), speech apraxia (\textit{P} = .01), visual motor tracking (\textit{P} = .01), and phonologic awareness (\textit{P} = .0003) than children in whom low-flow CPB was used.\textsuperscript{12} In adults in whom circulatory arrest is used, increasing age is an important predictor of both stroke and
Temporary neurologic dysfunction is a marker for long-term functional neurologic deficit.\textsuperscript{E14,E15}

**Effects of Brain Damage**

**Choreoathetosis** has occurred early postoperatively in infants and children undergoing hypothermic circulatory arrest.\textsuperscript{B20,B58,C21,S31} When it occurs, it usually develops 2 to 6 days postoperatively. As time passes, the movements usually lessen in severity. If mild, they disappear completely, but if severe, they or hypotonia may persist. Brunberg and colleagues found no correlation between circulatory arrest time or depth of cooling (between 16°C and 20°C) and development of choreoathetosis.\textsuperscript{B58} These reports suggest that this specific complication occurs in 1\% to 12\% of patients and that its residual effects are permanent in some. When choreoathetosis occurs, it is often in the setting of prolonged circulatory arrest.\textsuperscript{S31}

Choreoathetosis has been observed in infants and children subjected to hypothermic CPB without circulatory arrest.\textsuperscript{D8}

**Figure 2-4** Distribution of nasopharyngeal temperatures at which various electroencephalogram (EEG) landmarks occur. A, Appearance of periodic complexes. B, Appearance of burst suppression. C, Electrocerebral silence. Examples of typical EEG patterns during cooling are also shown: D, Precooling. E, Appearance of periodic complexes. F, Appearance of burst suppression. G, Electrocerebral silence. Each of the EEG samples represents four channels recorded from the left hemisphere. (From Stecker and colleagues.\textsuperscript{S28})

**Figure 2-5** Relationship of interval (seconds) from beginning of circulatory arrest to appearance of electroencephalographic quiescence, and nasopharyngeal temperature at time of circulatory arrest. (Note reversal of temperature scale.) (Redrawn from Harden and colleagues.\textsuperscript{H13})
There are suggestions that this complication can result from perfusion of the brain with very cold blood for a prolonged period at relatively high flows.18,20 This is the basis for the recommendation that arterial temperature not be reduced to less than 15°C.

The cause of choreoathetosis is unclear. Deep hypothermia per se may cause neurologic injury. Egerton and colleagues reported that continuous hypothermic perfusion at 10°C to 12°C produced moderate or severe brain damage, including choreoathetosis, in 10 of 16 patients (63%; CL 46%-77%).19 Air or particulate embolization to the brain may be a contributing factor. When circulatory arrest is used, choreoathetosis may be related to uneven brain cooling, leading to continued metabolic activity in the white matter and cerebellum (as reported by Reilly and colleagues21), and possibly to uneven brain reperfusion related to vascular changes associated with the no-reflow phenomenon. The latter finding lends support to the rationale for using hemodilution during cooling, because absence of red cells in the perfusion used just before circulatory arrest to the brain eliminates the no-reflow phenomenon.22 Use of the alpha-stat strategy of acid-base balance has also been implicated as a causative factor.18

Seizures have occurred in the early postoperative period in 5% to 10% of patients undergoing hypothermic circulatory arrest.23,24,25,26,27 Because seizures are usually transient and followed by uneventful convalescence, they have not been considered major neurologic events. However, in an analysis from the Boston Circulatory Arrest Study involving 171 children with D-transposition of the great arteries, transient postoperative clinical and EEG seizures were associated with worse neurodevelopmental outcomes at ages 1 and 2.5 years, as well as neurologic and MRI-detected abnormalities at age 1 year.28 At age 4 years, occurrence of perioperative seizures was associated with lower IQ scores \( (P = .01) \) and increased risk of neurologic abnormalities (odds ratio 8.4, \( P = .05)\).29

In a more recent prospective study of 178 neonates and infants less than age 6 months undergoing CPB with or without hypothermic circulatory arrest for a variety of congenital heart defects, including hypoplastic left heart syndrome and other forms of single ventricle, EEG-recorded seizures occurred in 20 patients (11.2%, CL 8.8%-14.2%).30 Patients with duration of circulatory arrest of more than 40 minutes had more seizures (14 of 58, 24%; CL 18%-31%) than those with a duration of 40 minutes or less (4 of 59, 6.8%; CL 3.5%-12%; \( P = .04 \)). Occurrence of seizures among patients with a duration of circulatory arrest of 40 minutes or less was similar among those in whom circulatory arrest was not used \( (P = .58)\).

The comments concerning possible causes of choreoathetosis are applicable to seizures. However, it is well known that infants are highly susceptible to seizures from other causes, such as disturbances of thermoregulation and fluid balance, as well as from metabolic disorders, especially those related to glucose and calcium, and many of these factors may be operative in these patients.

Severe gross evidence of brain damage occurs uncommonly after hypothermic circulatory arrest in infants and children, including coma either dating from surgery or developing some hours later, followed by lasting impairment or death. In a study by Stewart and colleagues, 3 (1.4%; CL 0.6%-2.7%) such instances occurred among 218 young patients undergoing repair of the common types of congenital heart disease with hypothermic circulatory arrest; 5 other patients developed choreoathetosis.31 All these events occurred in the group of patients in whom core cooling alone was used. None occurred in patients in whom the duration of circulatory arrest was less than 45 minutes, and the probability of developing major neurologic events increased as circulatory arrest time increased beyond this (Fig. 2-6).

Focal neurologic damage resulting in serious neurologic impairment (stroke) occurs in adult patients following hypothermic circulatory arrest. Ergin and colleagues demonstrated that this form of injury is related to older age \( (P < .0001) \) particularly beyond 60 years, presence of clot or atheroma in the aortic arch \( (P < .0001) \), as well as longer duration of hypothermic circulatory arrest \( (P < .0001)\).32 In the series of adult patients reported by Gega and colleagues in whom hypothermic circulatory arrest was used as the sole means of brain preservation, prevalence of stroke was 13.1% (8 of 61; CL 8.6%-19.1%) among patients in whom the duration of circulatory arrest exceeded 40 minutes.33 Computed tomographic (CT) scans demonstrated that 62% of these strokes were embolic in origin and 38% were related to hypoperfusion.

**Postoperative Intellectual Capacity**

The effect of hypothermic circulatory arrest on late postoperative intellectual capacity and behavior in infants and children has been difficult to study. Problems in testing infants preoperatively so that each may serve as his or her own control contribute to the difficulty. Associated congenital developmental disorders, possible adverse effects before operation of severe congenital heart disease, and effects of other perioperative events complicate interpretation of the data.

Results of psychomotor testing in 146 children undergoing cardiac surgery during hypothermic circulatory arrest early in the experience with this technique, obtained by combining the three largest reported series, are summarized in Table 2-3.34,35 Late postoperatively, 23 of the 146 (16%; CL 13%-19%) had an IQ of 80 or less, more than 1 standard deviation below the test mean. In approximately half these patients, preoperative events were considered likely to account for the low scores. In the remainder, an occasional child

![](https://i.imgur.com/3Q3Q3Q.png)
suffered an adverse perioperative event, but the low scores were unexplained in nine (6.2%; CL 4.1%-9.0%) patients.

Wells and colleagues obtained data on intellectual and psychological development in children that caused them to question the idea that 60 minutes of circulatory arrest at 18°C is safe.\textsuperscript{W12} They found that verbal ($P = .06$), quantitative ($P = .07$), and general cognitive ($P = .003$) IQ scores of patients with an arrest time of 50 minutes or more were lower late postoperatively than those of patients with an arrest time of less than 50 minutes.

The first randomized clinical trial comparing prevalence of brain injury after corrective heart surgery in infants with D-transposition of the great arteries using deep hypothermia, predominantly with circulatory arrest or low-flow CPB, was conducted at Boston Children’s Hospital.\textsuperscript{N8} This study demonstrated that infants in whom circulatory arrest was used had a higher prevalence of neurologic abnormalities and poorer mental function at age 1 year, and poorer expressive language and motor development at age 2.5 years. Follow-up studies of the same cohort at age 4 years showed that use of circulatory arrest is associated with worse motor coordination and planning but not with lower IQ or worse overall neurologic status.\textsuperscript{R14} However, neither IQ nor overall neurologic status was correlated with duration of circulatory arrest. In the cohort as a whole, cognitive, language, and motor performance were reduced relative to the general population.\textsuperscript{R14}

In summary, there is increasing evidence that intervals of hypothermic circulatory arrest of 40 minutes or more are associated with brain injury in infants, children, and adults. Early experience at the Mayo Clinic suggested that 45 minutes was the maximum safe duration even when nasopharyngeal temperature was reduced to 20°C.\textsuperscript{K11}

### Spinal Cord Function

The spinal cord is less susceptible to ischemic injury than the brain, as evidenced by absence of sensory or motor deficits of the trunk or the upper and lower extremities of infants, children, and adults who have been subjected to intervals of hypothermic circulatory arrest of up to 60 minutes. Hypothermia also provides important protection of the spinal cord during ischemic intervals produced by aortic clamping. In a clinical study of hypothermic CPB and circulatory arrest (mean interval of arrest, 38 minutes; range, 8-62 minutes) for operations on the descending thoracic and thoracoabdominal aorta in 161 patients, prevalence of paraplegia or paresis (severe injury resulting from spinal cord ischemia) remained constant and less than 3.5% for ischemic (but hypothermic) intervals of up to 138 minutes\textsuperscript{K20} (Fig. 2-7).

### Renal Function and Structure

#### Experimental Studies

At normothermia, at least in rats, 20 minutes of circulatory arrest to the kidney produces no histochemical evidence of cell death, whereas 30 minutes produces extensive cell death in the distal portion of the proximal convoluted tubules, with scattered areas of cell death being seen at 25 minutes.\textsuperscript{V15} Vogt and Farber identified progressive accumulation of lactic acid during ischemia as a causative factor, and rapid decrease of ATP to 20% of control values as an indicator of impending renal death.\textsuperscript{V18}

Hypothermia prolongs the safe circulatory arrest time for the dog kidney. Ninety minutes of circulatory arrest after surface cooling to 18°C to 20°C produces no late morphologic changes in the kidney,\textsuperscript{R16} but precise relationships among temperature, duration of circulatory arrest, and morphologic and functional renal damage are not clear. Gowing and Dexter suggest that minimal morphologic changes evolve in the rat kidney after 60 minutes of circulatory arrest at 21°C.\textsuperscript{S22} It is apparent, however, that at any temperature, the safe circulatory arrest time for the kidney is longer than it is

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### Table 2-3 Results of Intelligence Testing Some Years after Surgery Performed in Infancy Using Hypothermic Circulatory Arrest

<table>
<thead>
<tr>
<th>Investigators</th>
<th>No. of Patients Tested</th>
<th>“Explained” by:</th>
<th>Preoperative Events</th>
<th>Postoperative Events</th>
<th>Unexplained</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stevenson et al.\textsuperscript{S10}</td>
<td>36</td>
<td></td>
<td>3</td>
<td>0</td>
<td>1</td>
<td>4 (11)</td>
</tr>
<tr>
<td>Dickinson and Sambrooks\textsuperscript{S10}</td>
<td>38</td>
<td></td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>7 (18)</td>
</tr>
<tr>
<td>Clarkson et al.\textsuperscript{S21}</td>
<td>72</td>
<td></td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>12 (16)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>146</strong></td>
<td></td>
<td><strong>12 (8%; CL 6%-11%)</strong></td>
<td><strong>2 (14%; CL 0.5%-3.2%)</strong></td>
<td><strong>9 (6.2%; CL 4.1%-9.0%)</strong></td>
<td><strong>23 (16%; CL 13%-19%)</strong></td>
</tr>
</tbody>
</table>

Key: CL, 70% confidence limits; IQ, intelligence quotient.
for the brain and shorter than it is for the liver. In addition, a scattered loss of cells through cell death probably results in no detectable loss of renal function, whereas this may not be true in the brain.

As with other organs, the question of damaging effects of hypothermia per se is not fully resolved. Ward found fewer morphologic and functional derangements of the kidney after 90 minutes of circulatory arrest at 15°C than at either lower or higher temperatures.\textsuperscript{58} This suggests that temperatures less than 15°C may damage the kidney.

Studies in Humans
Important oliguria beginning about 12 hours postoperatively occasionally complicates recovery of infants operated on with hypothermic circulatory arrest for less than 60 minutes. Venugopal and colleagues reported 4 deaths (3%; CL 2%-6%) from renal failure among 130 patients operated on with surface-induced hypothermic circulatory arrest.\textsuperscript{510} Among patients who died, renal failure was the mode of death in 14%.

The primary cause of the renal failure appears to be low cardiac output after operation. However, in at least some cases, severe oliguria develops when the hemodynamic state of the patient appears to be adequate. In view of the finding in experimental studies that morphologic and functional damage to the kidney does not occur after 60 minutes of circulatory arrest at temperatures of 18°C to 20°C (Fig. 2-8), damaging effects from CPB must be implicated. In part, this may be the result of low cardiac output preceding and following the interval of circulatory arrest. In part, it may be due to damage to the kidneys by free hemoglobin and circulating toxins that appear during CPB (see Section II). Free hemoglobin has been found in the renal tubules of some of these patients at autopsy.

In 161 adult patients undergoing resection of the distal aortic arch and descending thoracic and thoracoabdominal aorta in whom hypothermic circulatory arrest was used (mean nasopharyngeal temperature, 14.5°C; mean interval, 38 minutes; longest interval, 62 minutes), prevalence of postoperative renal failure requiring dialysis among 157 operative survivors was 2.6% (4 patients; CL 1.3%-4.6%).\textsuperscript{320} Among the subgroup of 18 operative survivors who had evidence of renal dysfunction preoperatively (serum creatinine level > 1.5 mg · dL\textsuperscript{-1}), none developed renal failure that required dialysis.

Liver Function
Studies in dogs suggest that complete hepatic circulatory arrest for 45 minutes or more at 37°C is followed by serious functional derangements.\textsuperscript{20,82} The normothermic liver of humans resumes normal function after its complete isolation from the circulation for 35 to 40 minutes.\textsuperscript{514} With hypothermia (20°C-22°C), 60 minutes of circulatory arrest does not produce structural or functional abnormalities in the liver.\textsuperscript{R16}

SAFE DURATION OF CIRCULATORY ARREST

The preceding information does not allow formulation of a table or an equation relating safe duration of circulatory arrest to various temperatures based on rigorously derived rules. Knowledge of biological systems in general indicates that if adequate information were available, relationships should be expressed as probability of no functional or structural damage (i.e., probability of safe circulatory arrest) at a given temperature, rather than as an absolute value.

Fig. 2-9, A shows three curves relating probability of safe circulatory arrest to arrest time at nasopharyngeal temperatures of 37°C, 28°C, and 18°C. These estimates are based on available information, but because of lack of data they have not been rigorously derived. To emphasize that each curve would have a degree of uncertainty even if considerable data were available, the 70% confidence limits around the continuous point estimate for 18°C are shown in Fig. 2-9, B. The preceding pages indicate that histologic changes in the central nervous system, without functional abnormalities, are the most sensitive indicators of lack of complete safety of the arrest period used. The portrayal at 18°C of essentially complete safety of 30 minutes of circulatory arrest is consistent with all available information. The portrayal of essentially complete safety of arrest of 45 minutes for at least 70% of subjects is also consistent with the facts, and the damage produced within this period is likely to be structural and without permanent functional sequela. Most patients will have some structural evidence of damage from 60 minutes of arrest, but only about 10% to 20% will have evident functional damage, and in many of them the manifestations will be transient. It remains a vexing clinical problem that the probability of the safe period of circulatory arrest varies widely, especially because state-of-the-art medicine is not yet capable of defining specific patient genetic or phenotypic profiles that

![Figure 2-8](image-url) Freehand nomogram for the kidney of the relation between probability of safe total circulatory arrest and duration of circulatory arrest at two temperatures. Normothermic relationship is based on the work of Vogt and Farber\textsuperscript{915} and the hypothermic one on data presented in the text.
CPB for cardiac surgery is conceptually simple, and equipment is available to accomplish it with relative ease. Most or all of the patient’s systemic blood, which normally returns to the right atrium, is diverted into a device in which oxygen is supplied to the blood and carbon dioxide is removed. The newly arterialized blood is pumped from the device into the aorta. Among the complexities of CPB are that blood does not naturally (1) circulate through nonendothelially lined channels, (2) contain gaseous and particulate emboli, and (3) experience nonphysiologic shear stresses. Also, the body is unaccustomed to absence of any appreciable pulmonary blood flow and to presence of only minimally pulsatile aortic pressure. In addition to CPB, the patient undergoing cardiac surgery experiences all of the stress responses characteristic of major surgical procedures and trauma.

What is truly remarkable is that most patients survive operation and CPB and convalesce in a reasonably normal manner. For a time, however, almost every patient retains a few demonstrable stigmata from the procedure; some have major morbidity, and a few die of their response to CPB. Prevalence of these unfavorable outcomes in a group of patients is in part determined by identifiable risk factors, but determinants of their occurrence and severity in an individual patient remain incompletely defined.

When essentially all systemic venous blood returns to the pump-oxygenator instead of to the heart, the situation is termed **total cardiopulmonary bypass**. When some systemic venous blood returns to the right atrium and right ventricle and is pumped into the lungs, then passes back into the left atrium and is pumped by the left ventricle into the aorta, the situation is termed **partial cardiopulmonary bypass**. Partial CPB has long been known to be better tolerated than complete CPB. Reasons for this have not been clearly defined, but continuation of at least some pulmonary blood flow is a likely explanation. The remainder of this section is concerned with total CPB.

**HISTORICAL NOTE**

The historical aspects of CPB for cardiac surgery are not easily described, because it is almost impossible to determine who first conceived the idea of diverting the circulation of a patient to an oxygenator outside the body and pumping it back to the arterial system to allow surgery to be performed on or within the heart. References to extracorporeal gas exchange in blood go back to the last part of the 19th century. For example, Frey and Gruber worked with an oxygenator in 1885. Subsequently, scores of laboratory studies with oxygenators and pumps were reported. However, serious consideration of pump-oxygenators for cardiac surgery had to await development of modern anesthesia, modern surgical methods, and scientific developments such as discovery and use of heparin and manufacture of biocompatible plastic materials.

Without doubt, John Gibbon, with his pioneering experimental work at Massachusetts General Hospital in Boston in the late 1930s, was a major contributor to development of CPB and its advancement to the stage of successful clinical

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**Figure 2-9** Probability of safe (absence of structural or functional damage) circulatory arrest according to duration. **A**, Estimate at nasopharyngeal temperatures of 37°C, 28°C, and 18°C. **B**, Estimate at 18°C, with dashed lines representing 70% confidence limits. Number of experiments in the literature concerning 40 minutes of circulatory arrest at 18°C nasopharyngeal temperature is estimated at 20 as a basis for calculating these confidence limits. Note that at 30 minutes a safe arrest is highly likely and that at 45 minutes it is probable. Other data suggest that at 45 minutes, damage will probably be only structural and without evident functional sequelae.

...
application. Gibbon’s work was interrupted by World War II, but when he came to Jefferson Medical College in Philadelphia after military service, he resumed work with CPB, its pathophysiology, and the equipment required for it. Most of the medical and surgical world took little note of his work, considering it unlikely to lead to any useful purpose, but Gibbon persevered. In 1953, he performed the first successful operation in which the patient was totally supported by CPB when he repaired an atrial septal defect in a young woman using a pump-oxygenator. Unfortunately, his subsequent four patients died of a variety of problems, and he became discouraged with the method (Gibbon JH Jr: personal communication, 1955).

Meanwhile, a few others began to work with pump-oxygenators for CPB during the late 1940s. Among them were Clarence Dennis and his colleagues at the University of Minnesota. His laboratory studies led him to make what may have been the first attempt to use a pump-oxygenator for clinical cardiac surgery in 1951. Dennis and Richard Varco operated on a patient thought to have an atrial septal defect. These surgeons believed they had done a satisfactory repair, but the patient died. Autopsy showed that the lesion was in fact a partial atrioventricular septal defect, and misinterpretation of the anatomy was a major factor in the patient’s death. In Stockholm, Viking Bjork and Åke Senning also worked with CPB during the late 1940s and early 1950s. In related efforts, Clarence Crafoord was an early user of this method for removal of an atrial myxoma.

After Dennis’s unsuccessful effort, C. Walton Lillehei and his colleagues at the University of Minnesota began working in the laboratory with controlled cross-circulation, using another intact subject as the “oxygenator.” Their experimental studies led them to adopt the now discarded “azygos flow principle,” which presumed that only low perfusion flow rates were needed. In March 1954, they began a spectacular series of operations in 45 children with congenital heart disease using “controlled cross-circulation” with the mother or father as the oxygenator. A 53-year follow-up of the 28 hospital survivors documented only 8 late deaths, and of the remaining 20 survivors, none was limited by cardiac conditions. Although this particular technique was soon abandoned, the work of Lillehei and colleagues brought into being the modern era of open intracardiac surgery.

Experimental work at the Mayo Clinic with pump-oxygenators began in the early 1950s under the direction of John Kirklin. This led to the first use of CPB with a pump-oxygenator at the Mayo Clinic on March 22, 1955, when a ventricular septal defect was successfully repaired, and subsequently to the world’s first published series of intracardiac operations performed with use of CPB and a pump-oxygenator. These procedures were performed using the Mayo-Gibbon pump-oxygenator, which was designed and constructed in the engineering shops of the Mayo Clinic. Use of a pump-oxygenator for CPB during cardiac surgery expanded rapidly, and today the method is used many times a day in hospitals in almost every country in the world.

UNIQUENESS OF CARDIOPULMONARY BYPASS

The patient whose arterial blood flow is temporarily provided by means of a pump-oxygenator is in an abnormal state that affects most if not all physiologic processes. Throughout evolution, blood has passed only through channels lined with endothelial cells, but during CPB, it is passed across noneendothelial foreign surfaces. As a result, and perhaps because of other factors, virtually all humoral and cellular components of the inflammatory response are acutely activated, and probably some of the more slowly reactive specific immune responses are activated as well, at least initially. The general stress response seen after surgery and trauma also occurs to a major degree.

During total CPB, a number of physiologic variables are under direct external control, in contrast to the situation in intact humans. These include total systemic blood flow (“cardiac” output); input pressure waveform; systemic venous pressure; pulmonary venous pressure; hematocrit and chemical composition of the initial perfusate; arterial oxygen, carbon dioxide, and nitrogen levels; and temperature of the perfusate and patient.

Another group of variables is determined in part by the externally controlled variables but in large part by the patient. These include systemic vascular resistance, total body oxygen consumption (Vo2), mixed venous oxygen levels (Pvo2), lactic acidemia and pH, regional and organ blood flow, and organ function.

A third group of largely uncontrolled variables includes, to a greater or lesser degree, all components of the process of inflammation, incited in large part by the organism recognizing the foreign surfaces across which blood passes as “nonself.” These features make the patient who has undergone CPB a unique organism, at least for a few days. Recognition of this, as well as a detailed knowledge of the post-CPB state, is necessary for delivery of optimal postoperative care (see Chapter 5).

CONTROLLED VARIABLES

Arterial Output to the Patient

Arterial output (outflow) from the pump-oxygenator to the subject is achieved by generating a large pressure gradient by a pump. The most commonly used type of arterial pump is the roller pump (originally used by DeBakey for blood transfusion). It generates a relatively nonpulsatile flow and is simple, reliable, and relatively inexpensive. In clinical use, roller pumps are generally set to be nearly occlusive. When they are occlusive, trauma to the formed elements in blood is increased; when they are too nonocclusive, they are unable to maintain the same rate of flow against the wide range of resistances (pressure differentials of 30-300 mmHg) offered by arterial cannulae and the patient’s systemic vascular resistance. The tubing passing through the roller pump head is most often Tygon, a special nontoxic surgical grade of polyvinyl chloride. During hypothermia, Tygon tubing decreases in elasticity and filling volume, so stroke volume of the pump is slightly decreased. Silicone rubber tubing does not have this disadvantage and may be used in the roller pump head when hypothermia is required. Volume output of the roller pump head is controlled by creation of a pressure drop over 1 minute.
pump is more certain to be that predicted when output resistance is high than when a high negative pressure is generated on the input side. When generated negative pressure on the input side exceeds about 200 mmHg, volume output of the roller pump becomes less predictable.

The controlled vortex (centrifugal) pump is also commonly used for cardiac surgery and for closed-chest support of patients in whom both arterial and venous cannulation are accomplished centrally or peripherally (termed cardiopulmonary support [CPS]). Flow generated by a controlled vortex pump varies with changes in resistance to flow into and out of the pump. When pressure in the output line reaches about 500 mmHg, both outflow from and inflow into the pump become zero. When pressure in the inflow line decreases to about −500 mmHg, both inflow and outflow become zero. Therefore, in contrast to the roller pump, revolutions per minute (rpm) of the controlled vortex pump cannot be used to estimate flow. Instead, a flow meter must be placed on the arterial (output) or venous (input) line. However, if the arterial line becomes completely occluded, either intentionally or by accident, flow immediately ceases, but pressure in the arterial line will rise no higher than 500 mmHg, and it is unlikely that the tubing will rupture or a junction connector will give way. Blood trauma is similar in controlled vortex and roller pumps. Although air can be entrapped within the controlled vortex pump, it, like the roller pump, can transmit air bubbles from the venous to the arterial lines. (However, air entrapped in a vortex pump breaks down into microbubbles that eventually pass out of the pump; a roller pump will pump gross air presented to it.)

Venous Input from the Patient

The venous input (inflow) into the pump-oxygenter from the patient is achieved by a negative pressure gradient from patient to machine. The negative pressure required to move blood from the patient to the pump-oxygenter is considerably less than the pressure required to move blood from the pump-oxygenter to the patient, because of the different characteristics of the venous and arterial systems of the patient and to some extent of the venous and arterial cannulae.

Sufficient negative pressure for venous input into the pump-oxygenter can be generated by:

- Creating a controlled vacuum within a venous reservoir
- Using a siphon system in which gravity creates the negative pressure
- Using a controlled vortex pump to create the negative pressure within the venous line from the patient

Vacuum-Assisted Venous Return

The ideal method for creating negative pressure for venous input into the pump-oxygenter is by a regulated and monitored vacuum pressure system coupled to the venous reservoir. The patient and machine can be at or near the same vertical level from the operating room floor, the negative pressure does not rise above the controlled level if the cannula becomes occluded, and the amount of negative pressure can be varied as needed. Most importantly, the two pressures (i.e., output pressure to the patient and input pressure from the patient) are uncoupled and can be varied independently with an arterial roller pump. If a controlled vortex pump is used, the vacuum pressure in the venous system will reduce the outflow pressure of the nonocclusive vortex pump, thus requiring higher rpm to achieve a constant flow.

Use of a hard-shelled venous reservoir in currently available oxygenators and a vacuum regulator connected to wall suction set at −40 to −60 cm H2O has allowed vacuum-assisted venous return (VAVR) to become widely accepted. VAVR permits use of smaller venous cannulae, smaller reservoirs, considerably shorter tubing, and low priming volume. It is of considerable value for cardiac operations performed in infants and through small incisions in children and adults (see Special Situations and Controversies in Section III). In a study by Banbury and colleagues at Cleveland Clinic, VAVR was found to reduce priming volume from 2.0 ± 0.4 L to 1.4 ± 0.4 L (P < .0001), increase hematocrit both on bypass and immediately postbypass (P < .0001), and reduce use of blood products both intraoperatively and postoperatively from 39% of patients to 19% (P = .002).

Siphon (Gravity) Drainage

A common method of generating the negative pressure gradient is through siphonage. Disadvantages of this approach include an imposed difference in the levels of patient and pump-oxygenter, the relatively narrow range of negative pressures that can be generated in the operating room by its use, and its interruption by large boluses of air in the venous line. Most importantly, the need for a reservoir increases the filling (priming) volume of the pump-oxygenter. It is, however, simple, reliable, effective, and inexpensive.

Venous Pumping

The controlled vortex pump permits direct pumping from the patient’s venous system and is more effective and safer than a roller pump. The potentially large pressure gradient between the tip of the venous cannula and right atrium or venae cavae must be controlled in some way to prevent “fluttering” of their walls around the end of the cannulae. One way of accomplishing this is to use small venous cannulae to impose a considerable resistance between the pump and tip of the cannula, rather than between the tip of the cannula and the patient’s venous system. This is fortuitously advantageous in percutaneous peripheral cannulation, because an 18F or 20F venous cannula of some length can be easily passed into the venous system of a normal-sized adult and provides adequate venous drainage. It also facilitates minimally invasive cardiac surgery. By contrast, 28F to 32F catheters are required when gravity drainage is used.

Gas Exchange

The device for gas exchange, the oxygenator, is a highly important component of pump-oxygenators. Not only does it regulate tension of gases in the arterial blood emerging from the pump-oxygenator, it is also the largest area of foreign surface blood comes into contact with, and therefore probably the component of the pump-oxygenator where the most blood damage occurs. This contact occurs in the boundary layer of the blood, which is made very large in the oxygenator to facilitate gas exchange. Only a small proportion of the formed and unformed blood elements comes into contact with tubing and pump surfaces.

Gas exchange occurs directly across the blood/gas interface in bubble oxygenators, rotating disk and cylinder
oxygenators, and stationary vertical screen oxygenators used in the past. It occurs across a multitude of tiny pores in so-called membrane oxygenators of the hollow-fiber, microporous polypropylene and other types, in which there are still blood/gas interfaces. However, damage to the blood is less in these types of oxygenators than in bubble oxygenators. Only in the true silicone rubber membrane oxygenator of the type devised by Kolobow and colleagues, or the tightly woven microporous polymethylpentene membrane currently used for extended extracorporeal membrane oxygenation, is there no blood/gas interface. This allows CPB to be used for more than 24 hours with reasonable safety.

Because of their efficiency, hollow-fiber and true membrane oxygenators do not depend on minute ventilation (gas flow) to the oxygenator for CO₂ regulation under most circumstances. Rather, the ventilating gas flow rate and composition are regulated independently. This allows precise regulation of arterial Po₂ and PCO₂.

**Arterial Oxygen Levels**

With present-day oxygenators, maintaining PaO₂ at about 250 mmHg is easily accomplished. Higher PaO₂ is unnecessary and theoretically subjects patients to the risk of oxygen toxicity and bubble formation. PaO₂ lower than about 85 mmHg results in a declining arterial oxygen content (CaO₂) (according to the oxygen dissociation curve of blood) and a corresponding reduction of tissue and mixed venous oxygen levels. Shepard demonstrated that when arterial oxygen saturation (SaO₂) fell below 65% in dogs undergoing normothermic CPB, Vo₂ fell, indicating hypoxic cell damage.

PaO₂ is related to temperature of the patient, which is related to Vo₂ (see Fig. 2-1), blood flow rate (Q), performance of the oxygenator, and, in a complex fashion, to ventilating gas flow rate and composition (see “Gas Exchange,” earlier). Reducing the patient’s body temperature reduces Vo₂ and increases P⁰₂, resulting in increased PaO₂. During rewarming by perfusion from the pump-oxygenator, the increasing Vo₂ and the metabolic debt that has accumulated result in relatively low P⁰₂. **(Fig. 2-10).** This period, then, places maximal demands on the oxygen transfer capacity of the oxygenator.

**Arterial Carbon Dioxide Pressure**

Arterial carbon dioxide pressure (PaCO₂) is controllable during CPB by varying the ratio between gas flow rate into the oxygenator (V, or ventilation · min⁻¹) and Q through the oxygenator. This is facilitated by use of microporous or true membrane oxygenators, because V is not the force driving blood through the oxygenator, as is the case in bubble oxygenators, and PaO₂ is well maintained over a wide range of V. Inline P⁰₂ and pH meters facilitate control of PaCO₂ and pH.

Some clinical perfusions for cardiac surgery are performed at normothermia (=37°C) and others at various levels of hypothermia: mild (30°C-35°C), moderate (25°C-30°C), or deep (<25°C). Therefore, it is necessary to consider the strategy for controlling PaCO₂ and, indirectly, pH. The alpha-stat strategy is based on (1) using the pH measured at 37°C and uncorrected for the temperature of the patient’s blood, and (2) maintaining this level at pH 7.4. That is, the ventilation of the oxygenator is maintained at the level appropriate for a body temperature of 37°C, no matter how low the temperature. This hyperventilation during hypothermia results in a decrease in PaCO₂ and an increase in pH when the values for these are corrected for the temperature of the patient’s blood. Swan and Reeves and Rahn and colleagues have all emphasized that at low temperatures, neutrality exists at a higher pH than at normothermia, because of the change of the dissociation constant of water with temperature. The alpha-stat strategy results in optimal function of a number of important enzyme systems, including lactate dehydrogenase, phosphofructokinase, and sodium-potassium ATPase.

In contrast, the pH-stat strategy strives for the same values of pH and PaCO₂, corrected to the temperature of the patient’s blood, during hypothermia as at normothermia. This represents a state of respiratory acidosis and hypercapnia. Cerebral blood flow usually increases under these circumstances. This may be considered advantageous in some situations, but so-called luxury perfusion may expose the brain to a larger number of microemboli than would otherwise be the case, and therefore could be disadvantageous.

At a cellular enzyme level, the alpha-stat strategy may be preferable, but which is preferable in clinical cardiac surgery in neonates, children, and adults is the subject of continued investigation and debate. The alpha-stat strategy results in a lower PaCO₂, which may adversely affect cerebral blood flow. This may be of particular importance for patients with cyanotic congenital heart disease (e.g., tetralogy of Fallot with pulmonary atresia) for whom low PaCO₂ may result in pulmonary vasodilatation in addition to cerebral vasocostriction. Thus, there can be a steal of blood from the cerebral to the pulmonary vascular bed. Several studies in infants suggest that pH-stat management results in superior neurologic outcome during deep hypothermic CPB.
and hypothermic circulatory arrest.\textsuperscript{B13,K14,P11} The pH-stat technique may depress cardiac function.\textsuperscript{B10} However, at least in dogs, regional distribution of blood flow during normothermic and hypothermic full-flow CPB is similar with the alpha-stat and pH-stat strategies.\textsuperscript{B45}

A recent review of 16 best-evidence published papers concluded that better results were achieved with the alpha-stat technique in adult patients and with the pH-stat technique in pediatric patients.\textsuperscript{A1}

**Heparin Levels**

Before CPB is established, the patient is anticoagulated by intravenous or intracardiac injection of heparin, usually in a dose of 300 to 400 units · kg\(^{-1}\) body weight (sometimes expressed as 3 to 4 mg · kg\(^{-1}\)). (Details of dosage of heparin and protamine, and of activated clotting time (ACT), are given later in “Heparinization and Later Protamine Administration” under Preparation for Cardiopulmonary Bypass in Section III). Heparin, one of a heterogeneous group of glycosaminoglycans, has an approximate molecular weight of 3000 to 100,000. It binds to and greatly amplifies the effect of antithrombin III, which is responsible for virtually all of its anticoagulant activity. Currently, a purified form derived from porcine intestinal mucosa is commonly used, whereas the form derived from bovine lung was used more commonly in the past. Experimental and limited prospective clinical studies suggested that lung heparin may be preferable for CPB, because bovine lung heparin has a more reliable protamine neutralization response.\textsuperscript{F14} However, current supply of heparin in the United States is 100% derived from porcine intestinal mucosa.

Heparin concentrations in plasma can be measured directly; the usual values during CPB are 3.5 to 4 units · mL\(^{-1}\). Usually these measurements correlate well with ACT.\textsuperscript{W24} One exception is the situation of antithrombin III deficiency, a state of heparin resistance.\textsuperscript{B5,B26} Two or three times the usual dose of heparin may be required to produce satisfactory anticoagulation (i.e., ACT of 480 seconds); if only the heparin level is measured, initiation of CPB might produce thrombosis in the pump-oxygenator system and introduce thrombus into the patient. The most common cause of antithrombin III deficiency is previous exposure to heparin in a dose-dependent fashion.\textsuperscript{B5,B26} If repeated ACTs indicate an unsafe level for CPB, antithrombin III supplementation must be considered. This is accomplished with either fresh frozen plasma or antithrombin III concentrate.

Although heparin used in the manner described has been clinically satisfactory, activation of the clotting cascade during CPB is not completely neutralized. At least factor XI, factor X, and prekallikrein are activated, and high-molecular-weight kininogen is cleared.\textsuperscript{C2} Thus, markers of fibrin formation can be detected in most patients during and early after CPB, and fibrin deposition and embolization can occur.\textsuperscript{B33} In most patients, this subclinical coagulation does not cause the concentrations of the soluble coagulation factors to become sufficiently low during or early after CPB to cause bleeding.\textsuperscript{H15}

Increasing the dose of heparin does not prevent this subclinical coagulation during CPB,\textsuperscript{G23} so maintaining ACT at 300 to 350 seconds (rather than 450 seconds) results in no more subclinical plasma coagulation than does the traditional method, requires less heparin, and may be associated with less bleeding after operation.\textsuperscript{C2,G23} Yet a 2008 survey of 54 cardiac surgery centers in the United States and Canada indicated that the majority of institutions (71% for U.S. and 69% for Canadian sites) used a target ACT for instituting CPB of between 400 and 480 seconds.\textsuperscript{L18}

The former use of aprotinin affected the concepts of heparinization for CPB for intracardiac surgery, because this agent prolongs both clotting time and ACT, depending on the method of measurement (see “Fibrinolytic Cascade” under Details of the Whole-Body Inflammatory Response later in this section).\textsuperscript{H42,N3,W7} If aprotinin is used, an optimal recommendation is to administer the usual initial dose of heparin and add additional heparin to maintain the ACT above 700 seconds if the activating agent is Celite (diatomaceous earth). Kaolin is a more dependable activating agent, giving ACTs in the presence of aprotinin similar to those without aprotinin in vitro and during CPB.\textsuperscript{B7,W6} Therefore, a preferable method when aprotinin is used during CPB is to use kaolin as the activating agent and maintain the usual ACT at 480 seconds. Alternatively, the heparin concentration is measured at intervals and kept above 3 mg · kg\(^{-1}\). Because of results of randomized trials demonstrating that aprotinin was associated with a higher risk of death after cardiac surgical procedures than other antifibrinolytic agents used to decrease the need for red blood cell transfusions,\textsuperscript{C9} Bayer Pharmaceuticals withdrew their drug Trasylol (aprotinin) from the market in May 2008. Subsequent meta-analysis\textsuperscript{G3} has confirmed higher morbidity and mortality associated with use of aprotinin.\textsuperscript{A2}

It has been estimated that 1% to 5% of patients who receive therapeutic anticoagulation with unfractionated heparin develop antibodies, with concomitant development of thrombocytopenia defined as HIT (heparin-induced thrombocytopenia).\textsuperscript{C12} HIT may complicate management of patients who require cardiac surgery using CPB when a large dose of heparin is required. In patients with established or suspected HIT, all heparin must be withheld and alternative forms of anticoagulation used.

Bivalirudin, a synthetic 20-amino-acid peptide analog of hirudin, has become the anticoagulant most commonly used to replace heparin in patients with HIT who require cardiac surgery.\textsuperscript{C01,1,12} A randomized, open label, multi-institution trial comparing bivalirudin (101 patients) with heparin (49 patients) provided an interesting yet sobering insight into evidence-based medicine. Aprotinin was introduced for its serine protease inhibitory properties, which are relevant to the damaging effects of CPB discussed later in this chapter. Its profound effect on blood loss during cardiac surgery was a serendipitous pleiotropic finding,\textsuperscript{C19} although this had been observed in cyanotic children with hematologic derangement by Urban and colleagues\textsuperscript{C13} and others.\textsuperscript{H14,L12,L13,C17} What was considered by some an unethical number of small randomized trials repeatedly demonstrated this effect on blood loss.\textsuperscript{C19} Nevertheless, in a thoughtful assessment, Angoustides and Fleisher\textsuperscript{H33} pointed out that at least three essential issues remained unexplored: (1) safety in specific subsets of patients, (2) platelet protection, and (3) organ protection. For example, many studies, such as those of Koch and colleagues, have demonstrated that morbidity and mortality of cardiac surgery steadily increase with number of transfused red cell units;\textsuperscript{C13,64} yet despite the substantial decrease in transfusion requirement with aprotinin, morbidity did not proportionately decline. It was the observational study of Mangano and colleagues that focused attention on safety of aprotinin despite its efficacy.\textsuperscript{C31} This study with numerous flaws,\textsuperscript{C31} combined with another randomized trial\textsuperscript{C08} and concern about the transparency of reporting of safety by the manufacturer, led to withdrawal of aprotinin from the market.

In developing an evidence base, even randomized trials can be misleading when they (1) focus on efficacy without sufficient power (sample size) to identify possible safety problems; (2) do not compare against placebo, just other drugs of the same class; (3) do not take into account differential effects on different patient subsets; or (4) fail to assess known primary effects of the drug when interesting and unexpected efficacy is discovered. The result is incomplete evidence that clouds decision making.
Box 2-2 Algorithm for Calculating Patient-Machine Hematocrit

The need for and amount of additional packed red blood cells to achieve a desired hemoglobin concentration early after commencing bypass is determined by the patient’s blood volume (VmB) and hemoglobin concentration prior to CPB (expressed as hematocrit, HCTp), and the volume of pump-oxygenator prime (VmRBC) and its hemoglobin concentration (expressed as hematocrit, HCTm). Patient blood volume is estimated as

\[ \text{VmB} = 1000 f \cdot \text{wt} \]

where \( f \) is the proportion of body weight attributable to blood volume; \( f = 0.08 \) for infants and children up to 12 years of age, \( f = 0.065 \) for older patients, and \( \text{wt} \) is weight in kg. (These are average values for the proportion of body weight that is blood volume. More complex regression equations are available for more accurate estimates.)

Patient (VmRBC) and machine (VmRBC) red cell volumes are:

\[ \text{VmRBC} = \text{VmB} \cdot \text{HCTm} \]

Then, mixed patient-machine hematocrit (HCTpm) is:

\[ \text{HCTpm} = (\text{VmRBC} + \text{VmB})/(\text{VmB} + \text{VmRBC}) \]

If no blood is in the prime:

\[ \text{HCTpm} = \text{VmRBC}/(\text{VmB} + \text{VmRBC}) \]

These calculations may be included in a computer-prepared printout for the perfusionist, available before the patient comes to the operating room.

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patients) for operative procedures requiring CPB demonstrated similar procedural safety (freedom from death, Q-wave myocardial infarction, reperfusion for coronary artery surgery, or stroke) between the two groups at 7 days, 30 days, and 12 weeks.\(^22\) Secondary end points including mortality, 24-hour blood loss, transfusion requirements, and duration of operation were similar. Avoiding blood stasis was critical for patients receiving bivalirudin. A more recent single-institution study of 115 patients receiving bivalirudin during operations requiring CPB demonstrated procedural safety (similarly defined) of 99.4% at 7 days and 30 days.\(^6\) Although specific dosage protocols have not been determined, Czosnowski and colleagues, in a review of available randomized trials and other clinical studies, recommended a 1 mg · kg\(^{-1}\) bolus followed by a 2.5 mg · kg\(^{-1}\) · h\(^{-1}\) infusion (goal: ACT > 2.5 times baseline).\(^8\)

### Perfusate

**Diluent**

The diluent (which is used to prime the pump-oxygenator system, wholly or in part, and for any erythrocyte-free additions during CPB) is a balanced electrolyte solution with a near-normal pH and an ion content resembling that of plasma. There is some evidence for the concept that in both adults and young patients, it is disadvantageous to include either glucose or lactate in the priming solution\(^9\).\(^10\) (see “Biochemical Milieu” under Brain Function and Structure: Risk Factors for Damage in Section I). However, priming solutions containing glucose and lactate are used in some centers.\(^11\)

In pump-oxygenator systems without a venous reservoir or those using VAVR, mixing of blood and prime may be partially or wholly avoided, with residual prime discarded.

### Hemoglobin Concentration

At some institutions, in adult patients and even young patients, no effort is made to control hemoglobin concentration or hematocrit during CPB. Instead, the pump-oxygenator is routinely filled initially with a balanced salt solution. This provides sufficient oxygen delivery to maintain normal mitochondrial PO\(_2\) levels of about 0.05 to 1.0 mmHg, and average intracellular PO\(_2\) levels of about 5 mmHg, these being reflected in normal \( \text{Pvo}_{2} \) of about 40 (\( \text{Svo}_{2} \) of about 75%). When the hematocrit is abnormally high, oxygen content is high, but the increased viscosity tends to decrease microcirculatory blood flow. The rate of oxygen transport varies directly with hematocrit (because oxygen content varies directly with hematocrit), assuming normal red blood cell hemoglobin concentrations and adequate oxygenation) and inversely with blood viscosity (which is also determined primarily by hematocrit). Hypothermia increases blood viscosity; therefore, at low temperatures, a lower hematocrit is more appropriate than at 37°C.

A lower-than-normal hematocrit appears desirable during hypothermic CPB because the perfusate has a lower apparent viscosity and low shear rates and provides better perfusion of the microcirculation. Thus, a hematocrit of about 0.20 to 0.25 may be optimal during moderately and deeply hypothermic CPB, although a low hematocrit could predispose the patient to neurologic dysfunction, particularly when it exists during a period of low CPB flow and also in elderly and diabetic patients with poor cerebral regulation of blood flow. Several studies of infants suggest that a hematocrit of 0.25 is associated with better neurologic outcome than one of 0.20, but that there is no incremental improvement for hematocrit greater than 0.25 (up to 0.35).\(^12\)\(^13\) During rewarming, a higher hematocrit may be desirable because of increased oxygen demands, and the higher apparent viscosity of a higher hematocrit is appropriate during normothermia. This may be achieved by ultrafiltration (see “Components” under Pump-Oxygenator in Section III) or by adding packed red blood cells if the blood volume is too low to allow this.

The need for and amount of additional blood or packed red blood cells to achieve a desired hemoglobin concentration during CPB can be determined before the start of CPB (Box 2-2). If the calculated hematocrit is in the desired range, a blood-free priming solution is used. If the calculated hematocrit is lower than desired, an appropriate amount of blood (or packed red blood cells) is added.

**Banked blood** preferably less than 48 hours old is preferred, but older blood is accepted for adults when necessary. Banked blood is rendered calcium-free by the anticoagulant solution (citrate-phosphate-dextrose [CPD]) and is acidic, so additions of heparin, calcium, and buffer may be required before placing it in the pump-oxygenator, before or during CPB.
However, in at least a few institutions, no calcium is added before placing the blood in the pump-oxygenator, and none is added thereafter until the patient’s nasopharyngeal temperature reaches about 28°C during the rewarming process. It is important to monitor the ionized calcium level, and calcium is added if necessary. (The normal level is about 1.2 mmol · L⁻¹, with total calcium being about 2.5 mmol · L⁻¹ or 10 mg · dL⁻¹.) This practice results in extremely low levels of ionized calcium when CPB is first established. Unduly high levels of ionized calcium could be more deleterious (see “Damage from Global Myocardial Ischemia” in Chapter 3). A reasonable practice would be to initially add 3 mL of calcium chloride (10%) rather than 5 mL for each unit of banked blood used, and then add no more until the ionized calcium is measured.

**Albumin Concentration**

Concentration of albumin in the mixed patient-machine blood volume, as well as of hemoglobin, is affected by the amount of hemodilution. Theoretically, according to the Starling law of transcapillary fluid exchange (see “Pulmonary Venous Pressure” later in this section), a reduction of albumin and thus of the colloidal osmotic pressure of the plasma accentuates movement of fluid out of the vascular space into the interstitial space. That this occurs is indicated by the work of Cohn and colleagues, who showed that extracellular fluid volume increases more rapidly when hemodilution is used than when it is not.⁴²⁶

During CPB, microvascular permeability to macromolecules is increased;⁴²¹ some of the administered albumin leaks into the interstitial fluid and has an unfavorable effect on the relationships expressed in the Starling law. Homologous albumin may provoke an allergic response, which also increases microvascular permeability and causes leakage of albumin into the interstitial fluid.

These complex interrelations probably explain the failure of a randomized trial to find a favorable effect from adding homologous albumin to the prime in adults.⁴⁶⁷ It is not uncommon for cardiac surgical patients, particularly the elderly, to present with low-normal or below-normal albumin levels. Whether albumin concentration should be maintained at normal levels in some special situations such as this remains arguable.

Other colloidal solutions (dextran 40, dextran 70, hydroxyethyl starch) can also be added to the priming solution to attenuate loss of fluid from the intravascular space. However, none of them has been conclusively shown to have a beneficial effect.

**Other Additives**

Practices vary regarding addition of substances and drugs to the perfusate (by administering them into the priming volume of the pump-oxygenator or patient before CPB, or into the patient or pump-oxygenator during CPB), other than basic balanced salt solution and blood and its required additives.

Use of an osmotic diuretic may be advisable. Mannitol (=0.5 g · kg⁻¹), a pure osmotic diuretic, can be included as part of the prime. Mannitol also has the advantage of being an effective agent against oxygen free radicals generated during CPB.⁴¹¹,⁴¹² Glucose (added to the prime of the pump-oxygenator in sufficient quantity to obtain a glucose concentration of about 350 mg · dL⁻¹ in the prime) also produces diuresis. However, its use in the priming volume and its administration during and early after CPB, employing more than moderate hypothermia, may be unwise in view of the strong suggestion that hyperglycemia during cooling and early after hypothermic circulatory arrest increases the probability of brain injury.⁴¹⁸,⁴¹⁹,⁴₂⁰

Administration of a potent diuretic during CPB is generally useful. Incorporating furosemide in the pump prime is practiced by many groups. It may be more advantageous to give it as a bolus in a dose of 1 to 2 mg · kg⁻¹ at the start of rewarming, either after an interval of circulatory arrest or moderately or deeply hypothermic CPB.

The short-acting adrenergic α-receptor blocking agent phentolamine is capable of antagonizing the vasoconstriction produced by catecholamines and has been shown to produce more uniform body cooling and rewarming and improved tissue perfusion when given during CPB.⁴₅₂ A bolus of 0.2 mg · kg⁻¹ is administered just after the start of CPB and the initiation of cooling. When circulatory arrest is used, an additional dose of 0.2 mg · kg⁻¹ is administered with the resumption of CPB for rewarming.

Alternatively, the long-acting adrenergic α-receptor blocking agent phenoxybenzamine can be used in infants and children to produce total α-blockade for 8 to 10 hours. It is given in a dose of 1 mg · kg⁻¹ about 15 minutes before commencing CPB and at the beginning of rewarming after the period of circulatory arrest.⁴₅₃ A continuous infusion of nitropresside during cooling and again during rewarming is preferred to either of these agents by some groups. Nitropresside reduces arterial blood pressure (by = 25 mmHg), yet maintains cerebral blood flow during moderately hypothermic CPB.⁴₁⁹

Opinions differ about the advisability of routinely administering (or adding to the perfusate) corticosteroids and the appropriate agent to use. Available evidence suggests that corticosteroids improve tissue perfusion and lessen the increase in extracellular water that usually accompanies CPB.⁴⁰⁹ Although some studies have reported improved clinical status when steroids are given in the manner described, this matter remains controversial.⁴⁰⁸ Methylprednisolone in a single dose of 30 mg · kg⁻¹ or dexamethasone in a single dose of 1 mg · kg⁻¹ given at the onset of CPB and not repeated may be advantageous. These agents do not appear to reduce complement activation, but there is evidence to support the hypothesis that they attenuate complement-mediated leukocyte activation, particularly that associated with reperfusion of the heart and lungs in the latter part of CPB.⁴₁₃,⁴₁₅,⁴₁₆,⁴₁₇,⁴₁₈

In piglets, corticosteroids provide brain protection during operations that involve hypothermic CPB.⁴₁₈

The powerful antifibrinolytic agent aprotinin is a biological product that acts as a serine proteinase inhibitor. It may have a favorable effect on some platelet membrane-specific receptors, specifically GPIb. Aprotinin has been shown in several randomized studies to reduce bleeding after CPB by about 50%.⁴₂₇,⁴₂₈ F₂₀, F₂₈, R₂₄, V₆, V₇, W₁₇ but as mentioned previously, the drug is no longer available for use during cardiac surgical procedures. e-Aminocaproic acid (EACA) and tranexamic acid are two other antifibrinolytic agents that can be administered before, during, and after CPB to reduce bleeding and the need for allogeneic blood transfusions.⁴₅₅, C₄, G₂₉, L₄, L₅, M₃, M₃₂, N₁₅, T₇ EACA is administered using an empirical dose of 10 g before the skin incision, 10 g during the procedure, and 10 g early postoperatively.⁴₅₆
Alternatively, it can be given at a dose of 150 mg · kg⁻¹ at the time of the skin incision, with an additional 30 mg · kg⁻¹ for 4 hours upon initiation of CPB.⁵¹⁹ Tranexamic acid is given at a dose of 1 g before the skin incision, 500 mg in the pump prime, and 400 mg · h⁻¹ during the procedure.⁶⁴

Changes during Cardiopulmonary Bypass

During CPB for cardiac surgery, blood loss in the operative field and gradual increase in interstitial fluid and urinary output combine to steadily deplete the patient-machine blood volume. Usual practice is for the perfusionist to add increments of a balanced electrolyte solution to maintain the volume at a safe level; in adults, up to 2000 mL may be added. Unless special precautions are taken, such as avoiding return of irrigating fluids to the pump-oxygenator by cardiotomy pump suckers and using ultrafiltration during the final stages of CPB, severe hemodilution results and persists into the postbypass period.

In neonates and infants, ultrafiltration immediately after CPB (before removal of cannulae) is often advisable using the modified ultrafiltration (MUF) technique introduced by Elliot.⁵¹¹ Its efficacy has been confirmed by others.⁵¹²,⁵¹³ In children and adults, ultrafiltration may be performed during the latter part of CPB if the hematocrit is below about 0.25 and there is excess volume in the pump-oxygenator. If not, it may be performed after discontinuing CPB, slowly circulating blood through the patient before any cannulae are removed. A third option, and one that is frequently used, is ultrafiltration of the volume remaining in the pump-oxygenator after CPB is discontinued and the venous cannulae have been removed. Hemoconcentrated pump-oxygenator volume is then infused slowly into the patient before the arterial cannula is removed (see Pump-Oxygenator in Section III).

Total Systemic Blood Flow

Although total CPB has generally been considered to require two separate caval cannulae and occlusive tapes around each cannula, a single large, properly designed, and properly positioned venous cannula can direct all venous return to the pump-oxygenator and provide total CPB.

During total CPB, systemic blood flow (perfusion flow rate) is controlled by the perfusionist. It can be set at an arbitrary level or may be kept equal to the venous return from the patient. A rational approach is to set it at an arbitrary level.

In clinical practice, when body temperature is at 28°C or greater, a flow of 2.5 L · min⁻¹ · m⁻² is usually chosen for infants and children younger than about 4 years, and a flow of 2.2 L · min⁻¹ · m⁻² for older patients. For adults with a body surface area of 2.0 m² or more, a flow of 1.8 to 2.0 L · min⁻¹ · m⁻² may be chosen to avoid the disadvantage of high flow through the oxygenator. When moderate hypothermia is chosen, the CPB flow can safely be reduced to about 1.7 L · min⁻¹ · m⁻² for prolonged periods (Fig. 2-11). When cardiac operations are performed with body temperature reduced to 18°C to 20°C in neonates, infants, or adults, CPB flows of 1 L · min⁻¹ · m⁻² are adequate for prolonged periods, at least as judged by persistence of the somatosensory evoked response (SSER) under these circumstances.⁶²¹ Flows as low as 0.5 L · min⁻¹ · m⁻² (20-30 mL · min⁻¹ · kg⁻¹) have been shown to be adequate at these temperatures to maintain cerebral oxygen consumption and ATP levels for at least 30 to 60 minutes.⁵¹⁹,⁶²⁵,⁶³⁳,⁶³⁹

When flow rates are lower than optimal for more than a short time, VO₂ is considerably subnormal (<85% of the asymptote of the temperature-specific curve in Fig. 2-11 is considered subnormal), primarily as a result of perfusion of less than the total capillary bed. Also, the areas of the capillary bed that are open are underperfused, resulting in lactic acidemia and metabolic acidosis.

PO₂ and saturation (SVO₂) have been widely used as indices of adequate perfusion flow rate (see Box 2-3; for references, see Harris and colleagues⁵¹⁹), the assumption being that these values reflect average cellular PO₂. If Q is high and the entire microcirculation perfused, this is true. However, it has been shown that during CPB, with Q within the conventional range, SVO₂ is inversely related to VO₂.⁵¹⁹ This might have been predicted from the Fick equation:

\[
\dot{V}O_2 = \dot{Q} (CaO_2 - C\bar{V}O_2)
\]

(2-1)

where CaO₂ is arterial oxygen content, CVO₂ is mixed venous oxygen content, and Q is flow rate.

If VO₂ and CaO₂ are fixed, CVO₂ increases with Q. If instead Q and CaO₂ are fixed, CVO₂ increases as VO₂ decreases, and VO₂ may decrease, despite a perfectly adequate Q, if the capillary bed is not evenly perfused. In this case, the distance between perfused capillaries and many tissue cells increases, and these cells do not obtain their oxygen
requirement. In effect, this amounts to a shunt of arterial blood into the venous system. This effective shunt may at times amount to half the total flow. Rudy and colleagues, using microspheres in normothermic rhesus monkeys during CPB, found that shunting was only 1.4% of total $Q$.\textsuperscript{26}

A high $VO_2$ or $SV_0_2$ does not, therefore, mean that cellular oxygenation is satisfactory whatever the $Q$. A $VO_2$ at or around the whole-body requirement does. The $VO_2$ is not difficult to calculate during CPB; the problem is, rather, to decide what the oxygen requirement is in a given case.\textsuperscript{19,320} Moreover, if $VO_2$ is less than the usual levels at conventional $Q$, increasing $Q$ probably will not increase $VO_2$ (see Fig. 2-11). The fault is not in $Q$ but in the capillary bed or at the cellular level.

As might be expected, high $Q$ is achieved at the expense of some loss of safety and convenience in other variables. Blood trauma in the oxygenator is probably greater when high blood flows pass through it. With a bubble oxygenator, risks of gaseous emboli are also greater. Pressure gradients across the arterial cannula are greater at high $Q$. This increases cavitation, blood trauma, and the risk of bubbles forming as blood emerges from the cannula.

### Arterial Pressure Waveform

CPB is usually conducted in such a manner that the arterial pressure pulse is very narrow and essentially nonpulsatile, but if desired, a pulsatile arterial input can be achieved in several ways. One is by using left ventricular ejection. With no tapes around the caval cannulae, arterial flow to the patient may be temporarily increased over venous return, or venous return may be temporarily reduced by partially occluding the venous tubing. Atrial pressures and thus venous filling pressures are increased, left ventricular ejection augments systemic blood flow, and a somewhat pulsatile arterial blood flow results. In other words, pulsation is achieved by partial CPB. This mechanism is used during cooling and rewarming whenever cardiac action is sufficiently vigorous to prevent overdistention of the heart during the process. The procedure of partial CPB produces not only some arterial pressure pulsations but some pulmonary blood flow as well, with its favorable effect.

A pulsatile waveform can also be produced by using intraventricular balloon pumping during bypass.\textsuperscript{28} A third method is to use a pulsatile arterial pump.

Effects on the organism of using a system that results in a pulsatile rather than nonpulsatile arterial waveform during CPB have been questioned since the beginning of clinical CPB. Increasing the venous pressure requires more intravascular volume and often additional priming volume. Venous pressure should therefore be kept close to zero, and certainly not more than 10 mmHg, to minimize increases in extracellular fluid.

Extensive reviews of this subject have been presented.\textsuperscript{22,13}

A randomized clinical study by Singh and colleagues investigated pulsatile versus nonpulsatile flow during moderately hypothermic (25°C-30°C) CPB.\textsuperscript{319} No statistically significant differences between the two techniques were found in whole-body $VO_2$, blood lactate concentration, systemic vascular resistance, urine flow, or thermal gradients. Thus, no evidence was found that pulsatile flow improved perfusion of the microcirculation during clinical CPB. It is possible that pulsatile flow would result in fewer functional derangements at lower flows than were used in this study.\textsuperscript{321,322}

Bixler and colleagues found that nonpulsatile perfusion of a hypothermically fibrillating dog’s heart at a mean pressure of 50 mmHg resulted in subendocardial ischemia, whereas pulsatile flow did not.\textsuperscript{321} When the mean perfusion pressure was 80 mmHg, neither pulsatile nor nonpulsatile flow resulted in subendocardial ischemia.

It is also possible, but not proven, that pulsatile flow has an advantage over nonpulsatile flow in infants. Williams and colleagues drew this conclusion from a clinical study in which they found more rapid cooling and rewarming and greater urine flow with pulsatile flow.\textsuperscript{319} Results of this study are difficult to interpret, however. Finally, pulsatile flow could prove beneficial in high-risk patients who come to operation desperately ill with end-stage disease (low cardiac output, acidosis, or renal failure).\textsuperscript{319}

Currently, there is insufficient evidence to conclude that pulsatile flow from the pump-oxygenator importantly reduces the ill effects of the relatively short periods of CPB required for cardiac surgery in the great majority of patients.

### Systemic Venous Pressure

During CPB, systemic venous pressure is determined by the techniques used,\textsuperscript{13} because:

$$P_V = \frac{Q \times \text{viscosity}}{\text{Cannula size, venous tubing size}},$$

where $P_V$ is mean systemic venous pressure, $Q$ is systemic blood flow rate, and $f$ means “a function of.” The cross-sectional area and length of the single or multiple venous cannulae, and to a lesser extent (because it usually has a large diameter) those of the venous tubing, are fixed factors determining venous pressure during total CPB. For this reason, the largest venous cannulae compatible with the clinical situation are commonly used, mindful of the need for the cannulae to lie loosely, not snugly, in the caval veins. When smaller cannulae are used, the other variables in Equation 2-2 can be manipulated. For example, systemic blood flow can be reduced or suction applied to the venous return to ensure an acceptable venous pressure (see “Vacuum-Assisted Venous Return,” earlier).

There is no apparent physiologic advantage in having a central venous pressure greater than zero during total CPB. Increasing the venous pressure requires more intravascular volume and often additional priming volume. Venous pressure should therefore be kept close to zero, and certainly not more than 10 mmHg, to minimize increases in extracellular fluid.
Pulmonary Venous Pressure

Ideally, pulmonary venous pressure should be at zero during total CPB, and certainly not more than 10 mmHg. Undue elevations are dangerous because they produce increased extravascular lung water and eventually gross pulmonary edema, according to the Starling law of transcapillary fluid exchange (neglecting lymph flow):

\[ P_t - P_c = \pi_c - \pi_t \]  (2-3)

where \( P_t \) is effective blood pressure within the capillary, \( P_c \) is tissue turgor pressure (interstitial fluid pressure), \( \pi_c \) is osmotic pressure of the plasma (colloid) inside the capillary, and \( \pi_t \) is osmotic pressure of the extracellular fluid (tissue colloid osmotic pressure).

Increase in extracellular lung water is related to duration of elevation of pulmonary venous or pulmonary capillary pressure, other things being equal. Not only can pulmonary edema result, but a combination of the damaging effects of CPB and increased pulmonary venous pressure can lead to pulmonary hemorrhage. Maintaining a very low pulmonary venous pressure will not always eliminate these complications.

Maintenance of a low pulmonary venous pressure can be ensured by monitoring left atrial pressure in patients undergoing CPB (see Section III). In most clinical settings, there is little tendency for pulmonary venous pressure to increase. If it does, the pulmonary venous system can be decompressed by suction on either a catheter (or an opening) in the pulmonary trunk, because no valves are present in pulmonary veins, or a catheter inside the left atrium or left ventricle.

Temperature

Since the introduction by Brown and colleagues of an efficient heat exchanger for extracorporeal circulation, temperature of the perfusate, and secondarily of the patient, has been controlled by the perfusionist.\(^{854} \) In decisions regarding temperature of the patient during CPB, several facts must be considered. Flexibility of CPB is achieved when it is combined with hypothermia. Hypothermia of even moderate degree appears to blunt some of the damaging effects of CPB.\(^{855} \) It allows use of lower pump \( Q \) with less blood trauma and achieves better myocardial protection and protection of other organs than normothermic CPB.\(^{856} \) Systemic hypothermia also provides a margin of safety for organ protection if equipment failure occurs. The patient’s body temperature is the most important determinant of the length of safe circulatory arrest time (see Section I).

Moderate hypothermia is used in many patients, and we consider at least mild hypothermia (31°C-34°C) to be advisable in essentially all cases. A nasopharyngeal temperature of 14°C to 20°C is chosen when circulatory arrest is required.

During core cooling, blood entering the patient’s aorta should be kept no greater than 10°C to 14°C below the nasopharyngeal temperature to minimize the tendency for gas to come out of solution when the cold blood is warmed by the patient. This is a conservative recommendation, in that some groups use the coldest perfusate temperature obtainable (4°C-5°C) once CPB is initiated.

Because blood is damaged by temperatures greater than 42°C, and the boundary layer of blood next to the wall surface of the heat exchanger probably reaches the temperature of that surface and thus of the water on the other side of the wall, water temperature should not exceed 42°C during rewarming. Blood temperature should not exceed 39.5°C during rewarming. Solubility of gas in blood is decreased when blood is warmed, but this is not a problem when the heat exchanger is upstream (proximal) to the oxygenator. When it is downstream (distal) to the oxygenator, it is a potential problem during rewarming, and a bubble trap may be interposed in the arterial tubing downstream to both. In general, maintenance of a temperature gradient from the heat exchanger to the blood of not more than 10°C to 12°C will prevent bubble formation.

RESPONSE VARIABLES

Alberts and colleagues state in their textbook: “There is a paradox in the growth of scientific knowledge. As information accumulates in ever more intimidating quantities, disconnected facts and impenetrable mysteries give way to rational explanations, and simplicity emerges from chaos. The essential principles of a subject gradually come into focus.”\(^{857} \) The patient response to CPB using current techniques and equipment is still largely described by “disconnected facts and impenetrable mysteries,” but considerable effort has been made to develop simplicity and reduce chaos. Continued interest in this response has stimulated the search for more cohesive knowledge and ways of minimizing unfavorable outcomes of cardiac surgery using CPB and whole-body perfusion from a pump-oxygenator.

Unfavorable aspects of the response of the patient to CPB and use of a pump-oxygenator were evident during the early days of open cardiac surgery, but tended to be overlooked in the excitement generated by this new technology. Subsequently, surgeons observed that (1) diffuse bleeding was more common with CPB than after other types of surgery; (2) some patients, particularly small ones, became edematous during the procedure; (3) occasionally severe and truly malignant hyperthermia occurred with no demonstrable infection; (4) pulmonary dysfunction was sometimes unexpectedly prominent; and (5) the heart often did not perform as well as anticipated after its repair. Yet they also noted that many patients appeared to be free of these developments, and most survived. Since then, more information has been gathered, but not as much as is desirable.

Whole-Body (Nonspecific) Inflammatory Response to Use of a Pump-Oxygenator

Diversion of blood through nonendothelialized channels to, through, and from pumps and the oxygenator appears to stimulate the organism to recognize the extracorporeal system as nonself. Thus, potential is present for the specific immune and nonspecific inflammatory response systems to be activated. Specific immune responses of an immunologically naive (unprepared) patient are slow to develop and not in evidence during the first few days after CPB. In any event, they are generally not strong. Nonspecific inflammatory responses appear rapidly, and in a few patients they dominate the early minutes, hours, and days after use of a pump-oxygenator. We initially named this response the whole-body inflammatory response, which we hypothesized unified the many diffuse responses to exposure of blood to abnormal events.\(^{858} \) It is now often called the systemic inflammatory response.
response syndrome (SIRS) because processes other than CPB can stimulate it.

**Humoral Response**

Initial response is probably humoral, initiated by the contact of plasma with the foreign surfaces of the tubing and pump-oxygenator and with air. Gas exchange requires a large surface area; it is therefore in the oxygenator that the greatest stimulus to this response occurs. Humoral response appears to begin with activation of specialized plasma proteins, developed and conditioned throughout centuries of life to recognize and repel transcutaneous invaders. Whereas previously this invasion has generally been a relatively small, localized, and often extravascular process, in the patient exposed to a pump-oxygenator it is a massive intravascular process. Even though the patient is heparinized, parts of the coagulation cascade respond virtually immediately to the activating capability of the foreign surface, as do the complement, kallikrein, fibrinolytic, and other cascades. Activation of Hageman factor (factor XII) may be the initial event in activation of these cascades, although platelets appear to be independently activated at about the same time. Nearly all the split products resulting from these multiple activations can be found in the patient's blood during and, for a time, after bypass. Mechanisms for their disappearance have not been elucidated, but presumably they are to some extent metabolized, taken up by specific cell-surface receptors, dissipated into extravascular fluids, including peritoneal and pleural fluids, and excreted in the urine.

Products of activation of these cascades have powerful physiologic effects, both directly and by activation of other systems and cells. The complement cascade, once activated, results in the production of powerful anaphylatoxins (C3a and C5a) that increase vascular permeability, cause smooth muscle contraction, mediate leukocyte chemotaxis, and facilitate neutrophil aggregation and enzyme release. Complement activation occurs through either the classic or the alternative pathway.

Contact activation of Hageman factor also immediately initiates the kallikrein-bradykinin cascade, resulting in the production of bradykinin. Plasma kallikrein circulates in the blood as a precursor, prekallikrein, 75% of which is bound to high-molecular-weight kininogen (HMWK) in the plasma. Bradykinin, formed largely from HMWK, increases vascular permeability; dilates arterioles; initiates smooth muscle contraction, and elicits pain. Kallikrein also activates Hageman factor and plasminogen to form plasmin, again demonstrating the complex interactions and feedback loops between the various reactions of blood to nonself.

Once activated, the contact activation system overcomes its normal regulating system, and all the responses are amplified. Because plasma kallikrein leads to conversion of plasminogen to plasmin, whose basic function in the circulation is to digest fibrin clots and thrombi, the fibrinolytic cascade is activated by this and other humoral and cellular mechanisms.

**Cellular Response**

Blood cells and endothelial cells participate in the nonspecific inflammatory response to use of a pump-oxygenator. Lymphocytes (both antibody-forming B cells and T cells) are part of the specific immune system and, as indicated earlier, participate little in the response to CPB in the usual immunologically naive patient. Eosinophilic granulocytes also seem to have limited participation. Basophilic granulocytes (mast cells) may well participate, but the extent to which they do so is not clear, and the same is true of the natural killer (NK) cells within the leukocyte family. Monocytes, once activated, participate in the cellular response.

**Neutrophilic granulocytes** (polymorphonuclear leukocytes) play a major role in the response to CPB. Neutrophils are activated by complement and other soluble inflammatory mediators. When activated, they migrate directionally toward areas of higher complement concentration (usually in the tissues, but during CPB, probably in blood), change their shape, become more adhesive, and secrete cytotoxic substances, including oxygen-derived free radicals. Of importance—and possibly a clue as to why most patients recover uneventfully from cardiac operations in which CPB is used, despite the strong humoral and cellular response—is the fact that complement can also desensitize neutrophils, thereby reducing their ability to participate in the inflammatory response. Neutrophils are also activated by other humoral agents participating in the cascades in the blood, including kallikrein, as well as by other inflammatory mediators (cytokines) generated by cells, including tumor necrosis factor (TNF) and platelet activating factor (PAF). These molecules also have been shown to increase in amounts both during and early after CPB.

**Platelets** are strongly affected by CPB using a pump-oxygenator, but in a complex manner that has been well summarized by Edmunds and colleagues. As in the case of neutrophils, platelets must be activated from their normally passive state; this occurs within 1 minute of the start of CPB. The precise initial trigger is uncertain, but possibilities include direct surface contact, abnormal shear stresses, mechanical lysis, exposure to adenosine diphosphate, and unidentified chemical agonists. The mechanism for activation of platelets is exposure on the surface of the platelet of numerous specific membrane receptors. Exposure of the fibrinogen glycoprotein receptors (GPIIb-IIIa complex), and subsequent binding of fibrinogen to them, are essential for adherence of platelets to the foreign surfaces of the pump-oxygenator and for their aggregation. Many other specific receptor sites are expressed and exposed by activated platelets. Control, feedback, and amplification mechanisms regulate platelets as well as the humoral systems, all of which are involved in the response to CPB.

**Endothelial cells** do not pass through the pump-oxygenator, but their complex activities are affected while the patient is connected to it. Triggering mechanisms are not clearly defined, but they probably include abnormal pressures and shear stresses, localized ischemia, and increased concentrations of normal and abnormal substances and cells in the blood. As a result, endothelial surface receptors are exposed, substances are elaborated and extruded, and spaces between the endothelial cells and their membranes are enlarged. Endothelial and other cells, particularly those in the locally ischemic areas that surely exist during CPB, express phospholipid molecules derived from arachidonic acid (eicosanoids). These are important mediators of inflammation and include the prostaglandins, thromboxanes, leukotrienes, and lipoxins. Other cells in areas of acute inflammation that may be present during CPB can produce soluble factors (cytokines) that normally act on other cells to regulate their function; after
CPB, they can induce elevation of body temperature, among other things.

**Metabolic Response**
Magnitude of the acute elevation of catecholamine levels in the blood that develops during CPB (see “Catecholamine Response” later in this section) is a measure of severity of the stress reaction induced by most cardiac surgery using CPB. Thus, in addition to the responses induced by CPB, cardiac operations and CPB induce the important perturbations associated with other major operations and trauma. Characteristics of this “metabolic response to stress” have been intensively studied by a number of investigators and clinicians. Among the first was Cuthbertson in 1930, and among the most prominent, Francis D. Moore. The essence of this process has been well summarized by Wilmore.

The human body responds to these stresses with dramatic resilience. For example, following injury, clotting mechanisms are immediately activated to reduce blood loss; body fluids shift from the extravascular compartment to restore blood volume; blood flow is redistributed to ensure perfusion of vital organs; and respiratory and renal functions compensate to maintain acid-base neutrality and body fluid tonicity. Following these acute adaptations, other changes occur; these responses are more gradual and prolonged but are apparently necessary for recovery of the injured organism. A variety of immunologic alterations are initiated; leukocytes are mobilized, macrophages and specialized T cells are produced, and “acute phase” plasma proteins are synthesized by the liver. Inflammatory cells invade the injured area, set up a perimeter defense, and engulf the dead and dying cells and other wound contaminants. These initial steps are followed rapidly by ingrowth of blood vessels, appearance of fibroblasts that build collagen scaffolding, and a host of other local changes that aid wound repair.

Local changes that occur at the injury site are accompanied by systemic alterations in body physiology and metabolism. Cardiac output is elevated, minute ventilation is increased, and the patient becomes febrile. Lipolysis and skeletal muscle proteolysis are accelerated, providing an ongoing fuel supply and an immediate source of amino acids that are utilized for wound healing and synthesis of “acute phase” proteins and new glucose. The glucose provides essential energy for the brain and other vital organs and for healing of the wound.

Phenomena associated with CPB not only produce their own damage but also interfere with the metabolic response to stress, a process necessary for recovery. Uneventful recovery of most patients after cardiac surgery means that a vast array of control and counteractive phenomena of both humoral and cellular types is in place, many of which await discovery and exploitation.

**Details of the Whole-Body Inflammatory Response**

**Neutrophil Activation**
During CPB, an initial mild leukopenia develops, which soon returns to baseline values. Similar changes occur without an oxygenator in the system and are in part the result of transient movement of leukocytes out of the vascular system. By the end of CPB, leukocytosis is present, consisting primarily of mature segmented forms of neutrophils (coming primarily from the bone marrow, most of which are activated). Leukocyte count often increases to a peak of 12,000 to 24,000 cells · mL⁻¹ at 24 to 28 hours postoperatively. Both T and B lymphocytes are decreased early after CPB, and T-cell function is decreased.

Pulmonary sequestration of neutrophils occurs during CPB. An inflammatory response follows their disruption and release of proteolytic and vasoactive substances and powerful lysosomal enzymes, contributing to the increased vascular permeability associated with CPB (see “Complement Activation” later in this section). Also, activation of neutrophils during CPB by the C3a and C5a complement fragments liberates oxygen-derived free radicals; this contributes to the damaging effects of CPB. Neutrophil elastase, a connective tissue protease and product of neutrophil activation that appears in plasma, is considerably increased by CPB, and the peak concentration correlates positively and closely with the duration of CPB. Such proteases break down elastin, collagen, and fibronectin, destroying extracellular structures, and contribute to the capillary leak that leads to postoperative extracellular volume overload and electrolyte imbalance.

Neutrophils in healthy persons are distinct cells. By inference, these cells are inactive and unprepared for the numerous deleterious effects they exert during and early after CPB. However, when stimulated, neutrophils transiently aggregate and cluster with each other and to other cell types, such as vascular endothelial cells. The process of aggregation and clustering is rapid, mediated by cell adhesion molecules (CAMs), and a critical step in development of inflammatory and immune responses. In myocardial infarction, anti-CAM antibodies of specific types, which can be produced by monoclonal techniques and can attenuate or prevent neutrophil aggregation and clustering, have been shown to considerably reduce the extent of cell death produced by ischemia and reperfusion.

Gillinov and colleagues used the anti-inflammatory agent NPC15669 to inhibit neutrophil adhesion in a CPB model and found a marked decrease in pulmonary injury. Nifedipine, infused during CPB in doses of about 6 µg · kg⁻¹ · h⁻¹, appears to inhibit neutrophil activation. Hypothermia has been shown to delay, though not prevent, the expression of neutrophil adherence molecules. Other interventions that have been evaluated clinically and experimentally to reduce the adverse effects of neutrophil activation include leukocyte filtration and pharmacologic agents (aprotinin, oligosaccharide antagonists, antioxidants, corticosteroids, and omega-3 fatty acids).

**Platelet Response**
In vitro test circuits show that the platelet count (corrected for dilution) decreases within 2 minutes of the beginning of extracorporeal circulation to about 80% of the pre-CPB level. By 8 minutes, the count has decreased to about 70% of the pre-CPB level and then stays close to that level during the rest of CPB and the period thereafter. Decrease in platelet count during clinical CPB tends to be greater than this because of hemodilution. Cardiotomy sucker systems substantially reduce platelet count. Interestingly, membrane oxygenators are associated with greater reduction than bubble
oxygenators. As a result of these and other factors, the number of platelets in circulating blood post CPB decreases to about 60% of the prebypass value and does not correlate with duration of CPB.

Sequestration of platelets in the liver and other organs during CPB in humans is slight and therefore not a major factor in reducing the platelet count. Something other than mere loss of platelets by adhesion to foreign surfaces is involved, because the platelet count continues to be low in some patients for as long as 72 hours postoperatively. One factor may be reduced survival time of platelets after CPB. Shear stresses likely do not reduce either the number or function of platelets.

More complex and probably more important than the change in numbers are qualitative changes that occur in the platelets of patients undergoing CPB. Normally, platelets adhere only to cut ends of blood vessels and to subendothelial surfaces (presumably because subendothelial collagen causes them to adhere). Once CPB begins, platelets almost immediately adhere to foreign (nonendothelial) surfaces. Once this process begins, platelets also begin to clump (aggregate), primarily on the foreign surfaces they have already adhered to. There is some evidence that initial aggregation is in small clumps (primary aggregates) capable of deaggregating. If the stimulus is strong, however, these primary aggregates are transformed into larger aggregates. It is believed that only then do platelets begin to release the contents of their granules and become irreversibly activated. Aggregates break off on occasion and become particulate emboli. Either platelets aggregate and disaggregate for many days after CPB, or the aggregates formed during CPB persist in the circulation, because platelet aggregates can be seen passing through the retinal vessels of patients for days after cardiac surgery with CPB.

As blood circulates normally through endothelially lined tubes, platelets are generally inactive. The stimulus to platelet adherence and aggregation on the surfaces of the pump-oxygenator system, whatever it may be, also activates the platelets, a process that changes their form and internal architecture. This activation causes platelets to expose or assemble specific membrane receptors on their surfaces—for example, membrane glycoproteins Ib and IIa (which bind fibrinogen) and GPIb (which binds von Willebrand factor)—with a resultant cascade of further platelet adherence to the foreign surfaces and aggregation. The activation process simultaneously affects platelet granules, which are concentrations of selectively sequestered intraplatelet substances. These substances include (1) serotonin, ATP, adenosine diphosphate, pyrophosphate, and calcium in the “dense bodies”; (2) α-thrombin, β-thromboglobulin, platelet factor 4, and platelet-derived growth factor; and (3) lysosomes. When activated, prostaglandin synthesis (arachidonic acid cascade) and other reactions take place in the surface membrane of the platelet as well as within it and lead to external secretion of the highly reactive components of the platelet granules. The entire process may well contribute to a number of the damaging effects of CPB.

As is usual in the humoral and cellular cascades, the same processes that lead to platelet activation lead virtually simultaneously to processes that inhibit it. This proceeds because platelets, like most cells in humans, contain adenylate cyclase, which converts ATP to cyclic adenosine monophosphate (cAMP). This conversion is greatly stimulated by products of the arachidonic acid cascade, which is known to be accelerated by CPB. In sufficient amounts, cAMP leads to inhibition of platelet adhesion, aggregation, change of shape, and secretion. This is part of the normal autoregulatory process, but it may be abnormally amplified during CPB.

Although platelet adherence to the foreign surfaces of the pump-oxygenator is the initial feature of the platelet response to CPB, and is surely accompanied by other major and complex responses, there remains a degree of uncertainty about subsequent events. There are even doubts as to whether platelet depletion and dysfunction are the primary causes of the bleeding tendency usually present after cardiac surgery. In any event, a short time after the first few minutes of CPB, about 60% of circulating platelets have a normal smooth discoid form, as do about 80% 8 minutes after the start of CPB and at the end of CPB. The implication is that either these platelets have never been activated (because they have just been released into the bloodstream or because foreign surfaces of the pump-oxygenator, passivated by absorption and denaturation of fibrinogen and albumin, no longer activate platelets), or they have been reversibly activated and returned to an inactive state. The latter is supported by the work of Zilla and colleagues but is contested by Edmunds. Sufficient irreversible activation occurs that partially degranulated platelets, platelets with damaged membranes, and platelet fragments can be recovered both during and at the end of CPB, along with a large number of normal-appearing platelets. Thus, by the end of CPB, platelet aggregability is reduced by 60% and bleeding time is prolonged, abnormalities that may persist more than 24 hours.

Most events during CPB that profoundly depress platelet function appear to take place initially in platelet membranes. During CPB, there appears to be a loss or inactivation of the functionally important glycoprotein-specific surface receptor sites. It is possible that abnormal shear stresses are partly responsible. The GPIIb receptor (to which plasma von Willebrand factor must bind for platelet adhesion) is markedly reduced shortly after the onset of CPB and remains low throughout bypass (Fig. 2-12). The GPIIb and IIIa receptors...
(which bind fibrinogen in a process that leads to platelet aggregation in the presence of extracellular calcium) are markedly reduced by the end of CPB.²⁻¹¹ Other changes in the platelet membranes may occur. Zilla has postulated, as have others, that the key to preventing loss of platelet function during CPB, and therefore to preventing the sometimes strong bleeding tendency associated with cardiac surgery, is to avert loss of action of platelet membrane-specific receptor glycoproteins.²⁵

Whatever the mechanisms and despite the high probability that development of platelet abnormalities is inherent in CPB as it is currently used, these alterations can be favorably influenced. The true membrane oxygenator, made from silicone rubber, appears to cause less platelet (and erythrocyte) damage than occurs with bubble oxygenators.²⁴ Aprotinin, no longer available for clinical CPB, may further lessen the development of platelet abnormalities (see Fig. 2-12 and “Other Additives,” earlier).

**Complement Activation**

Complement is a group of circulating glycoproteins that function as part of the body’s response to various kinds of injury such as traumatic, immunologic, or foreign-body insults.³¹ The complement system can be activated upon contact of blood with nonbiological surfaces, perhaps by way of Hageman factor, but other substances (e.g., thrombin, plasmin) can also activate it.

Complement activation during CPB was reported by Hairston, Parker, and Hammerschmidt and their colleagues.²³,³⁰ Complement consumption during CPB was demonstrated by Chiu and Samson.²⁶ Chenoweth and colleagues identified C3a, a complement breakdown product, in blood shortly after commencing CPB for cardiac surgery, and found that its continuing production was directly related to body temperature and perfusion flow rate.²⁰ The result is that more than 50% of patients have serum C3a levels above 1000 ng · mL⁻¹ at the end of operation with CPB (Fig. 2-13). Complement activation has also been demonstrated to occur during hemodialysis from exposure of blood to the dialysis membrane.²⁹,³³,³⁴ Complement activation in this setting is through the alternative pathway, with depletion of C3 but not C1,³³,³⁴ During CPB, activation is also through the alternative pathway.²¹,²⁶ Further complement activation by the classic pathway occurs after administration of protamine at the end of CPB,²⁰ this may add to the whole-body inflammatory response in some patients.²⁶

Recent studies suggest that complement activation after CABG with CPB is biphasic, with a second phase occurring between 8 and 48 hours postoperatively.²⁵,²⁶ The second phase appears to be activated by the classical pathway, not by the alternative pathway.²⁶ Bruins and colleagues demonstrated that higher peak levels of C4b/c on the second postoperative day correlated with increased occurrence of arrhythmia.²⁶

Magnitude of complement activation is affected by several factors that probably interact with still other factors in complex ways.²¹,²³,²⁶ The nature of the foreign surface has some effect; nylon is apparently a particularly potent complement activator.²⁶ True membrane oxygenators are weaker activators of complement than bubble oxygenators.²³ Duration of CPB has a weak positive effect on the final level of C3a, but administration of protamine has a considerably stronger effect.²³,²⁶,²⁷ Pretreatment of the patient with methylprednisolone or other steroids may decrease the amount of complement activation.²³

Adverse effects of complement activation relate to depletion of a component (complement) necessary for normal immune response and to adverse effects of the intravascular production of anaphylatoxins (C5a and C3a). Hairston and colleagues showed a decreased ability of postbypass serum to inhibit the growth of certain bacteria and related this in part to complement depletion.²³ Adverse effects of anaphylatoxins probably account for the degree of complement activation as a risk factor for morbidity after clinical CPB (Table 2-4, Fig. 2-14).

Pulmonary sequestration of polymorphonuclear leukocytes and neutropenia have been shown to develop during hemodialysis and to be temporally related to complement activation.²³ Similar observations have been made during CPB (see “Neutrophil Activation,” earlier).²⁶,²² That these changes are functionally significant is evident from the increased alveolar-arterial oxygen difference that develops during hemodialysis and after CPB, and from the pulmonary edema observed after CPB.²³³ Activation of complement has

![Figure 2-13](image)

**Figure 2-13** C3a levels at end of cardiopulmonary bypass, expressed in a cumulative percentile plot. Steep vertical (blue) line on the left represents closed cases, 100% of which had near-normal or normal levels. Curve on the right (red line) represents open cases, virtually all of which had increased levels. Fifty percent of patients had levels greater than 1000 ng · mL⁻¹, and 25% had levels greater than 1600 ng · mL⁻¹. (From Kirklin and colleagues.²⁶)

**Table 2-4** Incremental Risk Factors for Morbidity after Cardiopulmonary Bypass

<table>
<thead>
<tr>
<th>Incremental Risk Factor</th>
<th>Logistic Coefficient ± SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher C3a levels (ng · mL⁻¹) 3 hours after CPB</td>
<td>.0006 ± 0.00033</td>
<td>.07</td>
</tr>
<tr>
<td>Longer elapsed time of CPB (min)</td>
<td>.017 ± 0.0048</td>
<td>.0004</td>
</tr>
<tr>
<td>Younger age at operation*</td>
<td>−.71 ± .131</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Intercept</td>
<td>2.0 ± 60</td>
<td></td>
</tr>
</tbody>
</table>

Based on data from Kirklin and colleagues.²⁶

*Natural logarithmic transformation.

Key: CPB, Cardiopulmonary bypass; SD, standard deviation.
been shown to be directly involved in production of pulmonary edema. These findings suggest that neutrophil-mediated pulmonary endothelial injury (see “Cellular Response,” earlier) and increased lung vascular permeability, perhaps also mediated by reactive oxygen metabolites, may contribute to the adverse effects of CPB on pulmonary function. Similar sequestrations may take place in other organs.

That important complement activation is dependent on a large proportion of blood in the boundary layer (e.g., in an oxygenator or hemodialysis coil) is evident from the demonstration in sheep that a simple venovenous shunt produces no adverse effects on white blood cells, platelets, or pulmonary artery pressure. Addition of an oxygenator to the circuit results in a decrease in circulating white blood cells and in platelets (presumably from pulmonary sequestration) and in a marked increase in pulmonary artery pressure. Fountain and colleagues showed that infusion of complement-activated plasma produces the same result.

**Kallikrein-Bradykinin Activation**

Another humoral amplification system involves kallikrein and bradykinin. Several studies have shown important amounts of bradykinin to be present during CPB. Hypothermia itself appears rather ineffective in production of bradykinin. Immaturity, such as is present in young infants, results in less effective elimination of bradykinin. Exclusion of the pulmonary circulation probably also reduces the ability of the organism to cope with circulating bradykinin, because the lungs are the main site of bradykinin elimination. Bradykinin, a small peptide, is a powerful vasodilator, and this effect is probably important in the overall response of the organism to CPB.

Nagaoka and Katori demonstrated a reduction in peripheral resistance and in fluid requirement during CPB accompanied by the administration of aprotinin. This agent is known to neutralize the kallikrein-bradykinin system.

**Coagulation Cascade**

Coagulation, the formation of fibrin clots, is largely inhibited by heparin during CPB (see “Heparin Levels,” earlier under Controlled Variables), but the coagulation cascade is in part activated. Related or unrelated to this, coagulation is often defective for a period of time after CPB.

Normally, in the presence of damaged endothelium or an exposed subendothelium, platelets and soluble components of the coagulation cascade are activated. Through the contact phase, intrinsic phase, and extrinsic phase of activation, prothrombin is converted to thrombin, which acts on fibrinogen to produce fibrin monomers that polymerize spontaneously to form a fibrin clot. Were CPB to be started in a nonheparinized patient, the contact phase and intrinsic phase would be rapidly activated, and within a short time the pump-oxygenator would be filled with clot.

Because of the incomplete blockade of the coagulation cascade by heparin, small amounts of fibrin form even during routine CPB. Many of the soluble coagulation factors are mildly reduced by the end of CPB. Most authorities believe these changes are insufficient by themselves to be responsible for the bleeding tendency following CPB.

**Fibrinolytic Cascade**

The fibrinolytic cascade, another humoral amplification system, is probably activated to some degree in all operations in which CPB is used. Important hyperfibrinolysis was shown to be present in 159 (20%) of 774 patients undergoing CABG.

Naturally occurring inactive plasminogen (normally incorporated within thrombi) is transformed into the active fibrinolytic agent plasmin under certain circumstances, and measurable blood plasmin levels have been demonstrated in patients shortly after initiation of CPB. Because conversion of plasminogen to plasmin is facilitated by kallikrein, which also results from activation of Hageman factor, the fibrinolytic cascade may be initiated during CPB by activation of factor XII. However, extrinsic plasminogen activator expressed by endothelial cells has been shown to be the major stimulant for conversion of plasminogen to plasmin, and thus for the fibrinolytic cascade. A reasonable explanation for this behavior of endothelial cells during CPB is the abnormally high levels of such substances as catecholamines, bradykinins, and other molecules that are generated.

Because plasmin also serves as an activator of complement, prekallikrein, and possibly Hageman factor, the intravascular activation of plasminogen into plasmin (which in intact humans is usually a localized phenomenon) may continue to stimulate cascades of all the humoral amplification systems. Breakdown products of fibrinogen (produced to some extent by the coagulation cascade during CPB), when acted upon by plasmin, have been shown experimentally to lead to important pulmonary dysfunction. This is another example of the powerful effects of the intravascular occurrence of events that are usually localized and extravascular in intact humans.

For a time, it was conventional wisdom that excessive bleeding after CPB was primarily the result of platelet depletion and dysfunction. More recently, several lines of information strongly suggest that activation of the fibrinolytic cascade also contributes importantly to postoperative bleeding after cardiac surgery in which CPB is used. One of these is the favorable effect of aprotinin on bleeding, with most reports indicating a 50% reduction in bleeding after CPB when this drug is administered. However, its action is probably not limited to the antifibrinolytic effect of inhibition of plasmin. Plasmin itself appears
to cause platelet aggregation, and its inhibition by aprotinin could therefore favorably affect platelets as well as fibrinolysis.\textsuperscript{16}

**Arachidonic Acid Cascade**

The completely cellular arachidonic acid cascade is activated by a disturbance of cell membranes, which in turn activates phospholipase A\textsubscript{2}. This releases arachidonic acid from the phospholipid fraction of cells, but the arachidonic acid can also come from intracellular lipid pools. The cascade proceeds through the prostaglandin-endoperoxide (cyclooxygenase) pathway. Stationary, migrating, and intravascular cells are susceptible to the arachidonic acid cascade and liberate the active products, which exhibit a short half-life.

The lung, bypassed during CPB, is a major site of synthesis, release, and degradation of eicosanoids (products of the arachidonic acid cascade), although not necessarily the cellular source of those compounds. Prostacyclin and prostaglandin E\textsubscript{2} (PGE\textsubscript{2}) production appears to be sharply increased shortly after CPB is begun, but later when CPB becomes partial and some blood again passes through the lung, levels decrease.\textsuperscript{15} By contrast, thromboxane B\textsubscript{2} production (thromboxane B\textsubscript{2} is a stable metabolite of thromboxane A\textsubscript{2}) becomes apparent and reaches peak levels when total CPB becomes partial as the lungs again are perfused.\textsuperscript{15} Many researchers believe that most of the thromboxane A\textsubscript{2} comes from platelets, even though release occurs to a great extent in the lungs. PAF, another product of the cascade, appears to be an important mediator of inflammation.\textsuperscript{11,13}

Leukotriene B\textsubscript{4}, a product of the arachidonic cascade that promotes plasma leakage and leukocyte adhesion, is also increased during and for a time after CPB.\textsuperscript{15}

Details and overall effects of activation of the arachidonic acid cascade during CPB are not completely understood, but there is at least evidence that the magnitude of the release of both of these eicosanoids during CPB is greatest in the very young.\textsuperscript{24} The activation releases agents that are somewhat counteracting, including the vasoconstricting agent thromboxane A\textsubscript{2}, a PAF, and the vasodilating and platelet-inhibiting factors prostacyclin and PGE\textsubscript{2}.

**Cytokines**

Cytokines are soluble factors elaborated by cells of the immune system (e.g., T-cell lymphocytes) that normally act on other cells to regulate their function. During CPB, cytokines such as the interleukins (ILs) elaborate other mediators of the inflammatory process (e.g., TNF, leukocyte adhesion molecules, PAF), which in turn continue the process.

IL-1 is an intracellular derivative of stimulated mononuclear phagocytes and a mediator of fever, changes in endothelial cell function and permeability, and decreased vascular resistance.\textsuperscript{12,22} Its concentration in monocytes is increased during CPB and again 24 hours later.\textsuperscript{12} A positive correlation has been found between intracellular IL-1 activity and the patient’s temperature 24 hours after CPB.\textsuperscript{12} The interrelation between complement activation (which activates monocytes), prostaglandins (which also mediate IL-1 production), and IL-1 illustrates the complexity of the whole-body inflammatory response to CPB and the problems inherent in efforts to prevent its damaging effects.

IL-6 and IL-8 levels rapidly increase after initiation of CPB.\textsuperscript{12,25} Degree of cytokine response appears to correlate with duration of CPB and aortic clamping.\textsuperscript{12,3}

**Other Mediators of Inflammation**

TNF is released by activated monocytes (and macrophages) and is increased in many patients in the later stages of CPB and during subsequent hours.\textsuperscript{13} It is known to increase endothelial cell permeability and open interendothelial cell spaces, thereby promoting development of interstitial edema.\textsuperscript{52,53}

Endotoxin, a powerful stimulant of complement and endothelial activation, is also a potent agonist of release of TNF from macrophages and is elevated in some patients after CPB.\textsuperscript{14,60,61,62} Endotoxin release may be the result of translocation of bacteria from the gut as the result of splanchnic ischemia and possibly impaired function of Kupffer cells in the liver.\textsuperscript{72}

**Protein Denaturation**

Proteins are denatured by a blood/gas interface, such as in a bubble or stationary vertical film oxygenator, but are denatured considerably less in microporous and true membrane oxygenators.\textsuperscript{17} Denaturation of albumin has a nonspecific effect, but denaturation of immunoglobulins yields degradation products that activate the complement cascade.\textsuperscript{75}

**Oxygen Consumption**

**Total Body Oxygen Consumption**

Theoretically, total body \( \dot{V}_O_2 \) during CPB at normothermia (37\(^\circ\)C) should be that of an intact human under anesthesia, if all parts of the microcirculation are perfused. Yet, in two studies in humans, \( \dot{V}_O_2 \) during normothermic CPB at flows of 1.8 to 2.4 L \( \cdot \) min\(^{-1} \) \( \cdot \) m\(^{-2} \) was highly variable. Values of 74 to 162 mL \( \cdot \) min\(^{-1} \) \( \cdot \) m\(^{-2} \) were found in one study\textsuperscript{12,16}; in the other study, which consisted of 12 patients, mean \pm standard deviation of \( \dot{V}_O_2 \) was 131 \pm 20 L \( \cdot \) min\(^{-2} \).\textsuperscript{1,11}

A combined analysis of experimental studies in animals during normothermic CPB\textsuperscript{89,94,95} indicates a best-fit hyperbolic relationship between the perfusion \( Q \) and \( \dot{V}_O_2 \) (Fig. 2-15). \( Q \) in these studies was expressed in L \( \cdot \) min\(^{-1} \) \( \cdot \) m\(^{-2} \). (These units were not used in the excellent study of Andersen and Senning, nor could the data be recalculated in these terms, hence their exclusion.\textsuperscript{117}) The following linear regression equation was derived from the data:

\[
\dot{V}_O_2 = 0.4437 \cdot (Q - 62.7) + 71.6 \quad (2.4)
\]

where \( \dot{V}_O_2 \) is oxygen consumption expressed as a percentage of measured control value before bypass, and \( Q \) is flow from the pump-oxygenator, expressed as mL \( \cdot \) kg\(^{-1} \) \( \cdot \) min\(^{-1} \) (correlation coefficient = 0.83). Andersen and Senning noted, however, that \( Q \) and \( \dot{V}_O_2 \) must meet at zero and that the control value for \( \dot{V}_O_2 \) was usually reached at high flows (100-125 mL \( \cdot \) kg\(^{-1} \) \( \cdot \) min\(^{-1} \)).\textsuperscript{117} Visual observation of their scattergram suggests that the hyperbolic model derived from the combined analysis fits their data and ideas well.

Temperature of the patient is also related to \( \dot{V}_O_2 \) during CPB, as it is in intact, anesthetized, nonshivering subjects. Harris and colleagues were first to express mathematically the interrelation among \( Q \), temperature, and \( \dot{V}_O_2 \), but their data covered a narrow range of temperature.\textsuperscript{12,10} Complete data of the type desired are not available. Using the experimental data at 37\(^\circ\)C just described and the relation of \( \dot{V}_O_2 \) to flow at 20\(^\circ\)C measured during CPB in humans, a multivariable
Relationship of total body oxygen consumption \( (\dot{V}O_2) \) to perfusion flow rate \( (Q) \) at normothermia during nonpulsatile cardiopulmonary bypass. Figure contains two depictions. One is a scattergram of data from animal experiments \( (n = 213) \) performed at about 37°C by Cheng and colleagues\(^{23} \) \( (n = 33) \), Paneth and colleagues\(^{25} \) \( (n = 60) \), and Starr\(^{27} \) \( (n = 120) \). Note that scatter of data increases as flow increases. Second depiction is solid and dashed lines (presented as in Fig. 2-1), which is a solution of the hyperbolic equation (Appendix Equation 2A-2) derived from these data. The hyperbolic equation is chosen because the correlation coefficient, \( r \), was .69, whereas it was .39, .54, and .52 for the linear equation, log-log equation,\(^{106} \) and Arrhenius equation,\(^{81} \) respectively.

Cerebral Oxygen Consumption

Cerebral oxygen consumption is important during CPB, particularly hypothermic CPB at low flow, because cerebral \( \dot{V}O_2 \) that is reduced below the usual (normal) value at a given temperature implies incomplete or uneven cerebral perfusion (decreased effective capillary density). An equation has been developed from the data of Croughwell and colleagues that is reduced below the usual (normal) value at a given temperature implies incomplete or uneven cerebral perfusion (decreased effective capillary density). An equation has been developed from the data of Croughwell and colleagues that appears to be the best expression available of the normal relation during CPB at full flow \( (2.0 \text{ L min}^{-1} \cdot \text{m}^{-2}) \) between cerebral \( \dot{V}O_2 \) and temperature during CPB. It is presumably applicable to all ages\(^{37} \) (Fig. 2-16). Assuming that cerebral oxygen consumption at 37°C before CPB is the same as that at 37°C during CPB is inappropriate, because whole-body \( \dot{V}O_2 \) on CPB is a little less than off CPB. This may be from presumed uneven perfusion on CPB.

Cerebral oxygen consumption does not appear to change with the variations in cerebral blood flow that occur during clinical CPB.\(^{18,23} \) This is consistent with findings in experimental studies. For example, Fox and colleagues found that in monkeys on CPB at 20°C, cerebral oxygen consumption was the same at CPB flow rates of 0.5 and 1.6 L · min\(^{-1} \) · m\(^{-2} \), even though cerebral blood flow at 0.5 was 50% of that at 1.6.\(^{19} \)

Mixed Venous Oxygen Levels

Although mixed venous oxygen levels are related to the controlled variables of \( Q \), hemoglobin concentration of the perfusate, and \( P_aO_2 \) as expressed by the Fick equation (see Equation 2-1), they are also related to the patient’s response in terms of \( \dot{V}O_2 \) and thus to some partially controllable variables that affect \( \dot{V}O_2 \), such as pH and 2,3-diphosphoglyceric acid levels in red blood cells.\(^{341} \)

When most of the microcirculation is known to be perfused, \( P_vO_2 \) levels reflect the mean value for tissue oxygen levels. Thus, the assumption can be made that when \( P_vO_2 \) levels during CPB are relatively normal \( (P_vO_2, 30-40 \text{ mmHg}; S_vO_2, 60\%-70\%) \) and \( \dot{V}O_2 \) is relatively normal, tissue oxygen levels are relatively normal, and the whole-body perfusion is meeting the patient’s metabolic demands (see “Total Systemic Blood Flow,” earlier under Controlled Variables).

Metabolic Acid-Base Status

Metabolic acidosis tends to develop during CPB, even when apparently adequate flow rates are used.\(^{62} \) This is probably related to uneven distribution of flow during CPB, with the consequent development of underperfused areas that release lactic acid.\(^{22} \) Resultant metabolic acidosis is usually not severe, and the concentration of lactic acid rarely exceeds 5 mmol · L\(^{-1} \).\(^{318} \)

Hemolysis

Hemolysis of red blood cells during CPB has long been recognized. During the early years of open heart surgery, plasma hemoglobin levels during and after operation were monitored.
as an index of damage caused by the pump-oxygenator. However, serum hemoglobin levels during clinical CPB do not accurately reflect the amount of hemolysis, because hemoglobin either bound to haptoglobins or free when haptoglobin binding sites are saturated is continuously removed from the circulating blood by the reticuloendothelial system and kidneys. When the plasma free hemoglobin level exceeds about 40 mg · dL⁻¹, hemoglobin casts may form in renal tubules. There is little likelihood of renal shutdown from this effect unless the plasma hemoglobin level exceeds 100 mg · dL⁻¹.

Han and colleagues found plasma free hemoglobin levels to be 8.3 ± 1.3 mg · dL⁻¹ before CPB, 33 ± 3.6 mg · dL⁻¹ 10 minutes after the start of CPB, and 91 ± 8.4 mg · dL⁻¹ after CPB. The plasma free hemoglobin level may be still higher several hours after CPB. Classically, this has been explained as continuing destruction of erythrocytes damaged but not destroyed during CPB.

Red blood cell mass often declines still further during the first 3 or 4 postoperative days. Although in the past this has been attributed to the shortened half-life of damaged erythrocytes, the entire matter of hemolysis during and after CPB may be considerably more complex than this finding suggests. C₅b-₉, a product of complement activation, is deposited on the surface of erythrocytes during CPB. This may play a major role in hemolysis associated with CPB.

**Systemic Vascular Resistance and Arterial Blood Pressure**

At the onset of normothermic or moderately hypothermic CPB, systemic vascular resistance usually decreases abruptly. It then gradually increases toward normal throughout the period of CPB and may become higher than normal. Considerable variation exists from patient to patient in systemic vascular resistance and thus in systemic arterial blood pressure during perfusion. In patients with coronary artery disease, a high systemic vascular resistance tends to develop during CPB.

Precise mechanisms underlying these variations in systemic vascular resistance during clinical CPB have not been identified, except in one situation. When, after a protracted period of global myocardial ischemia, cardiac reperfusion is commenced, systemic arterial pressure and resistance decrease within about 30 to 45 seconds. This interval coincides with the time it takes the cardiac reperfusate to appear in the coronary sinus, return to the pump-oxygenator via the venous cannula, pass through that machine, and be returned to the patient. Contents of the coronary sinus blood first appearing after an appreciable period of global myocardial ischemia likely contain vasodilating substances that develop in the heart during the ischemic period. Some studies have suggested that this blood contains a large number of leukocytes that have been sequestered in the heart during global myocardial ischemia.

In general, it is not necessary to pharmacologically manipulate systemic vascular resistance during CPB, but some evidence indicates that cerebral blood flow is lower than desirable when mean arterial blood pressure during normothermic or moderately hypothermic CPB goes below about 40 mmHg. Therefore, when mean blood pressure is lower than 40 mmHg for more than a few minutes during rewarming, the rational approach is to increase systemic vascular resistance with pharmacologic agents that will elevate arterial blood pressure (see Chapter 4). Increasing Q above usual values during rewarming is generally ineffective in increasing arterial pressure. When systemic vascular resistance becomes so high during this phase of CPB that mean arterial blood pressure increases to more than 100 mmHg, it is prudent to reduce it pharmacologically to less than that level (see Chapter 4).

A vasoplegic syndrome (low systemic arterial pressure despite high cardiac output or CPB Q and adequate fluid infusion with low systemic vascular resistance) has been observed following onset of CPB. Patients who have a significant decline in mean arterial pressure early after initiation of CPB are more likely to become vasoplegic postoperatively and are more likely to die in the hospital or have a prolonged length of stay. Patients with the vasoplegic syndrome generally respond to an increase in systemic vascular resistance with an increase in mean arterial pressure.
syndrome have inappropriate low serum arginine vasopressin concentrations.\textsuperscript{21} Infusion of vasopressin increases blood pressure and reduces catecholamine requirements.\textsuperscript{21,112} Methylene blue has also been used to treat patients with catecholamine-resistant vasoparesis.\textsuperscript{114}

Other risk factors for developing the vasoplegic syndrome after CPB include preoperative angiotensin-converting enzyme inhibitor or beta-blocker use, low ejection fraction, use of pressors or aprotinin before CPB, low pre-CPB mean arterial blood pressure, longer length of CPB, higher temperature on CPB, and higher pre- and post-CPB hematocrit.\textsuperscript{21,10}

**Distribution of Blood Flow**

Distribution of blood flow during CPB cannot be assumed to be similar to that when the circulation is intact. Distribution (and thus regional and organ blood flow) during CPB may vary according to age of the patient, amount of hemodilution, $Q$, arterial pulse contour, any pharmacologic manipulation, temperatures of the perfusate and patient, and arterial $P_{CO_2}$, pH, and $P_O_2$. The specific effect of some of these variables on distribution of blood flow is unclear. There may well be species differences, making data based on human subjects the most useful.\textsuperscript{226}

**Cerebral Blood Flow**

Under conditions that often pertain in adults undergoing cardiac operations (nonpulsatile perfusion; flow 1.6 L · min$^{-1}$ · m$^{-2}$; temperature ± 25°C), cerebral blood flow (measured by radioactive xenon clearance) is about 25 mL · min$^{-1}$ · 100 g brain tissue$^{-1}$, with some variability depending on $P_{CO_2}$.\textsuperscript{221} During CPB in monkeys, a similar value has been found (using microspheres), representing about 6% of total systemic blood flow.\textsuperscript{118}

In humans, cerebral blood flow during CPB is no less in elderly patients than in other adult patients, and it appears to be proportionally similar in neonates and infants to that in adults.\textsuperscript{859,226,227} Thus, age appears to have little effect on the proportion of total flow represented by cerebral blood flow under usual circumstances of CPB.

During normothermic and moderately hypothermic CPB in adults and elderly patients, cerebral blood flow is not importantly altered with variations of mean arterial blood pressure.\textsuperscript{209,226} This is similar to the situation in normal awake adult humans, in whom cerebral blood flow does not vary significantly with variations of arterial blood pressure (mean) from about 60 to 150 mmHg. When arterial blood pressure during CPB falls below about 40 mmHg, cerebral blood flow may decline appreciably, with a concomitant decrease in cerebral oxygen consumption.\textsuperscript{99,17} A reasonable inference is that in adults on CPB, arterial blood pressure need not be manipulated pharmacologically unless it is less than 40 to 50 mmHg.

By contrast, during hypothermic CPB—at least in neonates, infants, and children—cerebral blood flow is dependent on arterial blood pressure.\textsuperscript{225,226,227} Corresponding variations in cerebral oxygen consumption have not been established with certainty. In view of this, arterial blood pressure should probably be kept above about 25 mmHg in this setting in young patients.

The effect of decreased CPB flow rate ($Q$) on cerebral blood flow in humans is incompletely understood, in part because of the interaction between perfusion $Q$ and arterial blood pressure (see Chapter 4).\textsuperscript{99} However, during moderately hypothermic CPB at the usual flow rates, there appears to be a direct correlation between CPB and cerebral blood flow rates, despite the poor or absent correlation between arterial blood pressure and cerebral blood flow.\textsuperscript{223}

Cerebral blood flow during CPB is affected by arterial carbon dioxide pressure ($P_{CO_2}$). Hypercarbia increases cerebral blood flow, whereas hypocarbia decreases it.\textsuperscript{221,1033,118} In children undergoing hypothermic CPB, the flow increases 1.2 mL · min$^{-1}$ · 100 g brain tissue$^{-1}$ for every 1-mmHg increase in $P_{CO_2}$ (measured at 37°C) between 33 and 50 mmHg.\textsuperscript{115} Infants have a slightly blunted response. Data gathered by Kern and colleagues are compatible with the hypothesis that under usual conditions of hypothermic CPB, metabolic needs of the brain are met with a $P_{CO_2}$ value of 33 mmHg.\textsuperscript{115}

Although autoregulation of cerebral blood flow has been described during normothermic and moderately hypothermic CPB, it may well be that it is the remainder of the body, not the brain, that accomplishes autoregulation. This was suggested by the experimental studies of Fox and colleagues.\textsuperscript{118}

Cerebral blood flow during CPB may at times be excessive in relation to cerebral oxygen consumption. For example, Croughwell and colleagues found that during CPB and reduction of the patient’s body temperature from 37°C to 28°C, cerebral blood flow decreased less than cerebral oxygen consumption. This was referred to as a situation of luxuriant cerebral blood flow accompanied by a narrowing of the cerebral arteriovenous oxygen difference.\textsuperscript{113} Similar luxury perfusion can result from hypercarbia, and it has been argued that this increases the risk of cerebral damage by microemboli.\textsuperscript{125,117} This is an argument against use of pH-stat strategy for control of $P_{CO_2}$ during CPB.

**Cutaneous Blood Flow**

Clinical information strongly suggests that blood flow to the skin is severely reduced during nonpulsatile CPB in humans. The small bald spot that develops on the back of the head after CPB in some patients is probably the result of the pressure produced by weight of the head on an area of poorly perfused skin in contact with even a well-padded pillow during operation. Ease with which burns are produced by the cautery pad may also be the result of poor blood flow to the skin during CPB.

Of interest, a study of the sublingual microcirculation in humans has shown that the proportion of perfused small blood vessels decreases importantly and similarly with induction of anesthesia in patients undergoing thyroidectomy, and cardiac surgery with or without CPB.\textsuperscript{256} In the CPB group, the proportion of perfused small vessels decreased after induction, improved slightly thereafter, failed to return to baseline, and persisted after 24 hours (Fig. 2-17). The off-pump cardiac surgery patients had less severe but statistically significant microcirculatory alterations immediately postoperatively. These alterations improved slightly but also persisted after 24 hours. Thus, microvascular perfusion was altered similarly in CPB and off-pump patients 6 to 24 hours after admission to the intensive care unit. In thyroidectomy patients, early changes reversed rapidly in the postoperative period. Severity of microvascular alterations correlated with peak lactate levels after cardiac surgery ($P < .05$).\textsuperscript{256} These findings suggest that
changes in the microcirculation cannot be attributed entirely to CPB.

Venous Tone

Veins constrict during CPB, and venous tone is increased. This mechanism may persist for some hours afterward. The mechanism has not been determined with certainty, but high levels of circulating catecholamines probably play an important role.

Catecholamine Response

Response of circulating epinephrine (released primarily from the adrenal medulla) and norepinephrine (which overflows into the bloodstream from generalized sympathetic nervous system discharge) has been studied by many groups, with somewhat conflicting results. However, it is now clear that CPB is associated with a massive catecholamine release, greater than that from nearly any other form of stress. With onset of CPB in adult patients with coronary artery disease, plasma epinephrine levels increase; they begin to decline after discontinuation of bypass (Fig. 2-18, A). Persisting elevation 1 hour after operation occurs only in patients with postoperative hypertension.

Plasma norepinephrine levels do not increase in adult patients who remain normotensive postoperatively, but in those with postoperative hypertension, it increases at the start of operation and reaches a peak at the start of CPB (Fig. 2-18, B). It remains elevated at 1 hour postoperatively in this group. These patients show arterial blood pressure responses typical for patients undergoing CPB, with a striking decrease at the onset of CPB from reduced systemic arteriolar resistance (Fig. 2-18, C).

Mean arterial blood pressure 1 hour after operation correlates positively with both plasma epinephrine and norepinephrine levels. Neonates, infants, and young children also demonstrate marked increase in catecholamine concentration during CPB.15,16,12,24

Sympathetic–adrenal system discharge during, and in some patients after, operation is presumably related to use of CPB. The increased catecholamine response, particularly of norepinephrine, is partly attributable to the fact that during CPB, blood does not pass through the lungs, where norepinephrine is largely inactivated.12

Adrenal Cortical Hormones

Clinical studies nearly uniformly demonstrate large increases in cortisol and adrenocorticotropic hormones with initiation of CPB. After CPB, patients exhibit markedly elevated levels of cortisol (free and total) for more than 24 hours. It is not clearly established whether the elevated corticosteroid concentrations during CPB are deleterious or beneficial.

Vasopressin

Vasopressin, or antidiuretic hormone (ADH), is secreted by the pituitary gland and is a potent regulator of renal water excretion. Cardiac operations employing CPB are associated with large increases in ADH concentration that exceed those during other major surgical procedures; they can persist early postoperatively.35,7,14,29

Body Composition

After CPB, extracellular fluid volume is increased.40 The increase is in the interstitial fluid compartment, as shown by increased interstitial fluid pressure during CPB. The plasma volume tends to be decreased. Plasma volume is also greater with hypothermia and higher CPB Q. The large thoracic duct lymph flow occurring during CPB is related to this tendency of the interstitial fluid volume to increase. Also, exchangeable sodium is increased after CPB, while total exchangeable potassium is decreased.

Amount and concentration of intracellular potassium are decreased. These acute changes are probably, at least in part, the result of some of the damaging effects of CPB, including increases in capillary permeability, which probably facilitate the changes in body composition.

Thermal Balance

Heat is lost during CPB. A study of 6 adult patients cooled to 30°C during bypass lasting 130 minutes showed a mean net loss of 1000 kJ of heat (1 kilocalorie = 4.2 kJ) by the end of hypothermia. Loss to the heat exchanger and pump circuit was 840 kJ, and evaporative and convective loss was 380 kJ; the patient’s metabolism supplied 220 kJ. During rewarming to a nasopharyngeal temperature of 37°C, the pump-oxygenator returned 670 kJ to the patient. Loss of heat during the period of anesthesia preceding bypass was not accounted for. Patients therefore left the operating room with a deficit of at least 330 kJ, equivalent to more than 1.5 hours of basal energy production. This deficit has to be restored early postoperatively, and the extra metabolism necessary to
Figure 2-18 Plasma catecholamines and arterial pressures (mean ± SE) in patients undergoing cardiopulmonary bypass (CPB) for coronary artery bypass grafting at various stages of operation and early postoperatively. Blue lines represent patients who were normotensive early postoperatively, and red lines those who were hypertensive. A, Epinephrine (Epi). B, Norepinephrine (NE). C, Mean arterial blood pressure (MAP). Key: CICU, Cardiac intensive care unit. (From Wallach and colleagues.)

Figure 2.19 Relation between duration of cardiopulmonary bypass (CPB) and increment in extracellular fluid minus plasma volume soon after operation (patients with heart failure are not included). Key: ECF, Extracellular fluid; PV, plasma volume. (From Cleland and colleagues.)

do this places a strain on the circulation that at times may be substantial. When deeper hypothermia is used, the problem is magnified, because muscle rewarms slowly and heat loss during operation is greater. It is necessary to bear in mind that the temperature of the muscles and body fat remains considerably lower than that of the nasopharynx after a short period of rewarming.

After CPB, a hypermetabolic state exists for at least 6 hours, sometimes longer. $V_O_2$ and carbon dioxide production are increased during this period, and body temperature may rise precipitously. The possible relationship between intracellular levels of IL-1 and hyperpyrexia is discussed earlier in this section under “Cytokines.”

AGENTS OF DAMAGE

Foreign Surfaces

Recognition by the cells that the surfaces in the pump-oxygenator system are foreign is a fundamental inciting agent for the damaging effects of CPB, as previously described. All elements of blood, formed and soluble, are affected. These phenomena were perhaps first reported by Lee and colleagues in 1972 and termed protein denaturation. In subsequent years, further effects of CPB on the complement cascade, white cell, and platelet elements and humoral and endothelial systems have been elucidated. Selectins, kallikreins, kinins, leukotrienes, TNF, proteases, cytokines, and others are activated, liberated, or suppressed during CPB, presumably by exposure to foreign or nonbiological surfaces or the blood/gas interface.

Because it is only in the boundary layer of flowing blood that the foreign surface is encountered, opportunity for damage is directly related to the proportion of the blood flowing there. Thus, it is in the oxygenator, where this proportion is deliberately made as large as possible to promote efficient gas exchange, that the opportunity for surface
interactions and damage is greatest. This includes bubble oxygenators, because gases themselves are recognized as foreign surfaces when in direct contact with blood. It is next greatest in the heat exchanger, next in filters, and least in tubing and reservoirs.

Some artificial surfaces are more interactive with blood than others; nylon may be a particular offender. Surfaces may be passified to some extent in the initial few minutes of CPB by deposition on them of denatured albumin, platelets, and other substances, but in oxygenators this is disadvantageous to gas exchange. Experimentally, some of the surfaces of certain parts of pump-oxygenator systems have been seeded with endothelial cells, but this has not yet been made practicable.

Currently, most pump-oxygenator systems have coated circuits to reduce the formed blood elements’ response to the artificial surface of the perfusion circuit. These range from synthetic coatings, to covalent heparin bonded coatings, to albumin-based coatings. All have been associated with a decrease in the amount of formed blood elements deposited on the surfaces of the perfusion circuit.

Shear Stresses

Shear stresses are generated by blood pumps, suction systems, abrupt acceleration and deceleration of blood, and cavitation around the end of the arterial cannula. For the leukocyte, they are an important abnormal event during CPB. This is in part because leukocytes are the largest formed blood element and are normally exposed to nonendothelialized surfaces, and because they are capable of exiting from the vascular space by diapedesis and by migrating via chemotactic gradients. They are also capable of phagocytosis and, because of their proteolytic and enzymatic components, of digesting almost any biological material. Martin demonstrated that shear stresses not only increase leukocyte disruption but also increase degranulation and adherence and decrease aggregation, chemotactic migration, and phagocytosis in nondisrupted leukocytes.

Erythrocytes are damaged during CPB primarily by shear stresses. The amount of hemolysis and liberated free hemoglobin increases linearly as shear increases. In CPB systems, hemolysis is much less without the oxygenator in the system, and bubble oxygenators have been shown to produce more hemolysis than membrane oxygenators. Interaction of the damaging effects is again demonstrated by the fact that the critical shear stress for erythrocytes is lowered by presence of an unphysiologic surface. Intracardiac sucker systems are particularly damaging to erythrocytes, not only because of high shear stresses and deceleration injury but also because negative pressures are more damaging to erythrocytes than positive ones.

Incorporation of Foreign Substances

In intact humans, foreign substances rarely enter the arterial bloodstream, although when they do, the well-recognized pathologic state of arterial thromboembolism may develop. During CPB, air bubbles, particulate matter from the pump-oxygenator, platelet aggregates and fragments, fibrin aggregates, denatured protein particles, atheroma, and chylomicrons may be contained in the arterial blood and may be distributed throughout the patient’s arterial system.

Microembolization is greatest during the first 5 to 10 minutes of CPB. Perhaps related to this, the total amount of microembolization is not correlated with duration of CPB. The amount does seem to be decreased by a small-pore filter in the arterial tubing of the pump-oxygenator, but this is arguable. Microembolization is greater when bubble oxygenators rather than membrane oxygenators are used. Embolized particles, whatever they may be, usually cause only transient obstructions to flow; thus, after 5 to 10 days, there is usually little evidence of their presence. Nevertheless, there is some correlation between depressed neuropsychometric test scores postoperatively and number of microemboli.

There are many potential sources of microemboli. In some instances, pump-oxygenator surfaces have fine deposits of debris; this has led some to advocate preliminary filtration of blood that has passed through the system before CPB is established. Gas bubbles are commonly found in the arterial input to the patient; these must have multiple sources, although they have been shown to be more prevalent when bubble oxygenators are used. There is some suggestion from the work of Clark and colleagues and Donald and Fellows that large temperature gradients between the water bath and blood in the heat exchanger (i.e., rapid cooling and rewarming) are accompanied by a showering of gaseous microemboli. Adhesion and aggregation of platelets during CPB (see “Platelet Response,” earlier) and formation of fibrin despite heparinization (see “Humoral Response,” earlier) contribute importantly to microembolization. Intracardiac sucker systems incorporate gaseous macro- and microemboli, fibrin, platelet aggregates, and debris into the blood, some of which cannot be removed before the blood is returned to the patient.

Gradual improvements in techniques and equipment for CPB have decreased the prevalence of foreign substances and cellular debris entering the patient’s arterial system during cardiac surgery. This problem remains important and the subject of continuing research, because it probably contributes to neuropsychiatric abnormalities after CPB and to cardiac, pulmonary, and other subsystem dysfunction.

Heparin

Heparin is administered before and during CPB to prevent coagulation of blood (see “Heparin Levels” under Controlled Variables earlier in this section, and see “Heparinization and Later Protamine Administration” under Preparation for Cardiopulmonary Bypass in Section III). It is an agent of damage, in part because it is an imperfect anticoagulant that permits formation of microthrombi in the pump-oxygenator that can embolize to the patient. In rare instances, heparin produces an adverse effect such as severe thrombocytopenia.

Efforts continue to be made to avoid heparinizing patients in the usual manner, primarily by making surfaces of the pump-oxygenator biocompatible. The most common method involves bonding heparin to these surfaces.

Contraindications to use of unfractionated heparin include HIT, heparin allergy, or protamine allergy. Currently, alternative agents are undergoing laboratory and clinical investigation. These include low-molecular-weight heparin and heparinoids, ancord (a defibrinogenating agent derived from pit viper venom), hirudin (a coagulation
inhibitor derived from the salivary glands of the medicinal leech), and coagulation factor inhibitors such as factor IXa, an inhibitor of factor IXa, and argatroban, an inhibitor of factor IIa.

Protamine

Protamine is generally necessary after terminating CPB to reverse the effect of heparin. However, it is an agent with damaging effects because it activates the complement cascade through the classic pathway, and occasionally provokes temporary (5-15 minutes) severe bronchospasm, elevation of pulmonary vascular resistance, and hypotension.\textsuperscript{5,12} Whether prevalence of these undesirable reactions is reduced by slow administration of the drug or by infusing it into the left atrium or aorta rather than the right atrium is arguable.

PREVENTION OF UNDESIRABLE RESPONSES

True prevention of the fundamentally disadvantageous and undesirable responses to CPB has eluded the cardiovascular surgical community despite intensive efforts. Developments in molecular biology may provide techniques that some day accomplish this. To date, only palliative measures are available, some of which are described in “Other Additives” under Controlled Variables.

SAFE DURATION OF TOTAL CARDIOPULMONARY BYPASS

Partial CPB is better tolerated than total CPB,\textsuperscript{31} and its safe duration is measured in days if a true membrane oxygenator is used (see “Cardiopulmonary Support and Extra-corporeal Membrane Oxygenation” in Section I of Chapter 5). Safe duration of total CPB is much shorter and is measured in hours, although not fully defined. The safety of CPB is known to be adversely affected by certain incremental risk factors.

Duration of CPB is clearly a risk factor for morbidity (Fig. 2-20) and mortality after cardiac surgery, but the relationship between duration of total CPB and morbidity and mortality is affected by other risk factors as well. Type of oxygenator is probably one such risk factor; in general, true membrane oxygenators are the safest, followed by microporous oxygenators. Bubble oxygenators are generally the least safe. In contrast to moderate or deep hypothermia, normothermia throughout most of the period of total CPB is arguably a risk factor that affects the relationship between duration of CPB and unfavorable outcomes (see General Comments and Strategy in Section III). Absence of hemodilution is probably a risk factor. Very low venous oxygen levels, although no doubt interrelated with some of the previously mentioned risk factors, appear to increase the risk of unfavorable events after CPB.

It is arguable that patient age is a risk factor for unfavorable outcome events after CPB, but the impression is that very young (Fig. 2-21) and very old age have an unfavorable effect on the relation between duration of CPB and prevalence of unfavorable outcomes. Immature patients may have a greater tendency to develop increased capillary permeability than older patients, although this has not been well documented. Strength of the patient’s humoral and cellular responses to CPB also affects this relationship, with greater complement activation appearing to have an unfavorable effect (see Table 2-4).

Thus, the relationship between safety and duration of total CPB depends on a number of factors that have mitigated against a complete understanding of it. Duration of CPB has clearly been identified as a risk factor for poor outcome in a wide range of studies of open heart surgical procedures. Nevertheless, it remains a possibility, even a likely one, that longer duration of CPB is primarily a marker for an operation that has not proceeded as planned. For example, in fairly well standardized operations such as CABG or the arterial switch procedure for transposition, duration of bypass beyond the expected range likely is a marker for technical problems with the procedure. It is factors related to poor technical operation, and not CPB duration, that have a causal relationship with increased morbidity. Other indirect evidence suggests that safe duration of CPB may be many hours, rather than a
few. Patients can be supported on extracorporeal membrane oxygenation (ECMO) for days and even weeks without developing circulation-related complications. It must be fully acknowledged, however, that closed ECMO circuits and open CPB circuits have many differences.

Section III  Clinical Methodology of Cardiopulmonary Bypass

GENERAL COMMENTS AND STRATEGY

CPB should be used as a flexible clinical tool, recognizing its physiologic limitations, risks, and damaging effects. CPB is combined with at least some degree of hypothermia in many situations for the reasons given in Section II. An important advantage of hypothermia is that it allows safe periods of very low perfusion flow rate (≈0.5 L·min⁻¹·m⁻²) or circulatory arrest when needed, but the possible advantages of normothermic CPB continue to be explored. These include lower systemic vascular resistance and higher cardiac output in the early postoperative period and less blood loss. However, decreased oxygen saturation (<50%) in the cerebral venous blood has also been observed, particularly during the early period of CPB.

Size of the arterial and venous cannulae is determined primarily by perfusion flow rate and type of venous return, but total perfusion flow rate—even at normothermia—is not an absolute quantity but encompasses a range of acceptable values. Thus, if the surgical situation compels use of smaller cannulae, perfusion flow rate can be set at a smaller value, or assisted venous return (vacuum, centrifugal pump) can be used. Two venous cannulae may be used as a routine or only for congenital heart disease operations, including those in infants, and operations involving the right atrium, such as tricuspid valve surgery. A single two-stage venous cannula, having additional holes that come to lie in the right atrium while the tip is in the inferior vena cava (IVC), may be used for CABG; operations on the aortic valve, mitral valve, and ascending aorta; some operations for congenital heart disease; and combinations of these procedures. Such a cannula has been shown experimentally to efficiently decompress the right heart. On occasion, a single venous cannula may also be used with conventional CPB and without aortic clamping for simple operations such as replacement of a valved extracardiac conduit.

Method of cannulation, use of left atrial and left ventricular vents, monitoring catheters, and indeed all aspects of clinical CPB should be flexible within certain limits. The combined knowledge and experience of the surgeon, anesthesiologist, and perfusionist should allow adaptation to the surgical situation while ensuring the greatest possible safety for the patient.

Some operations traditionally performed with CPB support can be designed to avoid use of CPB. These include off-pump CABG (Chapter 7), bidirectional superior cavopulmonary shunt (Chapter 41, Section III), and extracardiac conduit Fontan operation (Chapter 41, Section IV). Percutaneous aortic valve replacement (Chapter 12), investigative percutaneous techniques to address mitral valve regurgitation, and intravascular aortic stent-grafting (Chapter 26) are examples of traditionally surgical procedures that are becoming catheter based or hybrid procedures that do not require CPB.

POSITIONING MONITORING DEVICES

Monitoring devices used for various cardiac operations in infants, children, and adults and specific positioning are discussed in Chapter 4.

POSITIONING PATIENT

The surgeon should collaborate with the anesthesiologist to position the patient correctly for operation, because an improperly positioned patient can make the operation more difficult and injure the patient. For a median sternotomy, both arms may be placed at the side to permit optimal access for the surgical team and avoid traction on the brachial plexus during operation. Alternatively, a carefully positioned arm board can be used for the left arm (and for venous and arterial catheters).

Particularly in infants, a pad is placed under the back to project the chest forward and extend the neck. The patient’s trunk must not be rotated, and the arms at the side must be secured and protected to prevent compression of the ulnar nerve at the elbow. A cauteried pad is placed under the buttocks or the back. Pads for external defibrillation may also be placed on the anterolateral left chest and the back. A draping framework is placed over the head of the patient and extended to either side to screen the patient’s head and the anesthesiologist from the sterile field. A urethral catheter containing a thermistor is inserted into the bladder. A thermistor probe is positioned in the nasopharynx.

PREPARING SURGICAL FIELD

The skin of the anterior thorax and abdomen is prepared with an antiseptic solution after mechanically cleansing it. In most patients, both groins should be prepared as well and draped into the surgical field so that the femoral vessels can be cannulated if necessary. Both legs are surgically prepared in their entirety for individuals undergoing CABG.

Appropriate sterile drapes are applied. Draping must shield the surgical field from the anesthesiologist, while at the same time allowing him or her an unobstructed view into the field.

Finally, the surgical field is covered by an impervious adhesive plastic sheet, in part to prevent the side drapes from falling away from the skin. It also prevents the drapes in the vicinity of the wound from becoming wet and thus losing their sterility.

Pump tubing is passed from the operating table to the perfusionist, who completes the CPB circuit. Tubing for infusion of cardioplegia, pericardial irrigation, suction, and venting is also positioned.

INCISION

Primary Median Sternotomy

A straight vertical midline skin incision is generally made in patients undergoing CPB through a median sternotomy. This incision commences several centimeters below the suprasternal notch and extends to the tip of the xiphoid.
An exception may be made in prepubertal girls in whom a bilateral submammary skin incision is made that follows the fourth intercostal space. A flap of skin and subcutaneous tissue is raised superiorly and inferiorly to expose the full length of the sternum for a vertical sternotomy. However, this incision may cause underdevelopment of the breasts in girls of this age and should be used judiciously. When used in female patients of all ages, this incision may cause hypoplasia or anemia of the anterior chest wall.

The exact midline over the sternum is scored with the cautery. A retractor elevates the upper angle of the vertical skin incision, placing the underlying tissues on tension. The soft tissue is separated from the superior surface of the manubrium, and a right-angled clamp is passed over the denuded manubrium into the space behind, hugging the bone. The clamp is spread to create a space for the tip of the sternal saw. The suprasternal ligament is cut with the cautery.

The blade of an electric or air-driven saw is held snugly against the posterior surface of the manubrium with the cutting edge against the superior manubrial surface. After activating the saw, the surgeon cuts the manubrium and sternum, staying precisely in the midline. The tip of the saw is kept elevated so that the toe of the saw hugs the back of the sternum. During sawing, the anesthesiologist should cease ventilating the patient and exert no pressure on the lungs, so that the soft tissue and pleura will fall away from the sternum. Drifting away from the midline with the saw must be avoided because the sternum will not spread evenly, and its later closure will be more difficult.

Alternatively, the sternum can be divided from the bottom up. The xiphoïd process is mobilized or excised, and the tip of the blade is introduced beneath it. In neonates and infants, the xiphoïd process may be excised, the costal margin on either side elevated by sharp retractors, and sharp, well-aligned scissors used to cut the sternum in the midline, from below upward.

When the incision is properly made, the pleural spaces are infrequently entered. A thin layer of bone wax is spread over the bone marrow, primarily where the bleeding is active. When the sternum is fragile, as in older patients, it is better to avoid wax altogether. Bleeding points in the cut edge of the anterior and posterior sternal periosteum are cauterized, but excessive cauterization should be avoided. A retractor is inserted and opened just enough to permit dissection. After a few minutes, it is opened further. It should be opened no more than is necessary for the procedure, because excessive retraction, particularly of the upper half of the sternum, may cause rib fractures, dislocation of costochondral junctions, injury to the brachial plexus, and damage to the stellate ganglion.

Dissection continues by incising the fascia that envelops the thymus gland. The right and left lobes of the thymus are separated up to the level of the brachiocephalic vein. In infants and children, and occasionally in adults, the thymus may be subtotally resected, leaving only the cervical portion cephalad to the brachiocephalic vein, to avoid expanding hematomas that may cause postoperative bleeding.

The pericardium is then opened longitudinally in the midline, from the diaphragm below to the brachiocephalic vein above. Where this incision meets the diaphragm, care must be taken not to incise the parietal peritoneum. If entry is made into the peritoneal cavity, the opening is sutured to avoid sequestration of blood and fluid in it. The pericardium is cut at right angles to the longitudinal incision at its diaphragmatic end, farther on the left than on the right, after pushing back the pleura to avoid entering the pleural spaces. Pericardial stay sutures are then placed.

Alternative Primary Incisions

Incisions other than a full median sternotomy are being used with increasing frequency. These incisions and the techniques of cannulation required for their use are described at the end of this section in Special Situations and Controversies.

The remainder of the general discussion on the clinical methods of CPB focuses on the median sternotomy approach to the pericardial cavity and its contents.

Secondary Median Sternotomy

The surgeon must estimate preoperatively the chances that catastrophic hemorrhage will develop from repeat sternotomy. This affects the decision regarding whether to cannulate peripheral vessels and establish CPB before sternotomy. It is helpful to study the chest radiograph and any available cineangiograms. However, cross-sectional imaging by CT or MRI provides the most useful information. When one of the great arteries, right ventricle, coronary artery bypass grafts, or a right ventricle to pulmonary trunk conduit is in close proximity to the back of the sternum, peripheral cannulation, establishment of CPB, and induction of moderate hypothermia before sternotomy are prudent precautions.

When a previous sternotomy has been performed, an oscillating saw is commonly used. Properly used with a light touch by the operator, this saw allows the sternum to be split without damage to underlying structures. Once the sternum is divided, a sharp handheld retractor is inserted to elevate the lower left sternal fragment. Dissection is commenced just beneath the xiphisternum, dividing the tissues just behind the sternum. Working from below upward, the surgeon frees the left sternal edge in this manner to the level of the suprasternal notch. The same maneuver is repeated on the right side. Returning to the left sternal edge, the surgeon fully elevates it with two retractors and carries the dissection leftward, keeping fairly close to the sternum until the divided edge of the pericardium is identified (when the pericardium has not been sutured at the first operation, it retracts well away from the midline). The left edge of the pericardium is separated from the underlying pericardial end, farther on the left than on the right, after pushing back the pleura to avoid entering the pleural spaces. Pericardial stay sutures are then placed.
of pericardium attached to the atrium if it is too densely adherent. This is often at the site of previously placed purse-string sutures.

It is very important during dissection of the aorta to remain outside the adventitial layer. The outer edge of the superior vena cava (SVC) is then dissected. To permit later clamping, the aorta requires further dissection, particularly posteriorly in front of the right pulmonary artery and on the left lateral margin.

Further dissection should be avoided unless it is necessary for proper exposure. Operations in which more extensive dissection may be necessary include redo CABG and repairs inside the right ventricle (see later chapters). When further mobilization is necessary, it is usually deferred until CPB has been established. The heart can then be emptied and dissection performed more precisely and more easily, with no hemodynamic disturbances. However, perfusion at this stage should be normothermic to prevent ventricular fibrillation and overdistention of the heart. If the heart cannot be completely mobilized, the left pleural space may be entered and opened widely, because this allows cardiac defibrillation and the usual de-airing maneuvers at the end of the operation.

**PREPARATION FOR CARDIOPULMONARY BYPASS**

Once the pericardial stay sutures are inserted, size and any abnormalities of the cardiac chambers are noted, anomalies of systemic venous return (especially a persistent left SVC) or pulmonary venous return are sought. A left atrial monitoring catheter, if indicated, may be inserted at this time or later, just before discontinuing CPB. For this, a 3-0 purse-string stitch is placed on the right superior pulmonary vein just posterior to the right atrium (Fig. 2-22). A fine polyvinyl catheter is threaded into a 16-gauge Tuohy needle, the needle is inserted into the left atrium through the purse string, the catheter is advanced about 2 cm, the needle is withdrawn, and the purse string is tied. A 5-0 stitch is placed in the adjacent pericardium and tied snugly around the catheter, very near the purse string. The other end of the catheter is brought through the skin and attached to a pressure gauge.

**Siting and Purse-String Sutures for Aortic Cannulation**

The site for cannulation of the aorta should be within the pericardial reflection whenever possible, because the aorta where the pericardium is fused onto the anterior surface is

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**Figure 2-22** Schematic representation showing positions of sites for cannulae and catheters. As indicated in the text, not all are used in every patient. Key: IVC, Inferior vena cava; LA, left atrium; RA, right atrium; SVC, superior vena cava.
tougher and better for cannulation than the part outside (beyond and downstream to) the reflection. In this location, the cannulation site is proximal (upstream) to the origin of the brachiocephalic artery. The site should be a little to the left side of the anterior aortic surface (to the right side in patients with right aortic arch) as an added precaution against the cannula tip entering the brachiocephalic artery. At times in infants, in children with a previously constructed Waterston anastomosis or with truncus arteriosus, in adults with short ascending aortas or ascending aortic aneurysms, and in those about to undergo primary or redo CABG, the pericardial reflection over the cephalad end of the ascending aorta can be dissected off the aorta, the aorta retracted inferiorly, and the purse-string sutures placed on the anterior aortic wall at the level of, or if necessary distal (downstream) to, the orifice of the brachiocephalic artery on the aortic arch. In such situations, care is taken to position the aortic clamp proximal (upstream) to the orifice of the brachiocephalic artery.

Two purse-string sutures of 2-0 or 3-0 polyester or polypropylene are placed. They should catch only the adventitia and must not penetrate into the lumen. Tourniquets are placed on these sutures. When the aorta is scarred from a previous operation, a single pledgeted 3-0 polypropylene box stitch may be used at the cannulation site. A purse-string stitch is also placed for the cardioplegic needle or venting cannula (see Fig. 2-22).

The aorta of older patients, particularly those with coronary artery disease, may be arteriosclerotic, and its manipulation, cannulation, and clamping may result in dislodging and embolizing atheroma. It is prudent to perform epiaortic ultrasonographic scanning of the aorta in such patients to detect severe arteriosclerosis and position cannulae and clamps in areas where arteriosclerotic disease is minimal or absent (see Chapter 26). Alternatively, off-pump coronary revascularization may be used or on-CPB beating heart revascularization with peripheral cannulation and without aortic clamping (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies later in this section). 79

Siting and Purse-String Sutures for Venous Cannulation

Purse-string sutures for venous cannulation can be placed before or after heparinization and aortic cannulation. Number and sites of these purse strings depend on the perfusion technique to be used. When a single venous cannula is used, only a right atrial appendage purse-string suture is needed.

When two venous cannulae are used, the SVC and IVC may be cannulated directly. This approach is an old one, but has been refined by availability of smaller cannulae. With this method, venous drainage and exposure within the atria and ventricles are excellent, even in infants. An oval-shaped purse string is placed on the presenting surface of the SVC (see Fig. 2-22), and a tape is placed around the SVC. For this, an incision is made in the pericardial reflection over the right pulmonary artery on the medial side of the SVC and again lateral to the SVC. These incisions allow a right-angled clamp to be passed easily around the SVC to grasp the tape and pull it through. The tape is placed in a rubber or plastic tourniquet. Alternatively, the SVC may be cannulated through a purse string in the right atrial appendage. To pass a tape around the IVC, the pericardial reflection posterior to the IVC and just inferior to the right inferior pulmonary vein is incised. This maneuver clearly delineates the inferior border of the right inferior pulmonary vein and left atrium. It establishes a free communication between the two pericardial spaces, which permits better circulation of the external cooling fluid, and provides a space for the IVC tape to be placed. Alternatively, the IVC can be mobilized by first passing the fingers to the right of and behind the caval and breaking down the pericardial reflection posteriorly by blunt dissection. The hand is then removed and a right-angled clamp substituted. The tip of this instrument is exposed by retracting the lateral right atrial wall superiorly and to the left. Usually, the clamp slides around the IVC without further dissection. Occasionally, tissue must be divided with scissors, working lateral to the right atrium and below the inferior pulmonary vein. Then the surgeon, with tissue forceps or a sponge, retracts the right atrium superiorly and to the left to expose the presenting surface of the IVC, which may require limited dissection from the diaphragm. A purse-string stitch is placed at the junction of the right atrium and IVC, or on the IVC itself, in a transverse oval shape (see Fig. 2-22).

Heparinization and Later Protamine Administration

Measurement of activated clotting time (ACT) and calculation of a heparin dose-response curve allows heparin and protamine doses to be individualized for each patient. 81 First a baseline, or control, ACT is established after sternotomy. Heparin (300-400 units · kg⁻¹ or 3-4 mg · kg⁻¹) is then given. After 3 to 5 minutes, the ACT is again determined. Additional heparin is given as needed to achieve an ACT of greater than 400 seconds. Cannulation is then performed. Heparin (3 units · mL⁻¹) is added to the priming volume of the pump-oxygenator (e.g., 5000 units for a 1600-mL clear solution). After CPB is established, the ACT is determined every 30 minutes, and additional heparin is given to maintain the ACT at greater than 400 seconds during normothermic CPB and at greater than 480 seconds during hypothermic CPB (<30°C). The ACT should be measured more frequently if it does not respond appropriately to additional doses of heparin. (See cautions about the interference of aprotinin and other factors with interpretation of ACT, particularly when measured with Celite, in “Other Additives” in Section II.)

Protamine sulfate is given at the end of CPB, after removal of all cannulae. This biological product, obtained from the sperm of fish, is a simple protein of low molecular weight. It is a heparin antagonist, forming with heparin a heparin-protamine complex. Protamine has a rapid onset of action, but the heparin-protamine complex may be partially metabolized or react with fibrinolysin, thus freeing heparin and causing a heparin rebound.

Several methods are available to calculate the dosage of protamine to be administered at the end of CPB. 150 These methods and their advantages and disadvantages are listed in Table 2-5. A widely used method involves administering 1 to 1.5 mg of protamine for each 100 units (or each mg) of heparin; 1 mg of protamine neutralizes approximately 85 units of heparin. Extra protamine is given to prevent heparin rebound associated with heparin release from tissue stores or from heparin-protamine aggregates, and to compensate for the probable shorter biological half-life of protamine. 151
Table 2-5  Comparison of Methods for Calculating Protamine Dosage

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fixed dose</td>
<td>Simple</td>
<td>Inadequate or excessive protamine</td>
</tr>
<tr>
<td>(1-1.5 mg heparin - kg⁻¹)</td>
<td>Not reliant on ACT</td>
<td>Potential for increased coagulation times with standard doses</td>
</tr>
<tr>
<td>ACT/heparin dose-response curves</td>
<td>Rapid, easy to use in OR</td>
<td>No correlation between ACT and heparin levels</td>
</tr>
<tr>
<td></td>
<td>More accurate protamine administration</td>
<td>Relies on ACT</td>
</tr>
<tr>
<td></td>
<td>Decreased blood product requirements</td>
<td>Dependence on plasma volume</td>
</tr>
<tr>
<td>Heparin levels</td>
<td>Less protamine given</td>
<td>Requires peripheral laboratory</td>
</tr>
<tr>
<td></td>
<td>Not reliant on ACT</td>
<td>Time consuming</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assumes point on static curve</td>
</tr>
<tr>
<td>Protamine titration</td>
<td>Less protamine required than fixed dose</td>
<td>Variability between heparin and protamine preparations</td>
</tr>
<tr>
<td></td>
<td>Decreased postoperative bleeding</td>
<td>Dependence on blood volume estimate</td>
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<tr>
<td></td>
<td>No rebound effect seen with small protamine doses</td>
<td>Several steps for potential error</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Assumes point on static curve</td>
</tr>
</tbody>
</table>

Modified from Moorman and colleagues.¹³¹
Key: ACT, Activated clotting time; OR, operating room.

Arterial Cannulation

After heparin has been administered, the adventitia within the purse string is incised. With the aorta stabilized by a gauze sponge under the surgeon’s left index finger, a digitally controlled stab wound of sufficient length is made within the purse string. The aortic cannula can then be slipped into the aorta easily and usually bloodlessly. Care is taken to adjust the cannula so that only 5 to 10 mm projects into the aorta. If an angled cannula is used, it is positioned so that the opening faces distally into the aortic arch. The tourniquet on the purse-string suture is secured, and the cannula is tied to it. The arterial cannula is connected to the arterial tubing from the pump-oxygenator and carefully de-aired. All clamps are then removed from this tubing if a roller pump is used, but not if the arterial pump is of the controlled vortex type. This technique may be used in adults, children, infants, and neonates.

Alternatively in neonates, infants, and small children, a fine side-biting clamp (Cooley or Castaneda) is used. All layers of the aorta, including the adventitia, are thicker in these small patients, and an excluding clamp will not damage the intima. The excluded portion of aorta is opened longitudinally with a knife. The purse-string stitch is then positioned, and the cannula tip is inserted into the opening while releasing the clamp. With this technique, the arterial cannula can have a long tip beyond the collar and is positioned so that this tip lies in the transverse portion of the aortic arch, safely beyond the origin of the brachiocephalic artery. Alternatively, the arterial cannula may have a very short tip beyond its collar, and the cannula will be perpendicular to the aorta after its insertion.

Venous Cannulation

When a single venous cannula is to be used, a suitable clamp is placed across the right atrial appendage, the appendage is opened, hemostats or forceps are placed on both edges, and the cannula is inserted into the right atrium. A single two-stage venous cannula of variable diameter may be used in adults undergoing CABG, aortic valve replacement, or in some cases of mitral valve replacement. When properly positioned, the tip will be in the IVC and the side holes in the mid-right atrium.

When two venous cannulae and caval taping are to be used, a clamp is placed across the right atrial appendage, the appendage is opened, and one and then the other venous cannula is inserted through this opening. One is guided into the SVC and the other into the IVC. Alternatively, direct caval cannulation can be used. The right atrium adjacent to the IVC is retracted by the surgeon with tissue forceps or a sponge, a stab wound is made in the center of the IVC purse string, and the cannula is inserted. A stab wound is made in the center of the purse string on the SVC, and this venous cannula is inserted. CPB is then established (see Commencing Cardiopulmonary Bypass and Left Heart Venting later in this section). Direct caval cannulation can be difficult in neonates and infants when the heart is large. In these small patients, maneuvers required for exposure of the IVC can lead to severe hypotension.

After the cannulae are inserted, each tip must lie directly parallel to the walls of the vena cava, with the tip of the SVC cannula pointing upward and that of the IVC downward. Otherwise, venous obstruction will result. Precision in positioning the tips of the cannulae can be obtained by attaching the cannulae to the Y connector on the venous line in exactly the right orientation before their insertion. When exposure of the IVC is particularly difficult, the SVC may be cannulated first, partial CPB established, and the IVC then exposed for placing the tape and purse-string suture and for inserting the cannula.

Two venous cannulae inserted directly into the cavae as described are well suited for operations in children, infants, and neonates down to a body weight of about 2.5 kg. When the cannulae are placed as described, venous drainage is excellent; this can be verified by routine measurement of SVC pressure through an indwelling small catheter previously introduced into the internal jugular vein. An advantage of direct caval cannulation in cases in which the major portion of the operation is performed during hypothermic circulatory arrest is that the heart may be opened and the exposure arranged during the latter part of cooling and before the arrest period. The cardiac chambers can be closed during rewarming. A disadvantage is that when the heart is closed,
the inferior caval cannula may have to be repositioned into the right atrium to prevent its distention by blood returning from the coronary sinus, SVC, or both.

COMMENCING CARDIOPULMONARY BYPASS AND LEFT HEART VENTING

On command from the surgeon, the perfusionist commences CPB. The surgeon removes the arterial and venous line clamps (if present). The perfusion flow is gradually increased to about 2.2 L · min⁻¹ · m⁻², and after the proper flow has been obtained, perfusion cooling (if indicated) is begun.

In neonates and infants, the priming volume of the pump may be maintained at a temperature of 18°C to 22°C, 30°C, or 37°C. If a cold prime is used, myocardial function is immediately affected after establishing CPB. Heart rate slows and contraction is impaired. The contribution to total blood flow by the heart rapidly diminishes. Therefore, the arterial pump must rapidly reach full flow to maintain adequate systemic perfusion. The heart should be carefully observed during this period for ventricular distention, especially in infants and neonates with high ventricular compliance and a heart less tolerant of excessive preload. If distention occurs, pump flow must be reduced and the venous cannulae repositioned. If cardiac contractility is maintained during initiation of CPB, it is preferable to maintain ventilation until full flow is achieved.

For operations in adults and older children, the left-heart venting catheter is inserted from the right side directly into the left atrium through a purse-string stitch positioned at the junction of the right superior pulmonary vein and the left atrium (see Fig. 2-22). The stitch should pick up atrial wall and the adventitia of the pulmonary vein, and should not be large enough to compromise the pulmonary vein orifice when tied down. In most cases a long, soft, angled catheter is used, and it is advanced through the mitral valve into the left ventricle. This must be done precisely if the heart is beating, in view of the possibility that air can be introduced into it and embolize to the brain unless the aorta has been clamped. Therefore, venous pressure is increased by reducing venous drainage to increase the volume of blood in the heart. A small incision is made within the purse string, and the venting catheter is introduced. After the venting catheter has been advanced into the left atrium, the left hand is placed behind the heart to palpate the tip of the vent and guide it toward the mitral valve and into the left ventricle. The same precautions with respect to air are necessary as the vent is withdrawn at the end of the operation.

For operations in the right atrium or right ventricle in which increased pulmonary venous return is anticipated, venting of the left heart can be performed as described in the previous paragraph. Alternatively, when two venous cannulae are used for operations in the right ventricle or right atrium, the caval tapes are secured after cooling has been initiated and the right atrium opened through a small oblique atriotomy. If a patent foramen ovale or atrial septal defect is present, a sump catheter is placed partially across it and into the left atrium. If neither is present, a stab wound is made in the fossa ovalis directly beneath the superior limbus. If this landmark is not used and the stab wound is imprecisely made, the vent may come to lie outside the heart rather than in the left atrium. Because the sump catheter lies only partially across the atrial septum, it removes both left and right atrial blood. The right atrium remains open during the repair.

If the right superior or inferior pulmonary vein is not accessible for venting, the pulmonary trunk and apex of the left ventricle are alternative sites. If the pulmonary trunk is used, a catheter or sump is inserted through a purse string in it immediately above the pulmonary valve. Drainage and decompression of the left heart may be suboptimal with this technique. If the left ventricle is to be vented directly, a pledgeted mattress suture of 2-0 or 3-0 polyester or polypropylene is placed near, but not at, the apex of the heart on the anterolateral wall, and a catheter or sump is introduced after the ventricle has been incised with a stab blade.

For operations in which the heart is not opened (e.g., CABG), the left heart can be vented through the ascending aorta proximal to the aortic clamp, using a needle vent that can be connected either to the venous line (gravity drainage) or directly to the reservoir of the pump-oxygenator using a roller pump.

CARDIOPULMONARY BYPASS DURING OPERATION AND REWARMING

When the desired perfusion flow rate is achieved, perfusate temperature is reduced, the aorta is clamped, and cardioplegic solution is infused (see Chapter 3). Cooling by the perfusate is continued until the nasopharyngeal temperature reaches the desired level, and then the perfusate temperature is stabilized at that level. A broad range of temperatures can be used. In most cases, the nasopharyngeal temperature should be lowered to at least 32°C. When the temperature is lowered to less than this level, perfusion flow rate can be safely reduced. For example, if 25°C is chosen, the flow can be safely reduced to 1.6 L · min⁻¹ · m⁻². Brief periods of lower flow may be used.

After completing most or all of the repair, rewarming is begun. It is usually at this point that preparation for myocardial reperfusion is commenced. The precise moment for commencing rewarming depends on the strategy used for myocardial management (see Chapter 3). For rewarming, the water in the heat exchanger is raised to 42°C; the arterial myocardial management (see Chapter 3). For rewarming, the water in the heat exchanger is raised to 42°C; the arterial blood temperature should not exceed 39°C. It is advantageous but not essential to have the nasopharyngeal temperature at 37°C for about 10 minutes before CPB is discontinued, lest there be excessive downward drift of temperature in the postbypass period.

DE-AIRING THE HEART

After completing the repair and as the cardiac chambers are closed or as CABG is being completed, the heart must be freed of as much air as possible before it begins to eject into the systemic circulation. Clinical studies have demonstrated a correlation between the number of gaseous microemboli and the severity of neuropsychological impairment after surgical procedures employing CPB. Thus, special maneuvers are necessary to avoid air embolism, as has clearly been demonstrated by intraoperative echocardiography. The exact steps and sequences and the time of de-airing may vary, but the principles are well established:

- The heart is filled with fluid (blood or electrolyte solution) before closing to minimize air entrapment.
- The heart must be reperfused and beating.
- Residual air is aspirated from the heart before allowing it to eject.
- The lungs are intermittently ventilated to express air from the pulmonary veins.
- Continuous suction is applied on a needle vent or catheter in the ascending aorta as the heart commences ejecting blood to retrieve any air that may have remained in the heart or pulmonary veins (alternatively, a freely bleeding stab wound may be used).\(^{116}\)

The exact technique used will depend in part on the method used for myocardial management (see Chapter 3). One technique can be illustrated with the procedure for aortic valve replacement:

1. As the suture line for aortic closure is being completed, suction on the left atrial vent is discontinued, and flow is reduced to allow the heart to fill with blood. If blood is not freely escaping from the most anterior portion of the aortotomy before completing this suture line, fluid (saline or Ringer’s lactate) is injected into the opened aorta with a syringe. The suture line is completed. A needle vent connected to tubing from the pump-oxygenator is inserted into the ascending aorta. The anesthesiologist gently inflates the lungs to remove air from the pulmonary veins into the left atrium; vigorous inflation is inadvisable because when the lungs collapse, air can be drawn into the left ventricle through the still-opened aorta.

2. With a large-bore needle connected to a 20-mL syringe or to tubing from the pump-oxygenator, the left atrium is aspirated through its dome beneath the aorta. Air is almost invariably obtained. Aspiration is combined with gentle ventilation on two or three occasions until no further air appears. The left atrial appendage is inverted to evacuate air.

3. The heart is gently pulled forward and to the right, and needle aspiration of the left ventricular cavity is performed through the front of the left ventricular apex. This is a simple and effective way of removing the pocket of air that is almost always present at this site. The maneuver can be repeated several times.

4. The operating table is tilted, with the patient’s head down.

5. Perfusion flow rate is temporarily reduced as the aortic clamp is slowly released. Blood and air are gently aspirated from the needle vent in the ascending aorta. Left ventricular overdistention must be prevented.

6. The left atrial vent is removed while the lungs are gently inflated, and the central venous pressure is slowly increased to evacuate any residual air. The purse-string suture is secured. The heart is electrically defibrillated if not already beating. The left ventricle is shaken with the left hand several times.

7. Central venous pressure is slowly raised by the perfusionist. The heart begins to eject. Air may then appear in the aortic vent suction line. When the central venous pressure has been elevated to 10 mmHg and the heart has ejected for several minutes, CPB flow is slowly reduced. The ventricle is again shaken, and CPB is discontinued.

8. The table is leveled. Suction on the aortic needle is reduced and then discontinued, the needle is removed, and the stitch is tied. These maneuvers should not be hurried. The longer the aortic needle vent is in use, the better, and it should not be removed until the heart has been ejecting well for some time.

Because small amounts of intracardiac air have a low probability of causing any detectable damage, adherence to a strict protocol for removal of air, such as the one described, will suffice for most patients.\(^{118,214}\) Transesophageal two-dimensional echocardiography (TEE) is commonly used to monitor removal of air from the heart before CPB is discontinued. TEE enables the operating team to identify the presence of even small amounts of intracardiac and intraaortic air.\(^{312,325}\) The clinical benefit conferred by TEE during operations in which standard de-airing procedures are used has not been conclusively demonstrated. However, TEE is of particular value during operations employing small incisions, when the left-sided cardiac chambers are not fully mobilized, or when some of the usual maneuvers for removal of air, such as aspiration and manipulation of the left ventricle, cannot be used.

Flooding the operative field with carbon dioxide is used for displacing air from the cardiac chambers. Its use was first reported by Nichols and colleagues in 1988.\(^{318}\) The theoretical value of this technique is that carbon dioxide will displace air from the operative field because it is a heavier gas and because carbon dioxide emboli, if they occur, are better tolerated than air emboli.\(^{323}\) In a randomized trial of patients undergoing single valve surgery, the number of microemboli assessed by intraoperative TEE was significantly less in the left atrium, left ventricle, and ascending aorta among patients in whom carbon dioxide (CO\(_2\)) insufflation was used than in those in whom it was not.\(^{536}\) The median number of detectable microemboli after CPB fell to zero 7 minutes after CPB vs. 19 minutes in the control group. CO\(_2\) may have an important role in operations performed through small incisions or during reoperative procedures, but the potential for inducing profound systemic hypercarbia and acidosis exists.\(^{860,331}\) Thus, frequent monitoring of arterial blood gases and electrolytes is necessary when the technique is used. Persson and colleagues have shown in vitro that efficient de-airing of a cardiothoracic wound by carbon dioxide insufflation depends on its flow and velocity.\(^{714}\) To compensate for diffusion with the ambient air, they observed that the flow of carbon dioxide should be 5 L · min\(^{-1}\) and the outflow velocity about 0.1 m · sec\(^{-1}\) or less to avoid turbulence in the wound. This was best obtainable with a gas diffuser apparatus (Cardiac Innovation AB).

**COMPLETING CARDIOPULMONARY BYPASS**

As rewarming is being completed, two temporary pacing wire electrodes are positioned on the lateral wall of the right atrium.\(^{935}\) The bared end of the shielded wire electrode is secured to the atrium with 5-0 sutures or with small clips. In most patients, one or two pacing wire electrodes are similarly sutured to the right ventricular myocardium on the anterior or inferior surface.

When the patient has been rewarmed to a nasopharyngeal temperature of 37°C, perfusion flow rate is gradually decreased until the right and left atrial and aortic pressures...
are adequate, and CPB is then discontinued. The venous cannulae are removed and the purse-string sutures are tied. Protamine is administered slowly (see “Heparinization and Later Protamine Administration” earlier in this section).

Positioning Chest Tubes

There is considerable surgeon-to-surgeon difference in the location and number of chest tubes placed before closure of the median sternotomy incision. In general, to avoid unnecessary bleeding, the tubes are placed after CPB is discontinued and protamine has been administered. If the pleural spaces have not been entered, then one or two tubes are placed. A single tube can be positioned in the anterior mediastinum and brought out through a stab wound in the midline just below the sternotomy incision. Alternatively, two tubes—one in the anterior mediastinum as described and one (an angled or flexible tube) in the inferior-posterior portion of the pericardial cavity—are brought out through stab wounds in the epigastric region on both sides of the midline. If a pleural space has been entered, as often occurs when the left internal thoracic artery is dissected from the parasternal area, a tube is positioned with the tip well posterior and inferior in the pleural space to ensure maximum removal of fluid. This tube can be brought out through the epigastrium in the midline below the sternotomy incision or through a stab wound on the lateral chest wall.

COMPLETING OPERATION

After CPB is discontinued, aside from ensuring adequate hemodynamics, the surgeon’s primary task is to obtain hemostasis. This should be accomplished in a systematic fashion. All cardiac and aortic suture lines and purse strings are inspected. Fine (4-0 or 5-0) single or pledgeted polypropylene sutures can be placed in the adventitia or epicardium to control bleeding from suture lines.

Generally, electrocautery suffices to control bleeding from the mediastinal tissues and around the sternum. Troublesome bleeding from the sternum itself can be managed by tying heavy, encircling, absorbable sutures around it. The wound should be closed only after hemostasis is secure.

The pericardium is generally left open after operations with CPB through a median sternotomy. A few sutures may, however, be placed at the upper end to partially cover a particularly prominent aorta or an aortic graft. Reoperations have not posed a major problem with this technique. Advantages of leaving the pericardium open are (1) good blood drainage into the pericardial cavity (and then out through the drainage tubes) from the mediastinal and substernal tissues, thus preventing hematomas from developing in that area; and (2) reduction (but not elimination) of the tendency of retained blood to produce a positive intrapericardial pressure, thus lowering ventricular transmural pressure (tamponade).

Secure closure of the sternum is critically important. Stainless steel wire sutures are used, with the most cephalad one or two placed through the manubrium, the next three or four through the sternum or around the sternum close to the bone, and the most inferior one or two through the sternum. Different sizes and types of stainless steel sutures are available to match the patient’s size. The wires are twisted, not tied, to bring the sternum together; in adults, these are further twisted with an instrument to ensure that the sternal fragments are securely approximated. If the sternal edges are thin or fragmented, wire sutures can be passed vertically in the parasternal position in front of and behind the costal cartilages on one or both sides. These vertical sutures can then be incorporated into the closure by the transverse wire sutures. Absorbable sutures are used for closing the muscles over the sternum and the linea alba. The skin is closed with a subcuticular absorbable suture or with metal staples.

Some patients have a suboptimal hemodynamic state as preparations are made to close the chest. In most of them, the sternum should probably not be closed, because this frequently further depresses cardiac function. Rather, the sternum, subcutaneous tissue, and skin are left unsutured. An impervious sheet of silicone rubber can be fit into the cutaneous defect and sutured to the skin edges with a running monofilament suture. Alternatively, the wound can be packed loosely with sponges and covered by an impervious, sterile adhesive sheet. This maneuver is lifesaving in some patients. Usually a secondary closure can be performed 24 to 48 hours later.

PUMP-OXYGENATOR

The available apparatus for CPB changes continually, but some general points are important.

Components

A venous reservoir is currently used and is positioned to provide adequate siphonage by gravity if gravity drainage is used. Alternatively, the venous reservoir may be a hard-shell device providing for vacuum-assisted venous return. Such a reservoir allows escape of any air returning with the venous blood and provides storage of excess volume. This reservoir is generally incorporated within the housing of the oxygenator. Although useful, venous reservoirs substantially increase priming volume of the pump-oxygenator system.

The oxygenator is probably the most varied and yet most important part of the system, while at the same time it is probably the most damaging part of the extracorporeal apparatus. Microporous and true membrane oxygenators have advantages over bubble oxygenators and are currently indicated for cardiac surgery (see “Gas Exchange” under Controlled Variables in Section II).

An efficient heat exchanger is necessary. This may be integral within the oxygenator or freestanding. Integrated heat exchangers have generally been less efficient than freestanding ones, but they reduce priming volume.

The arterial pump is most commonly a roller pump. It should be adjusted before each perfusion so as to be slightly nonocclusive, and should be calibrated at frequent intervals so that the flow rate can be accurately established. A centrifugal pump may also be used.

The arterial line pressure in the pump-oxygenator must be continuously monitored. When this pressure exceeds 250 to 300 mmHg, risk of disruption of the arterial line and of caviation in the region of the arterial cannula increases. A proper arterial line pressure is ensured by a properly positioned cannula of adequate size.

The advantages, disadvantages, and need for a low-porosity filter in the arterial line remain somewhat controversial. A randomized study by Walker and colleagues (Walker DR, Blackstone EH, Kirklin JW, Karp RB, Kouchoukos NT,
Pacifico AD, et al: unpublished data, 1976) showed good neuropsychiatric function (determined by specialized testing) in patients after CABG, whether or not a low-porosity arterial filter was present in the circuit. A similar study in patients undergoing open cardiotomy provided the same result. However, studies using transcranial Doppler ultrasound have shown that gaseous microemboli, more prevalent with bubble than with membrane or hollow-fiber oxygenators, can be considerably reduced by 40-µm filters in the arterial line of the pump-oxygenator. Currently, routine use of a low-porosity filter of this type in the arterial line appears to be beneficial. The exact filter to be used and its compatibility with the other components of the pump-oxygenator must be determined within each institution performing cardiac surgery.

A device for ultrafiltration is incorporated into the circuit of the pump-oxygenator, usually between the cardiotomy reservoir and the arterial line. During CPB, if there is excess volume in the pump-oxygenator, the device is activated for removal of serum water by ultrafiltration (see “Perfusate” under Controlled Variables in Section II).

The CPB circuit generally should contain at least two cardiotomy suction ports for return of blood from the opened heart. This blood may contain particulate matter and boluses of air and must be passed through a low-porosity filter and defoamed in a separate chamber open to air before it is returned to the circuit. During the perfusion, blood should be promptly aspirated from the pericardium with these suckers. Blood left too long in the pericardium before being aspirated can promote thrombolysis. Ideally, these lines should be activated by a continuously and rapidly variable high-capacity vacuum system. Because this has so far proved to be impractical, roller pumps are used. With this system, when the open end of the line is blocked, the suction rapidly increases; this may damage either the tissue or the blood. Thus, constant monitoring of the roller pumps is necessary.

### Priming Volume

Each component of the pump-oxygenator adds to the priming volume, which explains why many cardiac surgical groups are unwilling to add unessential components to their system. However, pump-oxygenator systems can be so oversimplified that safety may be compromised. Even with the most stringent efforts, the typical pump-oxygenator systems currently in use have a priming volume considerably larger than is ideal.

### Miniaturized Cardiopulmonary Bypass Circuits

Miniaturized CPB circuits have been developed with the objective of reducing the damaging effects of conventional CPB. It is hypothesized that minimizing hemodilution and mechanical blood trauma will improve outcomes. These closed circuits with little or no blood/air contact consist of a controlled vortex blood pump and a membrane oxygenator as the only components. There is no venous reservoir and no integral cardiac suction device. The components, including the tubing, are heparin coated.

Clinical studies (nonrandomized) in patients undergoing CABG suggest that use of these circuits is associated with fewer transfusions of blood products, less release of cardiac troponin, less postoperative atrial fibrillation, a lower prevalence of acute kidney injury, suppression of thrombin generation and coagulofibrinolytic activation, and lower levels of IL-6 and SC5b-9.

A meta-analysis of randomized clinical trials comparing conventional CPB with miniaturized CPB circuits indicated that miniaturized circuits are associated with substantial reductions in neurologic injury, number of patients requiring transfusion of blood products, and peak cardiac troponin release (Table 2-6). No difference in early mortality was noted. The majority of patients had CABG, and the remainder had aortic valve replacement. A separate meta-analysis examined only the need for red blood cell transfusion and demonstrated an absolute risk reduction in this variable among patients undergoing CABG.

### SPECIAL SITUATIONS AND CONTROVERSIES

#### One Versus Two Venous Cannulae

Use of a single two-stage venous cannula is optimal for many cardiac operations (CABG, aortic valve replacement, and in many instances mitral valve replacement) in adult patients and is widely practiced. The technique is likewise optimal in neonates, infants, and children when the entire repair (including closure of the cardiac chambers) is performed during hypothermic circulatory arrest.

A single venous cannula may also be used in operations in which part of the repair is done during circulatory arrest, but a portion is left to be performed during CPB. Although convenient, the method has some disadvantages. Unless assisted venous return is used, an air lock may occur in the venous line during operations within the right ventricle or

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**Table 2-6** Meta-analysis of Randomized Trials Comparing Conventional Cardiopulmonary Bypass with Miniaturized Cardiopulmonary Bypass Circuits

<table>
<thead>
<tr>
<th>Variable Examined</th>
<th>CPB</th>
<th>MECC</th>
<th>Odds Ratio (95% CL)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>CL (%)</td>
<td></td>
</tr>
<tr>
<td>Neurologic events</td>
<td>19/555</td>
<td>3.4</td>
<td>2.6-4.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4/58</td>
<td>0.73</td>
<td>0.37-1.3</td>
<td>0.30 (0.12-0.73)</td>
</tr>
<tr>
<td>Number of transfused patients</td>
<td>101/563</td>
<td>17.9</td>
<td>16.2-19.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>55/552</td>
<td>9.9</td>
<td>8.6-11.5</td>
<td>0.42 (0.28-0.63)</td>
</tr>
<tr>
<td>Reduction in peak cardiac troponin*</td>
<td>-0.15 ng·dL⁻¹</td>
<td>-</td>
<td>(-0.18-0.11)</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Zangrillo and colleagues.²¹

*Weighted mean difference.

Key: CPB, Cardiopulmonary bypass; MECC, miniaturized extracorporeal circuit.
pulmonary trunk, with the air entering the right atrium through the tricuspid valve. When this happens, venous return to the pump-oxygenator stops abruptly, and blood floods the right side of the heart. The perfusionist must not reduce the perfusion flow rate, but instead the intracardiac sucker is positioned outside the heart to keep blood from overflowing from the pericardial well, while the air lock is moved down the venous line and expelled into the venous reservoir. Principles for use of the single venous cannula in this setting are the same as those already described, including the need for the tip of the cannula to be in the IVC while its side holes remain in the right atrium.

Cardiopulmonary Bypass Established by Peripheral Cannulation

Femoral Cannulation

Closed-chest cannulation of the femoral artery and vein for CPB was practiced at the Mayo Clinic during the 1960s for establishing hypothermic circulatory arrest in patients undergoing intracranial operations. It has since been used with increasing frequency to establish CPB before opening the sternum in reoperations in which there is a high probability of entering a cardiac chamber or major artery during sternotomy. In these situations, a vertical or oblique incision in the groin crease is made over the femoral vessels. After identifying the inguinal ligament and working just inferior to it, the common femoral artery and vein are dissected, and a tape is placed around each. After the patient has been heparinized, a clamp is placed on the distal common femoral artery, any branches are temporarily occluded with ligature loops or small clamps, a clamp is placed proximally, and a transverse incision is made between the clamps. An arterial cannula of appropriate size is inserted into the vessel and, as the proximal clamp is removed, is gently advanced. The tape is snugged down around the cannula using a tourniquet, and the cannula is connected to the arterial line of the pump-oxygenator with the usual precautions to eliminate air. A large (28F-32F) long cannula is similarly inserted into the common femoral vein. This cannula must be advanced over the sacral promontory and into the IVC. When the right femoral vein is used, this is usually easily accomplished. If the left femoral vein is used, it is often necessary to first insert a guidewire, positioning the tip in the right atrium or the adjacent IVC, then a small-bore catheter which is passed over the wire, and then the venous cannula, which is inserted over the smaller catheter. After securing the tape and removing the smaller catheter and the guidewire, the cannula is connected to the venous line of the pump-oxygenator. Alternatively a two-stage cannula can be inserted over a guidewire from either femoral vein, positioning the tip in the SVC under TEE guidance. The upper openings in the catheter are located in the SVC and lower openings in the IVC. This permits placement of caval tapes and opening of the right or left atrium.

Axillary Artery Cannulation

Femoral artery cannulation may result in peripheral embolization, local thrombosis, or aortic dissection. Additionally, in the presence of an existing acute or chronic aortic dissection, retrograde flow from femoral artery cannulation may result in central malperfusion. An alternative is use of either axillary artery. Advantages include absence of malperfusion, establishment of brain blood flow during otherwise whole-body circulatory arrest, and presumably lack of retrograde particulate embolization. The axillary artery is exposed through a transverse incision below and parallel to the lateral two thirds of the clavicle. The pectoralis major muscle is divided in the direction of its fibers and the clavpectoral fascia incised, exposing the pectoralis minor muscle, which may be divided or retracted laterally. Using sharp dissection, the artery is dissected from surrounding tissue, taking care not to injure the branches of the brachial plexus. Proximal and distal control of the axillary artery is obtained. After administration of heparin, the artery can be cannulated directly. Alternatively, an 8- or 10-mm polyester or polytetrafluoroethylene graft is sutured end to side to the artery using a 6-0 polypropylene suture.

Other Sites

Other less commonly used sites for cannulation include the brachial, brachiocephalic, and carotid arteries. Another option for cannulation in high-risk reoperative sternotomy patients is to expose the brachiocephalic artery by dissecting just above the sternal notch, and the IVC by dissecting just below the xiphoid. The skin incisions used are simply the upper and lower poles of the sternotomy incision. Cannulation of the brachiocephalic artery with an appropriate-sized arterial cannula, and the IVC with a large, right-angled, venous drainage cannula can provide full CPB support while the sternum is opened. This technique is particularly useful for patients weighing 40 kg or less, in whom these vessels are easily accessible, and in very small patients in whom peripheral cannulation is not practical.

Indications

Indications for peripheral cannulation have been expanded to include operations performed through small midline or lateral chest incisions (see “Alternative Primary Incisions” earlier in this section), resuscitation of preoperative and postoperative cardiac surgical patients, and support of high-risk patients during percutaneous catheter interventions.

Both arterial and venous cannulation can be accomplished by percutaneous techniques. In this setting, the pump-oxygenator should be used in conjunction with a controlled vortex pump or vacuum-assisted venous return, which permits use of smaller (22F or 24F) venous cannulae.

Blood Conservation

Since the earliest days of clinical use of CPB, there has been concern about the relatively large amounts of allogeneic blood that often must be administered during and early after operations. This concern has been magnified by the prevalence of cardiac operations requiring CPB and the possibility of acquiring deadly diseases such as hepatitis and human immunodeficiency virus. Methods of testing the suitability of donor blood have improved greatly; in well-regulated institutional settings, the current risk of acquiring such diseases from transfused blood is small (see Chapter 5).

A major reason for the near-routine use of non-blood solutions for initial priming of the pump-oxygenator is the desire to minimize use of allogeneic blood. Removal of 500 to 800 mL of blood from adult patients with hematocrits greater than 33% to 35% after induction of anesthesia is safe and is commonly performed. The blood is collected in bags containing CPD anticoagulant, as used by blood banks, and
is left unrefrigerated in the operating room. (Refrigeration even for a short time renders platelets less effective.) This blood is not used during CPB, but rather is administered for its hemostatic and blood-volume effects after protamine is given and major bleeding has been controlled. Donation of blood by the patient several weeks before the operation, as well as by relatives and friends, is widely practiced. This blood has the disadvantages associated with stored blood.

The pump-oxygenator should incorporate one of the compact ultrafiltration devices currently available (see Pump-Oxygenerator earlier in this section). This provides the capability of concentrating the blood left in the machine after CPB, including plasma proteins (in contrast to blood salvage systems), and preparing it for prompt administration to the patient.

Blood aspirated from the surgical field by a standard high-power sucker during and after the cardiac operation can be processed through a blood salvage system. These systems separate, wash, and to some extent concentrate erythrocytes, which are then transfused to the patient. Anticoagulation is provided by heparin that is added to the apparatus. The components of plasma are lost. Postoperatively for about 12 hours, shed blood from the mediastinal and pleural tubes can be collected in the reservoir and returned intravenously to the patient. This blood has been defibrinated in the patient before its collection and has the disadvantage of having essentially no clotting factors.

Most bleeding after cardiac surgery results from coagulation disturbances associated with CPB, related primarily to platelet dysfunction and activation of the fibrinolytic cascade (see Chapter 5 and Response Variables in Section II). Prophylactic administration of antifibrinolytic drugs (epsilon-aminocaproic acid, tranexamic acid, and formerly aprotinin) decreases the frequency of reoperation for bleeding and need for allogeneic blood transfusions in patients after operations employing CPB. Comparative studies have demonstrated equivalent effectiveness of these three agents.

As mentioned earlier in this chapter, aprotinin was withdrawn from the market in May 2008.

Left Superior Vena Cava

A left SVC presents no problems in operations in which a single venous cannula is used. When other techniques for venous cannulation are used, several options exist. A simple method is to use cannulae in the SVC and IVC and to pick up the left SVC flow by the sump-sucker that is positioned partially across the atrial septum (see Commencing Cardiopulmonary Bypass and Left Heart Venting earlier in this section) or in the coronary sinus ostium.

Alternatively, the left SVC may be occluded with a tourniquet for short periods when exposure in the right atrium is suboptimal. As another alternative, a pressure-monitoring needle may be inserted into the left SVC, or the pressure in the left jugular vein may be monitored. As a test, the left SVC is clamped below the needle (downstream). If the monitored pressure does not increase, it may be assumed that the vein can be safely occluded during CPB (see Chapter 58). If the pressure increases substantially, an additional cannula is inserted into the left SVC either via the right atrium and coronary sinus ostium or directly via a purse string where the vein enters the pericardium lateral to the left atrial appendage. The latter is most easily done after CPB has been established but before the right atrium is opened. It is essential if cardioplegic solution is to be delivered retrogradely into the coronary sinus. When three cannulae are in use, two Y connectors are required to connect the venous return to the single venous pump line.

Other Systemic Venous Anomalies

Although a left SVC is the most common systemic venous anomaly that influences management of CPB, it is not the only one. Hepatic venous anomalies, which occur particularly in the various heterotaxy syndromes, can present similar challenges (see Chapter 58). The hepatic veins may attach to the right atrium or even the left atrium, independent of the IVC attachment. They may attach as a single confluent trunk or as several separate veins. The same concerns, considerations, and management options as described for the left SVC are applied to these anomalies.

Left Atrial Pressure Monitoring

Knowledge of left atrial pressure both intraoperatively and postoperatively is important. The most direct way of measuring this pressure is to insert a fine polyvinyl catheter into the left atrium. There is danger of accidental introduction of air into the left atrial line and of cerebral embolization from a tiny thrombus on its tip, but these complications are rare. The only major complication has been occasional bleeding when the catheter is removed. This can be sufficient enough in infants to require immediate blood replacement and, rarely, reoperation. Even in neonates and infants, bleeding after removal has not been encountered when removal is delayed until at least 48 hours postoperatively.

A less satisfactory but more commonly used alternative is to introduce a catheter into the pulmonary artery for intraoperative and postoperative monitoring (as discussed earlier). Unless pulmonary vascular disease is present, the pulmonary artery diastolic pressure approximates mean left atrial pressure. Many groups routinely insert a Swan-Ganz catheter after induction of anesthesia, rather than using a left atrial catheter as described.

Alternative Primary Incisions

Minimal Sternotomy and Thoracotomy

Currently, a number of smaller incisions are being used for procedures on the cardiac valves, the ascending aorta and aortic arch, and the coronary arteries in adults, and for correction of congenital cardiac defects in children and in adults. The various incisions used are shown in Fig. 2-23. They can be classified into three general types: a partial midline sternotomy (upper, lower, or middle), a parasternal incision with resection of one or more costal cartilages, and a more lateral approach through an intercostal space, with or without resection of a segment of costal cartilage or rib, and with or without partial or total transection of the sternum. The commonly used minimal incisions for CABG and for valve replacement or repair are described in Chapters 7, 11, 12, and 13.

Putative advantages of these less invasive incisions, when compared with the full sternotomy, include reduced blood loss, less pain and therefore a lowered requirement for analgesic agents, more rapid convalescence with
reduced hospital stay, reduced prevalence of infection, better cosmetic result, and lower overall costs. In a number of observational studies comparing minimal incisions with a full sternotomy, these advantages have not been consistently observed. In many instances, duration of CPB and total time of operation are prolonged with the minimal incisions. The resulting increase in operating room costs often offsets the reduced costs achieved by a shorter hospital stay.

It appears likely that the trend toward using smaller incisions will continue as new instruments and cannulae are developed that facilitate performing procedures on the heart and great vessels through smaller openings. However, until clear advantages of minimal incisions are demonstrated, full
sternotomy should continue to be used. Cardiac surgeons must be competent and experienced in use of the full sternotomy before attempting procedures through small incisions. Furthermore, they must recognize that the potential or real advantages of small incisions may be outweighed by the disadvantages that can result from limited exposure.

Right Anterolateral Thoracotomy
A right anterolateral thoracotomy through the fourth or fifth intercostal space may be used for cosmetic reasons in young women with developing breasts, for mitral and tricuspid valve operations, and for repair of atrial septal defects. It may also be used in patients who require reoperation only on the tricuspid valve and for reoperations on the mitral valve after one or more previous procedures. This approach provides excellent access to the left and right atria, although the field may be relatively restricted and cannulation of the ascending aorta may be difficult. When the aorta is inaccessible or when coronary artery bypass grafts have been anastomosed to the ascending aorta during a previous operation, the common femoral or axillary artery is used (see Cardiopulmonary Bypass Established by Peripheral Cannulation earlier in this section).

A double-lumen endotracheal tube is used to permit collapse of the right lung and enhanced exposure. The patient is positioned with the right side elevated 30 to 40 degrees. The right arm is flexed at the elbow and kept at the patient’s side. The left arm lies at the side. Groin areas are draped into the operative field. The skin incision follows the intercostal space to be entered and extends laterally to the anterior axillary line. The intercostal muscle is divided and a retractor placed. The pleural cavity is entered and the intercostal muscles are further divided laterally beneath the skin incision if exposure is not optimal. The collapsed lung is gently retracted posteriorly, and the pericardium is incised vertically 1 to 2 cm anterior and parallel to the phrenic nerve. If cannulation of both venae cavae is required, the cannulae are inserted through purse-string sutures in the SVC and in the right atrial wall adjacent to the IVC. Alternatively, a long cannula can be positioned in the IVC after insertion in the common femoral vein, or a two-stage long cannula can be inserted in the femoral vein and the openings positioned in the SVC and IVC. The aorta is cannulated on its right anterolateral aspect. For primary operations, the remainder of the procedure is similar to a median sternotomy approach.

For reoperations on the mitral valve, particularly after previous CABG, cannulating and clamping the ascending aorta may not be possible. In this situation, myocardial management is accomplished by hypothermic fibrillation. Temperature of the perfusate is lowered until the heart fibrillates or until the nasopharyngeal temperature reaches 18°C to 22°C. At that temperature, an external fibrillator is applied to the myocardium to induce ventricular fibrillation. The heart must be maintained hypothermic and in a fibrillating state to avoid ejection of air into the ascending aorta. Rewarming is not initiated until the left atrium has been closed. A soft rubber catheter attached to a cardiotomy suction line is positioned in the left ventricle through the mitral valve or a prosthesis, and is brought out through the atriotomy incision. Continuous suction is applied to this catheter during rewarming to evacuate air from the left ventricle. The catheter is removed just before CPB is discontinued and the left atrial suture line is secured.

Left Thoracotomy
A left thoracotomy may be used for primary or reoperative mitral valve replacement or repair, coronary artery bypass grafting (see Technique of Operation in Chapter 7). For mitral valve procedures, a standard posterolateral thoracotomy or minithoracotomy through the fourth or fifth intercostal space and a vertical incision in the left atrium anterior to the left pulmonary veins provide excellent exposure of the mitral annulus and valve. The procedure can be performed on a beating heart, with hypothermic fibrillation (see preceding Section), or with aortic occlusion and administration of cardioplegia. Peripheral cannulation is generally used (see earlier Section).

Port Access
Thorascopic, then robotically assisted, cardiac surgery through small thoracotomies and ports was introduced by Carpentier and colleagues in early 1996; length of incision for the first case was 5 cm. Subsequently, the technology has progressed to multiple degrees of freedom instrumentation, three-dimensional imaging, and 3- to 4-cm port incision. Conventional anesthesia is used with dual-lumen endotracheal intubation as for the anterolateral thoracotomy incision. CPB is established with peripheral cannulation (femoral artery and vein or venous cannulation via right internal jugular vein). The aorta is occluded either by an endoballoon or a trans-thoracic clamp and antegrade and retrograde cardioplegia are administered. For mitral valve repair, Mihaljevic, Gillinov, and colleagues insert the left arm of the robot through the third intercostal space in the anterior axillary line, the right arm through the fifth intercostal space in the midaxillary line, a working port in the fourth intercostal space in the midaxillary line, and a dynamic left atrial retractor in the midclavicular line.

Challenges of port-access surgery have led to a number of innovations, including new methods for mitral valve repair, arrested heart and beating heart CABG, atrial fibrillation surgery, epicardial lead placement for cardiac resynchronization, removal of cardiac tumors, atrial septal defect closure, and hybrid aortic valve replacement.

Port access procedures have permitted patients to proceed from surgery to a postanesthesia recovery unit rather than intensive care unit (Cleveland Clinic), with early extubation and shorter hospital stay than with conventional surgery via full sternotomy, partial sternotomy, or anterior thoracotomy, and with more rapid return to work (Jarrett C, Mihaljevic T: personal communication, 2010).

Section IV Clinical Methodology of Hypothermic Circulatory Arrest and Its Alternatives

GENERAL COMMENTS AND STRATEGY

Adults
Hypothermic circulatory arrest is widely used in adults for operations involving the ascending aorta, aortic arch, and descending thoracic and thoracoabdominal aorta. For operations involving the distal ascending aorta and aortic arch, it is used in conjunction with hypothermic CPB to provide
Brain protection and optimal exposure of the brachiocephalic vessels and proximal descending thoracic aorta. For operations involving the descending thoracic and thoracoabdominal aorta, it has been used in conjunction with hypothermic CPB, not only to provide brain protection and optimal exposure but also to eliminate the need to place occlusion clamps on the thoracic aorta, which reduces the risk for embolization of arteriosclerotic debris into the vasculature of the brain, kidneys, abdominal viscera, and lower extremities. Opinions differ regarding its use in these situations, because alternative methods of treatment exist. No studies to date have demonstrated the superiority of one technique over another. The various methods are discussed in detail in Chapter 24. Safe time limits of the arrest period are discussed in Section I of this chapter.

Neonates, Infants, and Children

Opinions differ regarding appropriate use of hypothermic circulatory arrest in the pediatric population. A 2003 survey of members of the Congenital Heart Surgeons’ Society indicated that about one third of respondents avoid using hypothermic circulatory arrest, and the frequency of use among the remaining respondents varied widely.

In previous eras, hypothermic circulatory arrest was essential for completing certain operations, such as neonatal operations requiring aortic arch reconstruction and a wide spectrum of other complex operations on neonates. Consensus opinion in the field also held that hypothermic circulatory arrest was a reasonable option for other operations, including most complex operations on full-term neonates and infants. Hypothermic circulatory arrest, however, was considered an unreasonable option for a large spectrum of congenital heart operations, including all simple operations regardless of age, and most if not all complex operations on older infants and children unless aortic arch reconstruction was involved.

In the current era, with technical- and equipment-related advances, it has been clearly established that all operations in neonates, infants, and children can now be performed using CPB strategies that do not use hypothermic circulatory arrest, but rather, continuous perfusion.

Hypothermic circulatory arrest is not essential for any operation, and becomes only one of several options for all operations. Currently, the primary alternative to hypothermic circulatory arrest is continuous full-body CPB for all operations not involving aortic arch repair, and continuous antegrade cerebral perfusion for operations involving aortic arch repair. The technique of continuous full-body CPB is described in detail in Section III. Continuous antegrade cerebral perfusion is described in this section. Controversy exists regarding the relative merits of both of these continuous perfusion techniques when used as alternatives to hypothermic circulatory arrest.

There are two major criteria for judging the efficacy of continuous full-body CPB and continuous antegrade cerebral perfusion relative to hypothermic circulatory arrest. First, in those operations that have traditionally utilized hypothermic circulatory arrest, continuous full-body CPB and continuous antegrade cerebral perfusion must achieve technical outcomes equal to or better than those using hypothermic circulatory arrest. Sufficient data have been accumulated over the last decade to confirm that this criterion is met.

All operations in neonates and infants, including those involving aortic arch reconstruction, can be performed using continuous CPB, including continuous antegrade cerebral perfusion when necessary, with technical outcomes that are at least as good as those achievable using hypothermic circulatory arrest. Second, continuous full-body CPB and continuous antegrade cerebral perfusion must preserve end-organ structure and function, particularly with respect to the brain, as well as or better than hypothermic circulatory arrest. This is a complex and controversial criterion with no definitive resolution at this time, and readers are referred to an editorial by Hanley that addresses the issue in depth. To date, no well-designed multicenter studies have addressed it.

TECHNIQUE IN ADULTS

The technique for establishing hypothermic circulatory arrest in adult patients is described in detail in Chapter 26 under “Aortic Arch Replacement” and “Thoracoabdominal Aorta Replacement.”

TECHNIQUE IN NEONATES, INFANTS, AND CHILDREN

Hypothermic Circulatory Arrest

Preparation for Cardiopulmonary Bypass

Preparation of the patient is the same as described for CPB in general (see Section III). Historically, surface cooling was used as an adjunct to core cooling. Now, most institutions use a cooling blanket and pack ice around the head. These maneuvers, plus a cool operating room, usually reduce the patient’s body temperature to 30°C to 32°C by the time CPB is initiated. The ice bags remain in place around the head until perfusion rewarming is begun after the period of circulatory arrest.

Cannulation

The aortic cannula is inserted into the ascending aorta in the usual manner. In some cases, particularly in infants, it is inserted near or into the brachiocephalic artery. It is critically important to remember that although the purse string around the aortic cannula may be hemostatic, it does not protect against the passage of air. This is important because when CPB is temporarily discontinued to establish circulatory arrest, the arterial pump may be sufficiently nonocclusive that suction initiated by gravity develops in the arterial system. With the aorta at essentially zero pressure, such suction draws air into the aorta and the cannula from the site of cannula insertion. The purse-string suture cannot be made snug enough to prevent this. Therefore, just before CPB is discontinued, the perfusionist clamps the arterial tubing and then discontinues CPB, making suction-driven air entry impossible because the arterial system has been “pressurized.” Just as CPB is recommenced, the perfusionist removes the clamp. These precautions are unnecessary if a clamp is placed on the aorta distal to the aortic cannula. The aortic cannula can then be used for delivery of cardioplegic solution.

Commonly, a single venous cannula is used (see “Siting and Purse-String Sutures for Venous Cannulation” and “One Versus Two Venous Cannulae” in Section III). Two venous cannulae and caval tapes may be used even if the patient weighs less than 3 kg. This allows maximal flexibility. The caval tapes are often left loose and then tightened during
cooling and periods of low flow. Some procedures can be performed at low flow rate with a single venous cannula.

**Cardiopulmonary Bypass for Cooling**

After CPB is established, cooling is begun as described in Section III. Relatively high CPB flows, 2.2 to 3.0 L·min\(^{-1}\)·m\(^{2}\), are used. The nasopharyngeal temperature in neonates and infants can sometimes decrease to 18°C within 10 minutes. However, rapid cooling has been demonstrated to be suboptimal for circulatory arrest (see “Characteristics of the Cooling Process” in Section I), probably because it is not homogeneous. Therefore, the cooling period should last at least 20 minutes and may at times approach 30 minutes.

The target temperature and its most appropriate site of measurement remain controversial (see “Brain Function and Structure: Risk Factors for Damage” in Section I). A nasopharyngeal temperature of 16°C to 18°C is a reasonable criterion to establish circulatory arrest.

Management of gas exchange during cooling is also controversial. The two management options, pH-stat and alpha-stat, each have advantages and disadvantages (see “Arterial Carbon Dioxide Pressure” in Section II). In any event, arterial P\(_{\text{CO}}\), and thus arterial pH—the important variables—are quite controllable with membrane oxygenators and online measurement of arterial pH and P\(_{\text{CO}}\). Mounting evidence suggests that pH-stat management results in superior neurologic outcome.\(^{113,114,111}\)

Hematocrit should not be allowed to drop below 0.25 throughout the operation. Although this variable has not been studied in enough detail to develop a linear relationship between hematocrit level and risk of neurologic injury, evidence suggests that levels of 0.20 result in greater neurologic injury than levels of 0.25, and there is no improvement with higher hematocrit levels.\(^{118,117}\)

During cooling, dilatation of the heart must be avoided. It may be necessary to manipulate the position of the venous cannulae to ensure adequate drainage. A single infusion of cardioplegic solution will usually suffice if circulatory arrest does not exceed 30 minutes.

**Circulatory Arrest**

Time constraints of safe circulatory arrest are discussed in Section I. There is no secure evidence that interposing a short period of CPB increases safe duration of circulatory arrest, presumably because cerebral blood flow is low early after resumption of CPB and presumably inhomogeneously distributed under that condition.\(^{59}\) (see Fig. 2-3). However, when time constraints are anticipated, intermittent perfusion to interrupt hypothermic circulatory arrest may be useful.\(^{11,3}\)

**Cardiac Operation**

The right atrial cannula is often removed from the heart. If arch reconstruction is part of the operation, the aortic cannula is removed as well. The heart and great arteries are opened where appropriate, and repair is performed. The right atrium is usually opened to close any atrial communication, including a patent foramen ovale, or to perform atrial septectomy, as appropriate. When the intracardiac repair is completed, the cardiotomy is closed.

**Rewarming**

The aortic and right atrial cannulae are inserted through the previous purse strings (if arch reconstruction is performed, depending on what reconstructive technique is used, a new arterial purse string may be needed). Extreme care should be taken to ensure that air entry into the aorta does not occur at the initiation of perfusion. Precise details of rewarming with CPB and time of its initiation, myocardial management, cardiac de-airing, and removal of the aortic clamp are highly interrelated and primarily dependent on the method of myocardial management. Each surgical group should determine these protocols individually, using the principles described in this chapter and in Chapter 3.

**Continuous Antegrade Cerebral Perfusion**

**Preparation for Cardiopulmonary Bypass**

This technique is reserved for operations in which aortic arch reconstruction or important aortic manipulation is to be performed. Preparation of the patient is the same as described for CPB in general (see Section III), with a few notable exceptions and areas of emphasis. Regional cerebral oxygen monitoring using near-infrared spectroscopy is performed routinely and has been shown to be beneficial.\(^{716}\) To achieve a technically precise repair using continuous CPB, exposure is of prime importance. The skin incision is taken to the sternal notch, with a retraction stitch placed at the upper pole of the incision. The thymus, when present, is completely resected. It is critical to both mobilize the brachiocephalic vein in its entirety and to open the fascia above the vein to fully expose the brachiocephalic artery. The dissection is continued by complete mobilization of the three major arch vessels and the ductus arteriosus. Mobilizing the left pulmonary artery to the pericardial reflection facilitates exposure of the aorta distal to the ductus arteriosus (if present).

**Arterial Cannulation**

Arterial cannulation is accomplished by direct cannulation of the brachiocephalic artery,\(^{341}\) although alternative methods exist.\(^{716}\) The arterial purse string is placed inferior to the brachiocephalic vein while retracting the vein superiorly using 6-0 polypropylene suture (Fig. 2-24). Care is taken to limit the width of the purse string to prevent narrowing the artery. For cases of interrupted aortic arch, a second arterial purse string is placed into the pulmonary trunk in preparation for lower-body perfusion through the ductus arteriosus. Standard setup also involves placing purse strings in the superior vena cava (SVC) and inferior vena cava (IVC) for bicalveal venous cannulation, and in the right superior pulmonary vein for venuing.

A 6F or 8F arterial cannula is selected for neonates, based on the patient’s weight and brachiocephalic artery size. Larger cannulae are used for larger patients. Before insertion, the obturator is withdrawn until it is flush with the catheter tip (Fig. 2-25). The artery is carefully cannulated to avoid obstructing flow in the brachiocephalic artery. Typically, the artery is opened with a fine-blade knife and the cannula placed directly, without using a vascular clamp. The cannula is advanced to the start of the wire spiral and no farther than 2 mm. The arterial line is then rigorously de-aired.

The cavae are cannulated with right-angled 12F venous drainage cannulae (for neonates weighing 2.0 kg or more), and CPB is initiated at a flow rate of 200 mL·kg\(^{-1}\)·min\(^{-1}\). The IVC cannula is initially oriented superiorly into the atrium to avoid any potential obstruction of lower-body venous return at these high flow rates. A vent is placed into the left side of the heart through the right upper pulmonary
Cardiopulmonary Bypass and Cooling

Once CPB is initiated and adequate venous drainage is confirmed, the patient is cooled to 22°C to 24°C for a minimum of 15 minutes to ensure uniform cooling of the central nervous system. The acid-base status is initially managed according to an alpha-stat strategy, and the perfusate hematocrit is maintained between 25% and 30%. After the cooling period is completed, flow is reduced to $120 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, and the IVC cannula is redirected downward into the IVC. The aorta is clamped and cardioplegia administered through the aortic root in an antegrade fashion. This is achieved using a standard neonatal cardioplegia needle in cases of interrupted aortic arch, coarctation, and Damus-Kaye-Stansel procedure, and using a 22-gauge angiocatheter in cases of hypoplastic left heart physiology with very small ascending aorta. Snares are placed around the two vena caval cannulae.

Preparation for Cerebral Perfusion

The arch vessels are now prepared for cerebral perfusion. The brachiocephalic artery, left carotid artery, and left subclavian artery are each individually clamped with atraumatic neurovascular clips (Fig. 2-26). At this point, direct perfusion is isolated to the head and right arm, the flow rate is reduced to $40 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, and acid-base management shifts to pH-stat. The ductus arteriosus is now formally ligated and transected (as appropriate), and the descending aorta, which has been extensively mobilized previously, is clamped distally.

Arch Reconstruction

At this point, any type of arch reconstruction can be performed. Specifics of the repair are tailored to the particular morphologic lesion. Associated intracardiac anomalies can be repaired during continuous antegrade cerebral perfusion; however, the preferred method is to reestablish total body perfusion (as described in the following text) after the arch repair, and then proceed with the intracardiac component of the repair.
Reestablishing Total Body Perfusion and Associated Intracardiac Repairs

After the arch reconstruction is completed, the descending aorta is unclamped. The neurovascular clips on the base of the brachiocephalic artery and the other arch vessels are also removed. Flow is increased to 120 to 150 mL · kg⁻¹ · min⁻¹, reestablishing total body perfusion. If no additional repairs are needed other than arch reconstruction, reestablishment of total body perfusion coincides with myocardial reperfusion. If any remaining intracardiac lesions are present, a standard aortic clamp is placed on the ascending aorta before the descending aortic clamp and the neurovascular clip on the brachiocephalic artery are removed. Additional cardioplegia is administered as necessary according to the general guidelines outlined in Chapter 3, and the intracardiac repair is performed.

Rewarming

After the arch repair (or combined arch and intracardiac repair) is completed, reestablishment of myocardial perfusion, de-airing, and rewarming are begun, again following general guidelines outlined in Section III of this chapter and in Chapter 3. Snares around the vena cava cannulae are removed, and the IVC cannula is again repositioned up into the right atrium. CPB flow rate is increased to 200 mL · kg⁻¹, and the patient is rewarmed using an alpha-stat strategy. Once normothermia is achieved, the patient is weaned from CPB support and the caval cannulae removed. To prevent obstruction or arterial thrombosis, it is important to remove the arterial cannula from the brachiocephalic artery immediately after separation from CPB.

Equations

The equation derived from the data in Fig. 2-1 is:

\[ \log_{10} V_{O2} = -0.69 \pm 0.061 + 0.043 \pm 0.0021 \cdot \text{temperature} \]

where \( P \) for intercept and slope < .0001, SD of regression = 0.12, and \( r^2 \) = .80.

Correlation (\( r^2 \)) of the data in Fig. 2-15 to a linear model \[^{127}\] was .39; to a log-log model \[^{128}\] .54; to the Arrhenius \[^{129}\] equation (log \( V_{O2} \) proportional to \( Q^{-1} \)) .52; and to a hyperbolic model.69. The equation for Fig. 2-15 is:

\[ 1 / V_{O2} = 0.0062 \pm 0.00024 + 0.0044 \pm 0.00020 \cdot Q^{-1} \]

where \( V_{O2} \) is oxygen consumption (mL · min⁻¹ · m⁻²) at 37°C; \( Q \) is perfusion flow rate (L · min⁻¹ · m⁻²) during CPB; \( P \) for intercept and slope < .0001; SD of regression = 0.0024; and \( r^2 \) = .69.

The equation represented by the nomogram in Fig. 2-11 is:

\[ 1 / V_{O2} = 0.168 \cdot 10^{-0.0587 \cdot T} + 0.0378 \cdot Q^{-1} \cdot 10^{-0.0253 \cdot T} \]

(2A-3)

where \( T \) is temperature in °C. This was derived as follows. The relationship between \( V_{O2} \) and \( Q \) at 37°C was established from published animal experimental data (Fig. 2-15 and Equation 2A-2). Fox and colleagues established these relationships at 20°C in humans during CPB.19 The equation is:

\[ 1 / V_{O2} = 0.0284 + 0.0118 \cdot Q^{-1} \]

(2A-4)

In mating these for the curves at intermediate temperatures, the first coefficient in Equation 2A-3 (relating to maximum \( V_{O2} \) at limitless flow) followed \( Q_{10} \), which happened to be 2.4. The second coefficient (relating \( Q \) slope change to temperature) followed a \( Q_{10} \) of 1.8. Both the experimental data at 37°C and the data of Fox and colleagues at 20°C are described by Equation 2A-3.

The logistic equation for Fig. 2-6 is:

\[ z = -7.3 \pm 1.56 + 0.08 \pm 0.026 \cdot \text{TCA} \]

(2A-5)
where TCA is circulatory arrest time (minutes), P for intercept < .0001, and P for TCA = .002. Also, among the 211 patients without such events, TCA time was 42 ±14.0 (SD) minutes, compared with 59 ±10.2 for the 8 patients with such events (P = .0008).

REFERENCES

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Chapter 2 Hypothermia, Circulatory Arrest, and Cardiopulmonary Bypass


Q


R


To whatever extent possible, injury to the myocardium must be avoided during operations utilizing cardiopulmonary bypass (CPB). During these operations, alterations of myocardial blood flow and oxygen demand are often imposed that, unmodified, might injure cellular energetics and morphology. We have chosen to call the following general discussion one of management rather than protection of the myocardium. Most efforts at management will result in protection of function. However, some techniques at times result in injury; at other times perhaps one or another technique may improve myocardial function. Almost all the techniques of myocardial management introduced in the past are in use.
today by one or more surgical groups, and at this time there is little secure evidence that one method is superior to another, or that the same method is optimal under all circumstances.\textsuperscript{19} This chapter is written, nonetheless, with the bias that few if any methods currently available perfectly protect the heart from the damaging effects of an appreciable period of global myocardial ischemia, but that such a method may evolve with additional knowledge. Emphasis is given to methods that are currently satisfactory.

**HISTORICAL NOTE**

In the early years of cardiac surgery, little mention was made of the possibility that fatal or nonfatal low cardiac output in the early postoperative period was related to damaging effects of the cardiac operation itself. Indeed, in two reviews of complications of open heart operations published in 1965\textsuperscript{182} and 1966,\textsuperscript{183} early postoperative low cardiac output was discussed extensively, but no mention was made of myocardial necrosis as a complication of the surgery or as a cause of low cardiac output, nor of temporary depression of myocardial function (stunning) as a result of the operation itself. Then, in 1967, Taber, Morales, and Fine described scattered small areas of myocardial necrosis, estimated to involve about 30% of the left ventricular myocardium, in a group of patients dying early after cardiac operations, and implicated this as the etiology of the patients’ low cardiac output.\textsuperscript{71} Najafi and colleagues showed in 1969 that acute diffuse subendocardial myocardial infarction was found frequently in patients who died early after valve replacement; these investigators suggested this was related to methods of intraoperative management of the myocardium.\textsuperscript{191} They discussed the possibility that disturbances of the myocardial oxygen supply/demand ratios might be implicated, and that proper perfusion of the subendocardial layer of the myocardium was a particular problem during CPB.

When coronary artery bypass grafting (CABG) began during the early 1970s, cardiologists and cardiac surgeons soon noted that a disturbingly high proportion of surgical patients developed a transmural myocardial infarction perioperatively (immediately before, during, or within 24 hours of operation).\textsuperscript{184,185} Although first widely publicized in connection with CABG, development of transmural myocardial infarction was soon shown to be a complication of cardiac surgery in general. In 1973, in a consecutive series of patients with normal coronary arteries who had undergone various open cardiac operations, Hultgren and colleagues documented a 7% occurrence of acute transmural myocardial infarction.\textsuperscript{185} These investigators recognized that “there is clearly a urgent need to further improve the protection of the heart during [cardiac] surgery.” Various autopsy studies have confirmed that acute transmural myocardial infarction, as well as scattered myocardial necrosis and confluent subendocardial necrosis, can occur after cardiac surgery in the presence of normal coronary arteries.\textsuperscript{186} The rarely occurring extreme manifestation of ischemic damage, “stone heart,”\textsuperscript{187} was recognized at about that time and has been confirmed to be essentially a massive myocardial infarction developing during reperfusion.\textsuperscript{182,183}

Development of knowledge in this area was facilitated by improved methods of identifying myocardial necrosis during life and, to some degree at least, quantifying its extent. Electrocardiographic criteria for diagnosing transmural myocardial infarction and ischemic changes were clarified\textsuperscript{188} and applied to postoperative patients. Appearance of cardiac-specific enzymes in plasma was shown to correlate well with other evidence of myocardial necrosis,\textsuperscript{189,190,191} and their concentrations were shown to correlate directly with amount of muscle that had become necrotic, as judged by other criteria.\textsuperscript{184,189} Isoforms of troponin I and T, sensitive and somewhat specific serum markers of myocardial injury following CPB,\textsuperscript{192,193} were found to be related to duration of ischemic time during cardioplegia, and elevated serum levels were associated with occurrence of delayed post-clamp recovery of ventricular function.\textsuperscript{191} Radionuclide imaging identified the presence and extent of perioperative myocardial infarctions.\textsuperscript{194}

With these methods, a number of clinical studies have supported the finding of autopsy studies that myocardial necrosis is an important and frequent complication of conventional cardiac surgery. In 1974, the frequency of myocardial necrosis in patients convalescing well was demonstrated in a study of isolated aortic valve replacement.\textsuperscript{195} Although hospital mortality was low (2%), 15% of the patients developed electrocardiographic evidence of transmural myocardial infarction, and 70% developed isoenzymatic evidence of myocardial necrosis. In 1974, it was shown that even after the short and simple operation for repair of an uncomplicated atrial septal defect, both adult patients and children developed isoenzymatic evidence of myocardial necrosis. Myocardial necrosis was demonstrated by enzymatic methods in children undergoing surgery for a number of different congenital cardiac defects.\textsuperscript{196}

In a 1975 study, early postoperative cardiac output was reported to be inversely proportional to the extent of myocardial necrosis, and thus the amount of myocardial necrosis was a determinant of the early postoperative condition of the patient and of the probability of survival\textsuperscript{186} (Fig. 3-1). Subsequently, it became clear that myocardial stunning also occurs after cardiac surgery, as well as after regional myocardial ischemia from coronary artery disease.\textsuperscript{197} This also results in a period of low cardiac output of variable duration, albeit without myocardial necrosis in some patients.

It is difficult to identify the individual who first thought about special methods of myocardial management to protect the heart itself from damage during operations. Probably the first special method was retrograde coronary perfusion for surgery on the aortic valve, reported by Lillehei and colleagues in 1956,\textsuperscript{198} and subsequently by Gott and colleagues.\textsuperscript{199} “Elective cardiac arrest” was advocated by Melrose in 1955,\textsuperscript{200} but its use at that time by Cleland in London was for intraoperative exposure, not myocardial management. The first deliberate attempts to protect the myocardium other than by simply perfusing it may have been made by Hufnagel and colleagues in 1961, who introduced profound cardiac cooling using ice slushes\textsuperscript{194} and Shumway and Gripp and colleagues, who used ice cold saline for the same purpose.\textsuperscript{201,202,203} Pharmacologic intervention, designed to provide myocardial protection against the damaging effect of ischemia, began during the 1970s as more knowledge of the pathophysiology of myocardial ischemia evolved.\textsuperscript{204} In the late 1970s, Clark and colleagues accumulated evidence of the favorable effect of nifedipine, a calcium channel blocking agent.\textsuperscript{205,206}

The concept of reducing global myocardial ischemic damage by inducing immediate cessation of electromechanical activity—cardioplegia—was discussed generally by cardiac
myocardial ischemic times greater than 150 minutes. About the same time, Hearse and Brainbridge and their colleagues in London were exploring induction of reversible cardiac arrest and its clinical application. Gay and Ebert studied and advocated potassium-induced cardioplegia in 1973, as did Roe and colleagues in 1977. Randomized trials soon confirmed the advantages of cold cardioplegia. Buckberg identified blood as the optimal cardioplegic vehicle in 1979. In the 1990s Wechsler, Damiano, and others began experiments using concepts of membrane hyperpolarization (nearer the resting state) via adenosine triphosphate (ATP)-sensitive K+ channels rather than hyperkalemic cell membrane depolarization; aprikalim and pinacidil are examples of K+ channel openers.

In 1960, Danforth, Naegle, and Bing showed the rapidity with which myocardial energy supply is replenished after ischemia when electromechanical quiescence is continued for a few minutes into the reperfusion period. This key observation remained unused until Buckberg and colleagues in 1978 showed experimentally that improved outcome could be obtained through use of an initially hyperkalemic reperfusionate. Subsequently, these investigators modified the reperfusionate: For acutely energy-deficient hearts, they introduced warm induction of cardioplegia with an enriched, modified, hyperkalemic blood perfusate. Control of perfusion pressure during reperfusion and continuance of controlled reperfusion until full recovery were additional contributions to cardioplegic and reperfusion techniques.

The mode of delivery of the cardioplegic vehicle was the latest contribution to cardioplegic management. Buckberg in North America and Menasche in Europe documented the efficacy and safety of retrograde and combined antegrade-retrograde infusion in valvar and coronary surgery. Metabolic demands of the heart were reduced by approximately 85% by sustained potassium arrest, even at normothermia. Therefore, using the delivery concepts of Buckberg and Menasche, Lichtenstein and Salerno reasoned that warm continuously delivered blood cardioplegia containing minimal amounts of potassium would provide adequate oxygen, substrate, and buffer to the arrested nonworking heart. They occluded the aorta and maintained the heart quiet and flaccid, but perfused.

### NEED FOR SPECIAL MEASURES OF MYOCARDIAL MANAGEMENT

**Conditions during Cardiopulmonary Bypass**

The heart of intact humans is perfused by blood, ejected from the left ventricle, that leaves the aorta via the right and left coronary arteries. Blood is continuously modified by the organism so as to be correct in its composition and free of damaging materials such as gaseous or particulate microemboli. The amount and distribution of myocardial blood flow (hence myocardial oxygen supply) are continuously regulated, primarily in response to myocardial oxygen demand. This flow is determined by coronary perfusion pressure (aortic pressure), tension in the various myocardial layers (related in part to ventricular wall thickness and size), and coronary vascular resistance. An appropriate coronary vascular resistance depends on proper function of the coronary endothelial cells and underlying smooth muscle. The ratio between flow to the inner one fourth of the myocardium (subendocardial
layer) and that to the outer one fourth (subepicardial layer) in normal hearts with intact circulation is maintained at 1 or a little greater. Although blood flow to the subepicardial layer occurs during both systole and diastole, blood flow to the subendocardial layer occurs almost exclusively during diastole, because intramyocardial tension during systole closes the branches of the coronary arteries that pass perpendicularly through the myocardium to arborize in the subendocardium. The well-known vulnerability to ischemia of the left ventricular subendocardial layer in shock, ventricular hypertrophy, and coronary artery disease, as well as during cardiac surgery, is dependent in part on this relationship, but in part on other factors as well, including a higher rate of oxygen consumption in the subendocardial layer.\(^{215}\)

During CPB, the heart is deprived of most of these protective regulatory factors. During total CPB, blood enters the arterial system through a cannula in the ascending aorta or at a more distal point. It then passes retrogradely into the most proximal part of the aorta and is distributed through the right and left coronary ostia into the coronary arteries. Arterial pulse pressure is narrow (essentially nonpulsatile), and mean arterial blood pressure is variable. The heart is usually more or less empty and thus smaller than usual, thereby increasing intramyocardial tension and transmural and subendocardial vascular resistance, and decreasing flow to the subendocardial layer.\(^{118,224}\) The effect is particularly powerful in the small heart and hypothermic heart.\(^{224}\) Ventricular fibrillation increases intramyocardial tension still more. Coronary vascular resistance during CPB is also affected by circulating vasoactive agents (see “Details of the Whole-Body Inflammatory Response” in Section II of Chapter 2). The perfusate is diluted blood of variable composition with highly abnormal physiochemical properties. The blood may contain microemboli of several kinds, and leukocytes and platelets with altered mechanical and humoral functions.

Thus, there is little reason to assume that the empty perfused human heart on CPB, even when beating, is managed optimally. Furthermore, clinical experience refutes that view.

Vulnerability of the Diseased Heart

In most patients undergoing cardiac surgery, coronary blood supply or the myocardium, or both, are not normal and are therefore particularly susceptible to ischemic and reperfusion damage. Hypertrophied ventricles have long been known to be particularly susceptible to ischemic and reperfusion damage.\(^{37}\) This vulnerability is a result of several factors. Transmural gradients of energy substrate utilization are markedly elevated, increasing the vulnerability of the subendocardium to ischemic damage.\(^{215}\) Xanthine oxidase levels are markedly elevated, increasing the opportunity for elaboration of oxygen-derived free radicals. Superoxide dismutase levels are markedly decreased, reducing the natural defenses against oxygen-derived free radicals.\(^{89}\) Also, wall characteristics of the hypertrophied ventricle make reperfusion of the subendocardium even more difficult than under normal circumstances.

The heart of the patient with chronic heart failure is chronically depleted in energy charge\(^1\) and is particularly susceptible to additional acute depletion and damage during ischemia and reperfusion.

The hearts of experimental animals made cyanotic have been shown to be considerably more susceptible to ischemic and reperfusion damage than are normal hearts.\(^{211}\) This may pertain also to severely ill, cyanotic patients. It is well known that the heart of a patient coming to the operating room in a hemodynamically unstable state or in cardiogenic shock is highly sensitive to the damaging effects of global myocardial ischemia.

Surgical Requirements

Cardiac operations can be performed with the heart perfused and either beating, in ventricular fibrillation, or in diastolic arrest. However, the probability of a precise and complete surgical procedure without air embolization is greatest when the heart is bloodless and mechanically quiescent. These optimal conditions are provided by global myocardial ischemia, but they necessitate appropriate myocardial management to limit the damage that would otherwise result from the period of global myocardial ischemia. The changes associated with myocardial ischemia and those associated with reperfusion are not often discussed as separate events; much of the literature does not allow interpretation of one or the other as a separate event. In contrast, the surgeon, by his or her manipulations, has a unique opportunity to control and influence each separately. Therefore, the following discussion must, for strategic purposes, attempt to distinguish the role of ischemia from that of reperfusion.

DAMAGE FROM GLOBAL MYOCARDIAL ISCHEMIA

Damage from a period of ischemia may result in a variable, and sometimes prolonged, period (many days) of both systolic and diastolic dysfunction without muscle necrosis.\(^{82}\) This condition is termed myocardial stunning.\(^{211,213}\) A period of ischemia may also result in irreversible damage (myocardial necrosis). Some investigators have obtained information indicating that this can develop in the subendocardium after as little as 20 minutes of normothermic ischemia.\(^{19,74}\)

Others have obtained evidence that at least 6 hours of normothermic myocardial ischemia is compatible with myocardial cell survival throughout the myocardium.\(^{82}\) Ischemic damage involves myocardial cells (myocytes), vascular endothelium, and specialized conduction cells (which, with many cardioplegic techniques, may be the last to recover).

Overall reviews of the damage from myocardial ischemia are available.\(^{156,224}\) Nayler and Elz stress the extreme heterogeneity among cells (and by implication among hearts) in the rate of progression of ischemic damage, as well as in the rapidity of the chain of events of ischemia (i.e., the switch from aerobic to anaerobic glycolysis occurs within seconds of onset of ischemia).\(^{224}\)

Although the phrase global myocardial ischemia is appropriately used to describe the situation during cardiac surgery when the aorta is clamped, some blood flow—originating in mediastinal arteries—continues from noncoronary collaterals.\(^{83}\) Generally, noncoronary collateral flow is less than 3% of total coronary flow. However, in patients with cyanotic congenital heart disease, advanced ischemic heart disease, extensive pericarditis, and other conditions, coronary collateral flow may be sufficient to initiate electromechanical

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\(^1\) Energy charge describes the energy-producing capacity of the particular combination of adenosine nucleotides present in mitochondria and cytoplasm of myocytes of a particular heart. Normally, it is 0.85. It would be 1.0 if the nucleotides were present only as ATP, but 0.0 if they were present only as adenosine monophosphate.\(^{80,222}\)
activity in the heart rendered quiescent by cardioplegia, but insufficient to prevent continuing and important ischemia.

**Myocardial Cell Stunning**

Surgeons have long known that patients may have severely depressed cardiac function after cardiac surgery without evidence of myocardial necrosis, and that the duration of the depressed function may last minutes or days. Some instances of delayed recovery of cardiac function after cardiac surgery may be related to initially incomplete reperfusion of the microvasculature of the heart. However, myocardial stunning probably underlies at least some instances of prolonged postoperative low cardiac output. In general, stunning occurs after a state of acutely diminished myocardial blood flow followed by adequate reperfusion. After establishing “normal” blood flow, there remains for a time diminished contractility; that is, perfusion/contractility mismatch.²

Myocardial stunning, which can follow even brief periods of myocardial ischemia, is characterized by systolic and diastolic dysfunction in the absence of myocardial necrosis.⁵¹,²,³⁴ Myocardial stunning has been attributed to reduced oxygen consumption, which might protect against myocardial necrosis. This hypothesis is denied by the fact that stunned myocardium has a high, not low, oxygen consumption.⁶¹ Some have suggested that stunning may be a consequence of abnormal energy transduction or utilization secondary to depletion of high-energy phosphates. Stunned myocardium, however, responds to inotropic stimulation, indicating the presence of adequate ATP to produce active contraction.³³ Myocardial stunning, then, is a form of myocardial cell damage caused by ischemia and reperfusion.⁸¹ Stunning, like myocardial necrosis, tends to begin in the subendocardial layers and progress outward; recovery during reperfusion proceeds in the reverse direction.²⁰

Current information makes it unlikely that stunning is the result of prolonged posts ischemic depletion of myocardial cell energy charge.²¹ It does not appear to be the result of a continuing posts ischemic impairment of coronary blood flow or coronary reserve.¹⁵ It may be caused in part by the release of oxygen-derived free radicals, presumably by activated neutrophils and probably occurring to a major degree during the first few minutes of reperfusion.²¹,²² Experimentally, introduction of superoxide dismutase and catalase (free radical scavengers) before an ischemic period results in nearly full reduction of superoxide dismutase and catalase (free radical scavengers) before an ischemic period results in nearly full protection of contractile indices upon reperfusion, compared with prolonged depression in controls.²¹ Stun ning may be caused in part by an ischemia-induced increase in influx of calcium into the myocardial cells.³⁶,³⁰,³² This possibility has led to the hypothesis that cardiac stunning is related to a defect in calcium-mediated excitation–contraction (EC) coupling that results from the excess calcium.³³ This hypothesis must be reconciled with evidence that after short periods of ischemia, excess intracellular calcium that rapidly accumulates with the onset of reperfusion soon leaves the cells.²⁴

Techniques of myocardial management designed to minimize myocardial necrosis are probably effective against myocardial stunning as well. Thus, for optimal results, these techniques should be used even when the period of global myocardial ischemia is less than that anticipated to result in myocardial cell death.

**Myocardial Cell Necrosis**

Myocardial necrosis after cardiac surgery is the end stage of a complex process initiated by the onset of global myocardial ischemia, maintained by continuing ischemia, and aggravated by reperfusion. The final link in the chain of events, reperfusion, can be favorably modified so as to prevent necrosis, unless the duration of myocardial ischemia is excessive; “excessive” in this context has not yet been defined.³⁰

Immediately after the onset of ischemia, contractile force declines rapidly, as does myocardial pH.¹⁴,³¹ Oxidative metabolism, electron transport, and ATP production by oxidative phosphorylation (which take place in mitochondria) decline rapidly. Some ATP is still produced by relatively inefficient anaerobic glycolysis. Fatty acid utilization is rapidly reduced, while fatty acid acyl-CoA derivatives accumulate because of continuing uptake of fatty acids by myocardial cells. Intracellular acidosis develops because of accumulation of lactate and protons in the myocardial cytoplasm, suppressing anaerobic glycolysis. These developments contribute to damage to the cell membrane and loss of control of cell size, with consequent cell swelling, intracellular accumulation of calcium, and other disturbances of membrane ion transport.¹⁵ This entire process acutely diminishes myocardial energy charge and glycogen reserves, while adenosine, inosine, and other nucleotides that are the results of ATP catabolism and the building blocks for ATP repletion leave the cell. Ultrastructural changes during this early phase are limited to loss of glycogen granules and some intracellular and organelle swelling.

As the duration of ischemia lengthens, intracellular metabolic deterioration continues, still more fatty acids accumulate within the myocytes, and diastolic arrest occurs. Loss of control of sarcoplasmic membrane permeability—which begins within 15 minutes of onset of ischemia—is continuous, and nonspecific membrane permeability increases. Adenosine, lactate, and other small molecules leak still more rapidly out of the cell, as do cytoplasmic proteins and enzymes; these appear in the cardiac interstitium and in the lymph.¹,⁵ As macromolecules within myocardial cells are converted to smaller, more osmotically active molecules by ischemic metabolic conversion, cell swelling proceeds more rapidly.¹² Cellular metabolism and ATP production nearly cease, and glycogen stores are depleted.²² As glycolysis and mitochondrial function are totally lost, cellular autolysis begins, and cell contents leak more extensively into the interstitial space and cardiac lymph.

In many laboratory preparations, as the depletion of ATP continues and finally reaches critical levels, myocardial contracture begins to occur.⁶ The classic belief has been that once contracture is completed, functional recovery is suddenly more difficult, and the time to this end point has been an important criterion in many studies in isolated rat heart preparations.¹¹ However, the time to contracture (1) is

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¹Myocardial hibernation vs. myocardial stunning: If stunning is characterized as a perfusion/contraction mismatch, hibernation is a perfusion/contraction match; in the latter, both are low.² Generally, hibernation is a chronic, potentially reversible state of segmental (less often, global) contractile dysfunction. Theoretically, dobutamine echocardiography, thallium scintigraphy, and positron emission tomography may distinguish hibernating from nonviable myocardium. However, the difference between stunned and hibernating segments may be vague. Marban³ suggests that a decrease in Ca⁺ transients at a cellular level is responsible for the contractile dysfunction in hibernation, whereas a decrease in myofilament Ca⁺ responsiveness accounts for the excitation–contraction decoupling seen in stunning.
endothelial cell activation following hypoxia, anoxia, or ischemia. Activated endothelial cells express proinflammatory properties, including induction of leukocyte adhesion molecules. These result in neutrophil accumulation at the arterial wall and release of oxygen-derived free radicals. Intracellular adhesion molecules (ICAM) are upregulated (see Fig. 3-2). endothelial cell swelling develops during ischemia and becomes more prominent during reperfusion, and secretion of endothelial relaxing factor, as well as of endothelin, the constricting factor, is affected. Boyle and Verrier have reviewed the role of the endothelium in events associated with ischemia and reperfusion (Fig. 3-2). There is

Figure 3-2  A, Hypoxic endothelial cell activation. Hypoxia stimulates Weibel-Palade bodies to release P-selectin and activates nuclear factor (NF)-κB. NF-κB is translocated to nucleus, where it promotes transcription of E-selectin, intracellular adhesion molecule (ICAM), tissue factor, interleukin (IL)-8, and IL-1. IL-1 feeds back to promote more endothelial cell activation through activation of NF-κB. B, Neutrophil adhesion is a multistep process that involves contact between neutrophils and members of the selectin family of adhesion molecules (P-selectin, E-selectin) expressed on activated endothelium. These low-affinity bonds result in rolling and slowing of leukocytes. As this occurs, neutrophils become activated, and a firm bond forms between integrins on the leukocyte surface (i.e., CD 11/18) and adhesion molecules on the endothelium (i.e., ICAM-1, vascular cell adhesion molecule, platelet-endothelial cell adhesion molecule). C, No-reflow phenomenon. Hypoxia results in activation of endothelial cell layer, which promotes leukocyte adhesion and degranulation, endothelial swelling, platelet activation, microthrombosis, and increased vasomotor tone. This contributes to impaired microcirculatory flow, despite what appears to be adequate perfusion through the large epicardial arteries. Adherent neutrophils infiltrate underlying myocardium and promote lipid peroxidation, enzymatic degradation of membranes, calcium overload, and excitation-contraction uncoupling. Collectively, these events result in impaired myocardial function. Key: LPS, Lipopolysaccharide. (From Boyle and colleagues.

highly species dependent, (2) is unknown but probably quite long in humans, and (3) in the rat heart, at least, has a greatly different implication in crystalloid vs. blood-perfused preparations. The appearance of contracture does indicate that the content of ATP has been depleted to a critically low level. Contracture first develops in the subendocardium, because of its higher metabolic rate and consequent more rapid depletion of ATP. Contracture develops more rapidly in hypertrophied than in normal hearts and is delayed in its onset by hypothermia.

Where the process becomes truly irreversible along this course of events, and cell death becomes inevitable, is not known with certainty.

Endothelial Cell Damage

As in the case of myocytes, distinguishing between ischemic endothelial cell damage and reperfusion damage is difficult. Endothelial cell swelling develops during ischemia and becomes more prominent during reperfusion, and secretion of endothelial relaxing factor, as well as of endothelin, the constricting factor, is affected. Boyle and Verrier have reviewed the role of the endothelium in events associated with ischemia and reperfusion (Fig. 3-2).
resistance that have been observed in humans during reperfusion after global myocardial ischemia, and in the no-reflow phenomenon seen after prolonged ischemia, particularly in the inner half of the myocardium. In children, cytokines such as interleukin (IL)-8 are liberated during CPB and may contribute to neutrophil adhesion and migration. Burns and colleagues\(^{B50}\) and Kilbridge and colleagues\(^{B55}\) report endothelial expression of P-selectin, E-selectin, and ICAM in myocardial biopsies taken during cardioplegic ischemic arrest in infants undergoing complex repairs. However, the degree to which endothelial activation and related subsequent events contribute to impaired microcirculatory flow and myocardial dysfunction during cardiac surgery is unknown.

Specialized Conduction Cell Damage

The specialized conduction cells become nonfunctional early in the course of global myocardial ischemia in humans; it may be speculated that their recovery takes longer than does recovery of myocytes. Some support for this is that 5 or so minutes after initially hyperkalemic reperfusion, the ventricular myocardium in some patients responds well and strongly to direct ventricular pacing, although it is quiescent with atrial pacing or without pacing. Then, after 5 or so more minutes, sinus rhythm may appear. Also, when blood cardioplegia and uncontrolled normokalemic reperfusion are used, about 50% of patients have atrioventricular (AV) conduction disturbances when CPB is discontinued.\(^{B3}\) This appears to be a form of specialized conduction cell stunning rather than necrosis, because these disappear by the time of hospital discharge in most of the patients in whom it had developed. Even third-degree AV block persisting as long as 2 months has been observed to give way to sinus rhythm.\(^{B3}\) Validation of this speculation remains to be obtained, however. These changes might also be ascribed to variation of specialized conduction fibers' sensitivity to chemical components of the cardioplegia infusate.\(^{B36}\)

DAMAGE FROM REPERFUSION

The morphologic changes following normal blood reperfusion of ischemic myocardium have been authoritatively presented by Jennings and Reimer.\(^{1,11}\) They stress the complexity of the process, including cell swelling, contraction band necrosis, calcium loading of mitochondria, accelerated washout of creatine kinase early in reperfusion, and the particular vulnerability of the subendocardium. It is clear that there can be no reperfusion damage in the absence of prior ischemia. What is not clear is whether there can be reperfusion damage in the absence of ischemic damage.\(^{S3,S41,S28}\) Clearly, limitation of the duration of ischemia and modification of the conditions during ischemia are fundamental to limiting reperfusion injury.

The following discussion assumes some degree of spontaneous ischemia (coronary obstructive disease) or induced ischemia (low blood flow or aortic clamping); it pertains to uncontrolled reperfusion, which is reperfusion by unmodified blood without control of pressure or flow.

Myocardial Cell Damage

The response of myocardial cells to uncontrolled reperfusion depends in large part on the time-related point along the pathway to cell death that has been reached during the ischemic period. Yet the critical point at which the “explosive cellular response” to uncontrolled reperfusion can be expected is not known with certainty. In the past, it has been defined (in the isolated rat heart) as the point at which contracture appears, a definition of little help in humans undergoing cardiac surgery, because the time to contracture—if it occurs—is unknown but probably quite long. Also, when the rat heart is blood perfused (rather than crystalloid perfused), reperfusion after contracture results in good return of function.\(^{W1}\)

When uncontrolled reperfusion is initiated after global myocardial ischemia in cardiac surgery, the response may be only myocardial stunning. A more severe response consists of reperfusion arrhythmias, particularly ventricular tachycardia and ventricular fibrillation. The more prolonged and the larger the area of myocardial ischemia, the more frequent, severe, and intractable the arrhythmias.\(^{B19}\) A still more severe response is the hard and fibrillating heart, sometimes termed stone heart.\(^{C18,414,214}\) The stone heart phenomenon may involve only some regions of the heart, typically the basilar portion of the left ventricle and the subendocardium. This phenomenon indicates that the heart has undergone severe damage and may be considered to have approached the critical “point of no return.” It has not necessarily reached this point, because the stone heart is, at least under some circumstances, capable of recovery. The histologic features of these advanced forms of reperfusion damage include disruption of the regular myofibrillar pattern and evident contraction bands.\(^{M5}\)

Clearly, the strong influx of calcium into myocytes, and particularly its accumulation in mitochondria, are obvious and fundamental features of reperfusion injury.\(^{22,23,35,314,415}\) Stiffness of cardiac muscle resulting from uncontrolled reperfusion after a period of ischemia is caused by the massive influx of calcium into mitochondria and cytoplasm of myocytes, as well as by edema and capillary disruption.\(^{B11}\) However, many other types of events are ongoing, most well underway within 1 or 2 minutes of uncontrolled reperfusion.

Chemotactic factors of cardiac subcellular origin, activated endothelial cells, activated complement fragments, such as C5a, and cytokines are generated locally in ischemic myocardium.\(^{D9,M6,R28}\) This process activates circulating neutrophils, which accumulate and play an important role in initiating and sustaining reperfusion injury.\(^{B44,C4,E7,M122}\) Neutrophils plug myocardial capillaries as reperfusion continues because of their large size and active adherence to ischemically damaged endothelial cells.\(^{M6}\) Leukocytes, and in particular neutrophils, release large amounts of oxygen-derived free radicals in these circumstances.\(^{155,M10}\) Activated neutrophils also release arachidonic acid metabolites that cause endothelial injury, vasoconstriction, and platelet aggregation. During reperfusion, certain leukotrienes are also released from platelets and endothelial cells.\(^{M3,R29}\)

Oxygen-derived free radicals generated during reperfusion represent one of the fundamental processes that produce damage.\(^{A13,P9}\) Oxygen-derived free radicals are characterized by presence of unpaired electrons and include superoxide (O2), hydrogen peroxide (H2O2), and the hydroxyl radical (OH). Normally, myocardial cells are constantly exposed to superoxide anions in very small amounts, produced in (1) mitochondria (where 95% of oxygen consumption occurs) during electron transport, (2) cell cytoplasm during prostaglandin synthesis and metabolism and oxidation of
tissue catecholamines, (3) vascular endothelium by xanthine oxidase-catalyzed reactions, and (4) extracellular fluids by activated neutrophils. Normally, these very small amounts of oxygen-derived free radicals are well controlled. Superoxide dismutase, which is normally present in myocytes, catalyzes the transformation of superoxide anions to hydrogen peroxide and water; metabolism of hydrogen peroxide to water and oxygen is accomplished by either catalase or glutathione peroxidase, or both.\textsuperscript{13}

The very onset of uncontrolled reperfusion can produce large amounts of oxygen-derived free radicals because of profound alterations imposed on this exquisite system by ischemia. Ischemia progressively decreases the cellular levels of the scavenger superoxide dismutase and also increases metabolic end products of ATP catabolism, such as hypoxanthine and xanthine. These catabolites may participate in producing oxygen-derived free radicals by supplying free radical substrates to endothelial xanthine oxidase.\textsuperscript{82} Also, during ischemia, normally present xanthine dehydrogenase is converted to xanthine oxidase. Superoxide anions are generated at the start of uncontrolled reperfusion. Xanthine oxidase is the catalyst for reoxygenation and metabolism of the considerable amounts of hypoxanthine and xanthine generated during ischemia. A chain reaction results, leading to the generation of other free radicals and of a direct attack by them on unsaturated fatty acids within cell membranes. As part of this chain reaction, iron plays a key role in converting relatively innocuous superoxide radicals into highly damaging hydroxyl radicals.\textsuperscript{82} Peroxidation of membrane lipids has been shown to result in increased membrane permeability, decreased calcium transport into the sarcoplasmic reticulum, and altered mitochondrial function,\textsuperscript{13} setting the stage for myocardial stunning or necrosis.

**Endothelial Cell Damage**

Reperfusion damage to the heart involves more than the myocytes. For example, myocytes surrounding a necrotic area of myocardium may be perfectly viable and functioning 1 hour after the start of reperfusion, only to become necrotic over the subsequent few hours.\textsuperscript{14} This has been shown to be due to delayed closure of coronary arterioles and capillaries and to the resulting no-reflow phenomenon.

The endothelial cells of large coronary arteries appear to be little affected by the damaging effects of ischemia and reperfusion.\textsuperscript{15} The coronary microvasculature is profoundly affected, however, and the resultant endothelial dysfunction appears to develop rapidly with the onset of reperfusion.\textsuperscript{14,15} This damage appears to be minimal after ischemia itself but is incited almost exclusively by reperfusion.\textsuperscript{14} In addition to changes in endothelial cell function, the endothelial cell swells, activated neutrophils and platelets aggregate and adhere to the endothelium, and microvascular obstruction can develop.\textsuperscript{14,15,16}

This rapidly induced reperfusion injury to the endothelial cells severely impairs normal endothelium-dependent relaxations to neutrophils and platelets as well as to thrombin, acetylcholine, and bradykinin.\textsuperscript{20,82,85,15} These alterations could play some role in the observed progressive increase in coronary vascular resistance during reperfusion. In addition, with damage to endothelial cells, smooth muscle beneath the cells is exposed, allowing additional mediators to induce direct smooth muscle contraction.

In addition to these phenomena, coronary vessels are compressed by myocardial areas with high wall tension and hemorrhage and by myocardial cell swelling. This all may lead to inhomogeneous distribution of the uncontrolled, unmodified blood reperfusate or actual “no-flow,” further aggravating reperfusion injury in the clinical setting. These unfavorable events are particularly damaging after prolonged (>24 hours) cardiac preservation,\textsuperscript{26} as may eventually be required for cardiac transplantation.

**Specialized Conduction Cell Damage**

Little specific information is available about reperfusion injury to the specialized conduction cells.

**ADVANTAGEOUS CONDITIONS DURING ISCHEMIA**

Advantageous conditions during ischemia delay the time required for the ischemic myocardium to reach the hypothetical critical point in the course of ischemic injury. This is classically considered the point at which uncontrolled, unmodified blood reperfusion produces explosive cell damage and accelerated myocardial necrosis, rather than recovery. For this discussion, it is this critical point that must be delayed. The common denominator may be delay in severe reduction of the energy charge of the myocardium.

Circumstances that decrease the rate of ATP utilization (or its surrogate, myocardial oxygen consumption) lengthen the safe ischemic interval. These circumstances include immediate cessation of electromechanical activity and hypothermia.\textsuperscript{112} The interrelationships are such that a great advantage is obtained by reducing myocardial temperature from 37°C to 27°C, a lesser advantage by reducing temperature from 27°C to 17°C, and a still smaller advantage by reducing temperature further (Fig. 3-3).\textsuperscript{118} However, for longer periods of arrest (6 hours), Rosenfeldt found an increase in protection with stepwise cooling from 20°C to 4°C.\textsuperscript{20} In a different experimental preparation, Balderman and colleagues\textsuperscript{84} found less satisfactory ventricular performance after 120 minutes of ischemia at temperatures of 6°C and 10°C compared with 14°C and 18°C.

Preoperative enhancement of cardiac substrates seems advantageous, but has been little used in cardiac surgery to date. Myocardial glycogen content can be increased by an intravenous infusion of a glucose-insulin-potassium solution during the 12 hours preceding operation.\textsuperscript{17,13} This can be combined with continuous retrograde coronary sinus infusion of a similar solution during the ischemic period.\textsuperscript{13,15,16}

Acute substrate enhancement before cold cardioplegia and ischemia by initial infusion of warm, hypokalemic, modified and substrate-enriched blood has been shown to benefit hearts that have become energy depleted before the cardiac operation.\textsuperscript{22,23,26} Continuation of the pressure-controlled, warm, enriched blood infusion for a few minutes after the onset of asystole takes advantage of increased coronary flow and better distribution brought about by cardiac asystole.\textsuperscript{31}

Preischemic administration of drugs such as lidoflazine has been shown to be advantageous,\textsuperscript{26,57} although the mechanism of their favorable effect remains arguable (see “Drug-Mediated Myocardial Protection” later in this chapter).
Preischemic myocardial conditioning may surface as an additional tactic to limit damage during an induced ischemic interval and as an adjunct to surgical myocardial management. The concepts of both ischemic preconditioning and postconditioning are well recognized in the science of myocardial ischemia and myocardial ischemia (reperfusion injury have not found general application in cardiac surgery. Ischemic preconditioning refers to brief periods of cessation of coronary blood flow prior to the longer ischemic event, and ischemic postconditioning refers to brief periods of coronary blood flow cessation during the early period of reperfusion. Ischemic preconditioning appears to stimulate potent innate cardioprotective mechanisms that attenuate ischemia-reperfusion injury. The protective mechanisms have been linked to stimulation of myocyte adenosine receptors, reduction of inflammatory responses to reperfusion, attenuation of endothelial dysfunction during reperfusion, reduction in tissue acidosis during ischemia, and prevention of ischemia-induced cell apoptosis.

Similar mechanisms have been invoked for ischemic postconditioning. Ischemia-induced cardiac preconditioning has been shown to reduce infarct size in dog, swine. Several reports suggest that in humans, prodromal angina may limit infarct size. Adenosine activation and α1-adrenergic stimulation are two pathways suggested as mediators of preconditioning. Protein kinase C has been identified as at least one of the factors that when activated by adenosine or phenylephrine results in protection by myocardial preconditioning in laboratory animals (Fig. 3-4). Experimentally in sheep, preconditioning has been produced by CPB alone and the response suppressed by α1-adrenergic blockade or adenosine receptor blocker.

Because of its simpler application to cardiac surgery, remote ischemic preconditioning is the object of numerous clinical trials. It refers to myocardial protection against ischemic injury by inducing ischemia in a distant organ, such as skeletal muscle of the arm. This, and the fact that a preconditioning factor can be transferred from animal to animal, suggests a humoral factor, although a mural component has been implicated as well. Remote ischemic preconditioning has been implemented during cardiac surgery simply by 5-minute cycles of upper-limb cuff inflation to 200 mmHg, separated by 5 minutes of cuff deflation. Clinical trials have thus far produced mixed results.

**ADVANTAGEOUS CONDITIONS DURING REPERFUSION**

Advantageous conditions during reperfusion (1) minimize the persistence of myocardial stunning into the post-CPB period, (2) provide for optimal recovery of function of reversibly damaged myocardium, and (3) resuscitate myocytes that would otherwise have undergone necrosis.

Buckberg and colleagues evolved the methods and demonstrated the advantages of controlling reperfusion. These ideas constitute a clinically useful body of knowledge. In essence, the advantageous conditions consist of:

1. Maintaining electromechanical quiescence during the first 3 to 5 minutes of reperfusion to permit more rapid repletion of myocardial energy charge, minimize regional heterogeneity of reperfusion flow, minimize myocardial energy expenditure until recovery has been established, and minimize intracellular accumulation of calcium.
2. Combating accumulated myocardial acidosis by controlling pH of the initial reperfusate and providing a large buffering capacity to permit more prompt morphologic, biochemical, and functional recovery.

3. Minimizing damage from oxygen-derived free radicals.

4. Reducing ionized calcium in the initial reperfusate to help minimize intracellular accumulation of calcium.

5. Increasing availability of substrate for repletion of myocardial energy charge.

6. Maintaining a low perfusion pressure (=30 mmHg) during the first 60 to 120 seconds of reperfusion to minimize endothelial cell damage and swelling, during which time reactive hyperemia, usually present, allows this low pressure to be maintained with adequate volume and distribution of flow.

7. Maintaining a flow sufficient to encourage near-uniform myocardial distribution of the reperfusate.

8. Continuing control of reperfusion pressure and flow until myocyte, endothelial cell, and specialized conduction cell recovery is essentially complete.

Specific comments about individual items follow, and the details of establishing these advantageous conditions during clinical cardiac surgery are described in “Cold Cardioplegia, Controlled Aortic Root Perfusion, and (When Needed) Warm Cardioplegic Induction” later in this chapter. New information continues to accumulate, and current practices must be changed whenever sufficient information becomes available to indicate the possibility of improving results by modifying methods.

Blood

Blood as the reperfusion vehicle has been shown to be superior to crystalloid solutions. The advantage is due in part to the red blood cell component, although it may not relate to the oxygen transport capacity of red blood cells. Among other things, red blood cells contain abundant oxygen-derived free radical scavengers, which have been shown to be important. The minimal effective level of hematocrit in the reperfusate is 0.15 to 0.20. The buffering capacity of blood proteins, especially their histidine and imidazole groups, is also advantageous.

Leukocyte Depletion

There is little doubt that activated leukocytes play an important role in reperfusion damage. Depletion of leukocytes from the blood reperfusate (by filtration) has been shown to reduce reperfusion injury considerably. Leukocyte fillers are commercially available for pediatric and adult CPB circuits.

Substrate

Addition of the amino acids L-glutamate and aspartate to solutions used to reperfuse the heart after an ischemic insult has been shown by Rosenkranz and by Buckberg and colleagues to be beneficial to metabolic and functional recovery. Their early work has been confirmed by Choong and Gavin and others. Addition of adenosine during reperfusion was theorized to improve postischemic function; there is experimental support for its efficacy. The delay in repletion of ATP after ischemic injury may well relate to lack of availability of adenosine, an important component of the process of rebuilding ATP stores because it is essentially converted to inosine and as such is washed out of cells during reperfusion.

Hydrogen Ion Concentration

The initial reperfusate should contain adequate buffering capacity to combat the intracellular acidosis developed during the ischemic period (see “Blood” earlier in this section). Various buffering agents have been used, but hydroxymethylaminomethane (Tris) and histidine have particularly favorable characteristics.

Calcium

During reperfusion, perfusate calcium content should be low to minimize the influx of calcium into potentially damaged myocytes. The special effects of calcium in the neonatal and infant myocardium are discussed under “Neonates and Infants” under Special Situations and Controversies later in this chapter.

Potassium

Hyperkalemic reperfusion permits rapid repletion of ATP and improved functional recovery, even in the face of ischemic contracture and myocardial accumulation of calcium. It also promotes better myocardial blood flow. Therefore, if controlled reperfusion is elected, the initial reperfusate should contain sufficient potassium to maintain electromechanical quiescence for at least 2 to 3 minutes, and preferably 5 to 10 minutes. The sufficient concentration is about 12 mmol · L⁻¹.

The advantages of hyperkalemic reperfusion in clinical cardiac surgery have been confirmed in a randomized trial by Teoh and colleagues, although these advantages may be difficult to demonstrate in low-risk patients undergoing uncomplicated CABG.

Pressure

After a period of myocardial ischemia, coronary vascular endothelial cells are in a state in which they are easily damaged by high reperfusion pressure, but that state appears to be rapidly reversed by gentle reperfusion. Therefore, in clinical cardiac surgery, it is prudent to keep reperfusion pressure at about 30 mmHg for the first 60 to 120 seconds of reperfusion. Because of reactive hyperemia present at that time, the reperfusion flow rate may nonetheless be large.

Some experimental studies have suggested that reperfusion pressure should be no higher than 50 mmHg, lest excessive myocardial edema develop; others have suggested that it may be as high as 100 mmHg. These differences may be the result of species differences. In a canine model, 1 hour of hyperkalemic reperfusion at 80 mmHg with electromechanical quiescence resulted in improved myocardial function with no more myocardial edema than from normokalemic reperfusion and rapid resumption of cardiac activity. The importance of maintaining a sufficient coronary perfusion pressure at this stage has been well documented in the
diastolically arrested canine heart exhibiting maximal coronary vasodilatation. In that model, endocardial flow falls steeply when coronary perfusion pressure is reduced from 70 mmHg to 40 mmHg. Reduction of perfusion pressure to 20 mmHg leads to substantially increased heterogeneity of flow (Fig. 3-5). Clinical experience at UAB demonstrated the efficacy and safety, after the first 60 to 120 seconds, of maintaining reperfusion pressure between 50 and 75 mmHg, or at the preoperative diastolic arterial blood pressure of the patient, whichever was lower.

Flow and Resistance

At the beginning of reperfusion, coronary resistance is very low, primarily as a result of reactive hyperemia, with additive effects from the cold temperature of the myocardium and the action of vasoactive substances, such as adenosine and lactic acid, that accumulate during the ischemic period. Thus, coronary blood flow is very high initially, even with low reperfusion pressure, but begins to fall within a few minutes of beginning reperfusion.

Subsequently, reperfusion flow is usually about 150 mL · min⁻¹ in adults (about 100 mL · min⁻¹ · m⁻² body surface area). This is about 40 mL · min⁻¹ · 100 g⁻¹ of heart muscle, approximately half the value for normal hearts, but it appears to be adequate in the nonworking empty heart being reperfused under these conditions. In similar experimental models of normal hearts, flow after the initial hyperemia is higher and near control level.

Temperature

In practice, the temperature of the reperfusate is initially about 35°C because of the characteristics of the heat exchange mechanism in the reperfusion circuit. After 2 to 3 minutes, the temperature rises to 37°C. There may be advantages to this gradual return to normothermia. Normothermia is advantageous to the normal function of enzyme systems.

Suppression of Formation of Oxygen-Derived Free Radicals and Enhancement of Free Radical Scavengers

Allopurinol, a xanthine oxide inhibitor, given just before reperfusion, protects the previously ischemic isolated rat heart from reperfusion injury, presumably by slowing conversion of hypoxanthine and xanthine to superoxide ions. Deferoxamine, given just before reperfusion, is also protective in experimental models, presumably by chelating iron and slowing formation of highly damaging hydroxyl radicals from superoxide radicals. Their use during early reperfusion has also been shown to be advantageous in experimental models. However, use of blood as the reperfusate, with its naturally occurring free radical scavengers, appears to obviate need for these agents in clinical cardiac surgery.

Duration

Recovery is not complete at the end of the hyperkalemic phase of controlled reperfusion. This may be because at this time (1) cellular recovery from ischemia is incomplete, and (2) inhomogeneity of myocardial perfusion probably persists. Controlled normokalemic reperfusion with adequate aortic root pressure should be continued until the heart is beating forcefully and is in sinus rhythm. This stage is usually reached 10 to 20 minutes after the beginning of reperfusion. In an experimental study, this length of time has been shown to be required for return of normal coronary vascular resistance, myocardial oxygen consumption, myocardial lactate levels, and ventricular function. Although ATP levels have not yet returned to normal, at this stage the heart itself is able to generate an adequate coronary perfusion pressure. Controlled aortic root reperfusion can therefore be discontinued by removing the aortic clamp, with proper precautions (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” later in this chapter).

Reperfusion with the aorta clamped, as described above, has been called “hot shot.” In practice, controlled reperfusion with the aorta clamped may not be necessary; reperfusion by pump flow supported by pharmacologic manipulation may be adequate.

Adenosine

Adenosine is a potent coronary vasodilator with effects that can reverse coronary artery spasm, increase flow to the myocardial microvasculature during reperfusion, replenish high-energy phosphates, and retard no-reflow effects through its antiplatelet and antineutrophil activity. Studies by Kim and
Ischemic Postconditioning

The proposed mechanisms of ischemic postconditioning are similar to ischemic preconditioning (see Advantageous Conditions During Ischemia earlier in this chapter). Although studies in cardiac surgery have shown a beneficial effect, this technique has not gained general application in clinical cardiac surgery.

METHODS OF MYOCARDIAL MANAGEMENT DURING CARDIAC SURGERY

The objective of any type of myocardial management during CPB should be limiting injury during ischemia by some combination of myocardial hypothermia, electromechanical arrest, washout, \( O_2 \) and other substrate enhancement, oncotic manipulation, and buffering.

No single method of myocardial management is unequivocally the best. Many different methods are in use by surgeons obtaining good results. Surgeons necessarily make a decision as to the method to be used each time they perform a cardiac operation, often based on “preferences” rather than on rigorous comparisons between methods. A number of factors influence the surgeon’s preference:

1. The surgeon’s specific surgical techniques or operative sequencing that influence duration of aortic clamping
2. Strength of the surgeon’s desire to have a quiet, bloodless heart
3. Strength of the conviction that cardiac surgery without myocardial necrosis or residual stunning is desirable and possible despite the added complexity to achieve these goals
4. Institutional environment
5. Costs

Continuous Normokalemic Coronary Perfusion

Empty Beating Heart

The earliest intracardiac operations were performed on normothermic, perfused, empty beating hearts. Experimental studies had been interpreted as showing “normal left ventricular function” after 30 minutes to 3 hours of CPB with the heart perfused, empty, and beating.

Current information indicates that the method is not ideal. Water tends to accumulate in the myocardium during CPB; as a result, ventricular distensibility in dog models is decreased by nearly 50% after 3 hours of CPB with the heart perfused, empty, and beating. The distribution of coronary blood is abnormal. The change in myocardial compressive forces and left ventricular wall geometry impede intracoronary collateral flow supplying potentially ischemic areas of myocardium. Occurrence of transmural myocardial infarction has been reported to be 15% when individual coronary artery perfusion was used for aortic valve replacement, with isoenzymatic evidence of myocardial necrosis in 70% of patients, proportions as high as in patients randomly assigned to cold ischemic arrest.

Despite these considerations, the method can serve well for various procedures and under certain circumstances may be combined with other methods of myocardial management. For example, in elderly patients or those with extensive arteriosclerosis of the aorta, CABG using both internal thoracic arteries may be performed using stabilizers without aortic clamping (“no-touch” technique) and CPB established by peripheral cannulation (e.g., axillary artery cannulation; see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Chapter 2). Tarakji and colleagues report that this technique reduces intraoperative and postoperative strokes in such patients (see “Coronary Artery Bypass Grafting Without Cardiopulmonary Bypass” in Chapter 7).

Mild or moderate whole-body, and thus cardiac, hypothermia are often combined with this method. McGoon and colleagues reported a series of 100 consecutive cases of isolated aortic valve replacement using this method, with no hospital deaths, evidence that, when properly used, the method can provide good results.

Perfusion of Individual Coronary Arteries

Individual coronary artery cannulation is necessary when perfusing the empty beating heart for surgery on the aortic valve. After CPB is established, the aorta is clamped (stopping flow of blood into the aortic root and ostia of right and left coronary arteries), and an incision is made into the first part of the ascending aorta. Small individual cannulae are placed into the ostia of right and left coronary arteries, and, by way of a separate pump, blood is infused into both. The cannulae tips are at least 3 to 4 mm long.

This technique works well in most patients, but it is not ideal. The tip of the cannula may extend beyond the bifurcation of the left main coronary artery, so that only the left anterior descending or circumflex artery is perfused. In about 1% of patients, these two arteries arise separately from the aortic sinus, making proper individual cannulation even more difficult. The prevalence of left dominant systems in patients with aortic stenosis secondary to congenital bicuspid valves is higher than normal; in left dominant systems, the left main coronary artery is shorter than normal, again making individual coronary perfusion more difficult. In about 50% of patients, the conus artery supplying the infundibulum of the right ventricle arises separately from the aortic sinus and is not perfused by a cannula inserted into the right coronary ostium. Also, mechanical injury to the coronary ostia can occur whenever techniques of direct coronary ostial cannulation are used; this results in intraoperative myocardial infarction and late coronary ostial stenosis.

The method in practice is not without periods of global myocardial ischemia. One occurs between aortic clamping and initiation of right and left coronary artery perfusion. This interval varies, depending on the sequences elected by the surgeon, but can seldom be reduced below 2 to 3 minutes.

If exposure for the operation is hampered by leakage of blood around the cannulae, coronary perfusion may have to be discontinued for short periods during the procedure.

When this method is used, the flow rate is of obvious importance, and information obtained for patients in whom...
the flow was delivered separately and directly into right and left coronary arteries during aortic valve replacement provides useful information in this regard.\textsuperscript{88} This information indicates that total coronary blood flow of about 200 to 250 mL·min\(^{-1}\) (≈120 to 150 mL·min\(^{-1}\)·m\(^{-2}\)) is optimal, at least at 30°C. This flow is below 300 mL·min\(^{-1}\), which under some circumstances produces histologic evidence of myocardial damage,\textsuperscript{52} yet is sufficient to prevent undesirable vasoconstriction, which leaves part of the microcirculation without flow or underperfused.

When this method is used, the heart should be kept beating; therefore, the perfusate should be warmer than 30°C. Sapon and colleagues\textsuperscript{522} showed that when ventricular fibrillation persisted throughout the period of coronary perfusion, risk of perioperative infarction and death was higher than if the heart were beating. This would be expected from knowledge of subendocardial blood flow during ventricular fibrillation.\textsuperscript{86,113}

**Hypothermic Fibrillating Heart**

In continuous coronary perfusion with ventricular fibrillation, fibrillation can be maintained by an electrical current, which is necessary when the perfusion is at 37°C, or it may be spontaneously or electrically induced and maintained by moderately hypothermic (25°C-30°C) coronary perfusion. The latter condition is desirable. Coronary perfusion can be through the intact aortic root (as in CABG) or by individual coronary perfusion cannulae during aortic valve replacement.

A number of theoretical objections to the method can be raised. For example, perfusion of the subendocardium is impaired during CPB and ventricular fibrillation, particularly in hearts with ventricular hypertrophy. However, good clinical results have been obtained using either normothermic CPB and electrically maintained ventricular fibrillation or moderate hypothermia and ventricular fibrillation sustained only by hypothermia, or profound cardiac hypothermia and ventricular fibrillation. Akins has reported excellent results from CABG using the latter method.\textsuperscript{55,66} Time constraints must apply to this method, as to most others, but they have not been defined. The surgical conditions that exist with this method are better than with the beating heart, but most surgeons find them less satisfactory than with a cardioplegic technique.

**Moderately Hypothermic Intermittent Global Myocardial Ischemia**

Use of intermittent cardiac ischemia with moderate cardiac hypothermia requires conducting CPB with the perfusate temperature at 25°C to 30°C. The surgeon works on or in the heart intermittently for periods of 10 to 15 minutes, during which time the ascending aorta is clamped (to stop coronary perfusion) or individual perfusion into the coronary ostia is interrupted. Between these periods, the aortic clamp is released (or individual coronary perfusion resumed) for 3 to 5 minutes. When the technique is used optimally, the heart is made to beat (not fibrillate) during this interval. This was the method most commonly used during the 1960s and early 1970s, but is used by some surgeons today.

The clinical results can be good, as was demonstrated by McGoon and by Bonchek and colleagues.\textsuperscript{116,24,111} McGoon’s analysis of one group of patients—those receiving valved extracardiac conduits—indicated no relationship between the proportion of nonsurvivors in the experience and cumulative aortic clamp time. However, because 35% of the 468 patients in the group had low cardiac output postoperatively\textsuperscript{111} (in which subset the mortality was 52%), the method must have been producing myocardial damage. Reduto and colleagues found no difference in left ventricular performance early after CABG, regardless of whether this or cold cardioplegic myocardial protection was used.\textsuperscript{65}

The method does not provide optimal exposure for operations inside the heart, but does provide reasonable working conditions for CABG. Unless the heart is electrically fibrillated just before aortic clamping, it continues to beat during much of the ischemic period, making precise repair difficult. Each time coronary perfusion is recommenced, coronary (and perhaps systemic) air embolization may occur, despite precautions against it. A considerable amount of blood comes into the heart during periods of coronary perfusion, stressing the intracardiac sucker systems and thereby increasing blood damage and interfering with the smooth and efficient flow of the operation. Moreover, each time the coronary arteries are perfused in this uncontrolled manner, a reperfusion injury may occur.

**Profoundly Hypothermic Global Myocardial Ischemia**

The heart may be profoundly cooled by the perfusate, by filling the pericardium with very cold saline solution, or by both, after which the aorta is clamped. The cardiac operation is done during a single period of aortic clamping.\textsuperscript{59,116,94,127,518} In clinical practice, myocardial temperature is generally about 22°C with these methods;\textsuperscript{117} most surgeons believe that this allows 45 to 60 minutes of safe global myocardial ischemia.

This technique provides better operating conditions than those discussed earlier, and good results have been obtained with it.\textsuperscript{110} Despite this important consideration, a randomized study of patients undergoing aortic valve replacement showed that this technique results in as much myocardial necrosis as does continuous individual coronary perfusion.\textsuperscript{54}

Profoundly hypothermic cardiac ischemia without cardioplegia may be preferred for infant cardiac surgery in which hypothermic circulatory arrest is used. Part of the rationale for this preference is that no perfusate passes through the heart to rewarm or inadequately reperfuse it during circulatory arrest, as may happen when CPB is continued.

**Drug-Mediated Myocardial Protection**

Both β-adrenergic receptor blocking and calcium channel blocking drugs, in conjunction with one of the other methods, have been used as part of the myocardial management by some groups.\textsuperscript{112,111} The calcium channel blocking agents verapamil and diltiazem have seemed particularly advantageous because of their prevention of calcium influx into cells and their coronary vasodilatory effects.\textsuperscript{85} However, these drugs are potent negative inotropes and produce prolonged electromechanical quiescence, at least when used clinically in cardioplegic solutions.\textsuperscript{67,110}

Particularly good results have been obtained by giving lidoflazine intravenously just before CPB and using moderately hypothermic intermittent cardiac ischemia.\textsuperscript{94,81} Lidoflazine is believed to be a nucleotide transport inhibitor, which
results in increased myocardial accumulation of endogenous adenosine during ischemia, increased lactate extraction during reperfusion, and improved postischemic function. The basic action of lidocaine is complex and appears to be different from that of β-blocking and calcium channel blocking drugs.

Certain drugs have been shown in experimental studies to reduce reperfusion damage related to oxygen-derived free radicals (see Advantageous Conditions during Reperfusion earlier in this chapter). However, when using blood cardioplegia and pressure-controlled, initially hyperkalemic, blood reperfusion, incorporation of free radical scavengers has not been demonstrated to provide additional protection.

Cold Cardioplegia (Multidose)

The underlying principles of all cardioplegic solutions are listed in Box 3-1. Inducing chemical arrest to conserve energy during the period of myocardial ischemia can be accomplished by one or more of the following methods:

1. Inhibition of the fast sodium current to prevent conduction of the myocardial action potential by one or more of the following methods:
   a. Extracellular hyperkalemia
   b. Sodium channel blockers (e.g., lidocaine)
   c. KATP channel openers (e.g., adenosine)

2. Inhibition of calcium activation of myofilaments to prevent myocyte contraction by one or more of the following methods:
   a. Zero extracellular calcium
   b. L-type calcium channel blockers (e.g., magnesium)
   c. Direct myofilament inhibition with agents such as 2,3 butanedione monoxime (BDM)

Cardioplegic Solution

There are both asanguinous solutions and those that are mixed with blood (at a 2 : 1 or 4 : 1 blood-to-solution ratio), and extracellular solutions and intracellular solutions as distinguished by their potassium concentrations (Table 3-1). Some believe that the components of the solution, particularly K+ concentrations, should be altered according to solution temperature, timing of infusion (initial, maintenance, and terminal), and presumed energy state of the myocardium. In general, K+ concentration is lowered for maintenance, and substrates are added for energy-depleted hearts. Delivery can be intermittent (multidose) or continuous; in the latter case the K+ concentration is lower than for intermittent delivery (Box 3-2).

Hyperkalemic cold sanguinous cardioplegia is advantageous and is preferred, although asanguinous cardioplegia may work equally well. The Buckberg formulation (cold, oxygenated, hyperkalemic blood-crystalloid mixture, with lowered free calcium concentration, added glucose, and added buffering capacity) may be preferable to simple hyperkalemic blood (see Table 3-1). The latter, however, is less costly because it involves only transferring blood perfusate from the CPB oxygenator to a separate reservoir–heat exchanger–pump system, adding sufficient potassium chloride to make it cardioplegic (potassium concentration about 22 mmol · L⁻¹).

Technique of Antegrade Infusion

After CPB is established with the perfusate at 32°C (under which conditions ventricular fibrillation should not develop), an aortic root catheter is inserted through a previously placed purse-string stitch, attached to the cardioplegia line, and de-aired. Optionally, the pressure line of the cannula may be attached to a strain gauge for continuous measurement of aortic root pressure. The aorta is clamped as soon as the aortic root catheter is in place, and in any event before the heart has been cooled sufficiently by the whole-body perfusion so that it becomes arrhythmic or develops ventricular fibrillation.

Cold cardioplegic infusion is begun promptly at a flow of 150 mL · min⁻¹ · m⁻² (based on the data for continuous direct coronary perfusion described earlier in this chapter) for

### Box 3-1 Principles of Cardioplegic Protection

**Arrest**
A rapid and effective induction of diastolic arrest to keep the myocardium relaxed and minimize cellular use of ATP

**Myocardial Protection**
Protective effects to delay the onset of irreversible injury caused by global ischemia and limit the extent of reperfusion injury

**Reversibility**
Readily reversible cardioplegic effects on washout of prompt resumption of heart function

**Low Toxicity**
A short half-life with no toxic effects on other organs after cessation of cardiopulmonary bypass

From Fallouh and colleagues.¹²
Table 3-1 Commercially Prepared Asanguinous Cardioplegic Solutions

<table>
<thead>
<tr>
<th>Components</th>
<th>Plegisol St. Thomas II</th>
<th>CAPS(^a) Buckberg</th>
<th>Bretschneider</th>
<th>ViaSpan UW</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>K(^+)</td>
<td>16</td>
<td>60</td>
<td>10</td>
<td>125</td>
<td>mmmol · L(^{-1})</td>
</tr>
<tr>
<td>Na(^+)</td>
<td>110</td>
<td>15</td>
<td>30</td>
<td>41.5</td>
<td>mmmol · L(^{-1})</td>
</tr>
<tr>
<td>Cl(^-)</td>
<td>128</td>
<td>50</td>
<td>41.5</td>
<td>25</td>
<td>mmmol · L(^{-1})</td>
</tr>
<tr>
<td>Ca(^{2+})</td>
<td>1.2</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>mmmol · L(^{-1})</td>
</tr>
<tr>
<td>Mg(^{2+})</td>
<td>16</td>
<td>4</td>
<td>2.5</td>
<td>—</td>
<td>mmmol · L(^{-1})</td>
</tr>
<tr>
<td>PO(_4^{3-})</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>25</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>Histidine</td>
<td>—</td>
<td>198</td>
<td>—</td>
<td>—</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>2</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>Ketoglutarate</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>Glucose</td>
<td>—</td>
<td>4</td>
<td>—</td>
<td>—</td>
<td>g · L(^{-1})</td>
</tr>
<tr>
<td>Mannitol</td>
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<td>—</td>
<td>30</td>
<td>—</td>
<td>mmol · L(^{-1})</td>
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<td>THAM (0.3 mol)</td>
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<td>—</td>
<td>—</td>
<td>mL</td>
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<td>CPD</td>
<td>—</td>
<td>50</td>
<td>—</td>
<td>—</td>
<td>mL</td>
</tr>
<tr>
<td>Raffinose</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>30</td>
<td>mmol · L(^{-1})</td>
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<tr>
<td>K-Lactobionate</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>100</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>Allopurinol</td>
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<td>—</td>
<td>—</td>
<td>1</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>Adenosine</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>3</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>Hydroxyethyl starch</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>50</td>
<td>g · L(^{-1})</td>
</tr>
<tr>
<td>Glutathione</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>5</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>pH</td>
<td>7.8</td>
<td>7.65</td>
<td>7.1</td>
<td>7.4</td>
<td></td>
</tr>
<tr>
<td>Osmolarity</td>
<td>280</td>
<td>—350</td>
<td>310</td>
<td>320</td>
<td>mOsm/L</td>
</tr>
<tr>
<td>Additives(^c)</td>
<td></td>
<td>—</td>
<td>25</td>
<td>—</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>NaHCO(_3)</td>
<td>10</td>
<td>—</td>
<td>25</td>
<td>—</td>
<td>mmol · L(^{-1})</td>
</tr>
<tr>
<td>0.46 mol aspartate glutamate(^d)</td>
<td>—</td>
<td>—</td>
<td>250</td>
<td>—</td>
<td>mL</td>
</tr>
<tr>
<td>Insulin</td>
<td>—</td>
<td>—</td>
<td>40</td>
<td>—</td>
<td>units · L(^{-1})</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>16</td>
<td>mmol · L(^{-1})</td>
</tr>
</tbody>
</table>

\(^a\)This formulation is intended for dilution by two or four parts blood (perfusate) to solution.
\(^b\)Concentration is diluent dependent.
\(^c\)Added to the commercially prepared solutions.
\(^d\)For warm induction and reperfusion strategies only.

3 minutes in adults; the average adult is given a dose of about 750 mL. In infants and children with a body surface area of less than 1 m\(^2\), the infusion is given at the same flow rate (150 mL · min\(^{-1}\) · m\(^{-2}\) body surface area), but for only 2 minutes. Occasionally the monitored aortic root pressure is less than 30 mmHg, in which case the flow rate, but not the total dose, is increased. However, low aortic root perfusion pressure may be due to aortic regurgitation, hidden by the action of a left ventricular vent; the surgeon must be certain that this is not the situation. In patients with severe ischemic heart disease, the aortic root pressure sometimes rises above 75 mmHg, but the flow should not be reduced.

External cooling of the heart may be established while the cardioplegic infusion is being administered. An isolating pad can be placed between the heart and the left side of the pericardium containing the phrenic nerve. A thin layer of ice slush (or ice-cold saline) is placed over the anterior surface of the heart. Later, whenever the heart will be in a stable position for a time, a thin layer of ice slush can be placed on the surface. The slush is never placed in the pericardial space itself, because left phrenic nerve damage may result. As the slush melts, the fluid is aspirated with the high-vacuum sucker. If it is surgically inconvenient, the slush is omitted.

Neither left nor right ventricle is allowed to become distended at any time. A left ventricular vent (introduced through a right pulmonary vein) is used for some operations, suction through an aortic root catheter for others, and simple needle aspiration of the ventricle across the ventricular septum for others.

Cardioplegic solution is reinfused about every 25 minutes. The initial flow rate is used, and the surgeon must be certain that the aortic valve has closed as the infusion begins. If it has not, a few pinches of the proximal aorta usually accomplish valve closure. Reinfusion is given for 30 to 60 seconds. After the first infusion, the potassium concentration of any subsequently infused cardioplegic solution is reduced to about 10 mmol · L\(^{-1}\).

Should serum potassium levels reach 7 to 8 mEq · L\(^{-1}\) (a rare occurrence), a bolus injection of 400 mg · kg\(^{-1}\) of glucose (as 50% glucose) and 0.2 unit · kg\(^{-1}\) of soluble insulin may be given after the beginning of myocardial reperfusion. Because the levels of both whole-body intracellular
potassium\textsuperscript{1} and circulating insulin\textsuperscript{2} are abnormally low at
this point, these maneuvers are physiologically reasonable. Alternatively, the technique of ultrafiltration during CPB (see “Changes during Cardiopulmonary Bypass” in Chapter 2) may be used to lower elevated serum potassium levels induced by multidose cardioplegia.

**Technique of Retrograde Infusion**

Retrograde infusion of cardioplegic solutions directly into the coronary sinus was suggested by Lillehei and colleagues in 1956.\textsuperscript{1,10} Many have found this technique as effective as antegrade infusion,\textsuperscript{2,20} although the right ventricle (particularly its midportion) and right atrium are less well perfused. When instead retrograde infusion is administered through the right atrium and right ventricle, this problem may be avoided.\textsuperscript{21} Retrograde coronary sinus infusion is particularly advantageous in the presence of acutely developing high-grade coronary artery stenoses or obstructions.\textsuperscript{22}

The surgeon should arrange to deliver either antegrade or retrograde cardioplegia, or both. Either before or after CPB has been established, a purse-string stitch is placed in the right atrial wall, and a small stab wound is made in the middle, through which the retrograde infusion catheter is introduced and under digital control manipulated into the coronary sinus.\textsuperscript{23} The catheter is attached to one arm of the cardioplegia infusion line and de-airred. The pressure measuring arm of the catheter is connected to a manometer. Coronary sinus pressure must not be allowed to rise above 50 mmHg during coronary sinus infusion.

Indications for combined antegrade-retrograde or totally retrograde infusion vary among surgeons,\textsuperscript{24} in part because no clear advantage of retrograde over antegrade infusion of cardioplegic solutions has been identified in patients undergoing elective operations.\textsuperscript{25} However, for aortic valve replacement and during mitral valve operations, refinements of cardioplegic solution are often more conveniently given by the retrograde method. The same may be true for many operations performed through the right atrium for congenital heart disease.

A conscious decision to use both the antegrade and retrograde routes of cardioplegia routinely, delivered in either an alternating sequential fashion or simultaneously, has evolved in the practice of some institutions.\textsuperscript{26,27} This method allows rapid electromechanical quiescence, protects against uneven cardioplegic distribution, and may maximize the duration of ischemia while avoiding cardioplegia overdose. The combined approach has also been successful in pediatric patients.\textsuperscript{28,29} Thus, we believe retrograde cardioplegia is better viewed as synergistic and complementary to antegrade cardioplegia rather than as the sole method of myocardial management.\textsuperscript{30}

Severe obstructive manifestations of coronary artery disease are perhaps the best example for the superiority of retrograde cardioplegia. These include left main lesions and acute coronary syndromes.

Various procedures on the aortic valve and the ascending aorta demanding long clamp times are safely accomplished using coronary ostial infusion supplemented by retrograde infusion. These include acute aortic dissections and the Ross procedure.

Retrograde cardioplegic myocardial protection has some disadvantages. It clearly has various degrees of maldistribution to the right ventricle.\textsuperscript{31,32} There is the occasion when a left superior vena cava is encountered and is unrecognized. Infrequently, the retrograde cannula cannot be placed or is dislodged. There may be less satisfactory protection in hearts with severe left ventricular hypertrophy. Application may be difficult in children and sometimes impossible in neonates. Coronary sinus rupture is a well-known complication (it can be dealt with before separation from CPB by closure of the rupture with fine suture or oversewing the sinus at the site of rupture). Finally, retrograde cardioplegia demands more cannulae, and in some situations seems to clutter the field in greater measure than its benefit.

**Results of Cold Cardioplegia**

Despite several randomized trials and numerous observational studies, the quantitative advantage of the cold cardioplegic technique over other methods of myocardial management in low-risk patients is not unequivocally defined. This alone suggests that it may be small in routine operations performed with reasonable dispatch. The technique facilitates the cardiac operation, and it is the technique most widely used today.

Even with cold cardioplegia, the safe duration of global myocardial ischemic time is not unlimited. Furthermore, it varies according to preoperative ventricular hypertrophy, ventricular function, and energy charge of the myocardium. In general, it is probably about 100 minutes with this particular technique and without controlled reperfusion.

Antegrade cardioplegia has proved safe and effective over many years and in many clinical settings. It is easily accomplished and requires little special equipment. However, myocardial protection in some situations is imperfect using classic antegrade cardioplegia, and thus outcomes may be improved with retrograde cardioplegia delivery.

Retrograde delivery may be superior or synergistic in redo CABG, particularly in the presence of narrowed or obstructed saphenous vein grafts or with an open left internal thoracic artery to an obstructed left anterior descending coronary artery. When CABG is planned in the presence of mild aortic regurgitation (valve not replaced), retrograde cardioplegia is optimal for induction and maintenance. This is also true for other procedures with mild aortic regurgitation in which the aorta need not be opened for direct infusion.

**Single-Dose Cold Cardioplegia in Neonates and Infants**

An opinion has been expressed elsewhere in this chapter that (1) no compelling evidence exists that a different method of myocardial management is required in neonates and infants than in older patients, even though some of the characteristics of the heart in these small patients are different from those in older patients, and (2) the optimal method of myocardial management in general remains arguable.

A method that has given excellent results in neonates and infants is single-dose, oxygenated St. Thomas solution (see Table 3-1). Using a simple pressure bag, it is infused into the aortic root proximal to the aortic clamp. The dose is 20 mL · kg\textsuperscript{-1} and is not repeated.

An exception is the first stage of the hypoplastic left heart operation (Norwood operation). The ascending aorta is thin and small in this situation. Simple cold ischemic arrest may be used, primarily because this avoids inserting a needle into
the delicate ascending aorta. However, because of the critical importance of right (single) ventricular function in this and other operations for single ventricle, many neonatal cardiac surgeons use single-dose cardioplegia administered through a fine catheter or other techniques (see Chapter 49).

The del Nido pediatric cardioplegic solution is discussed later under “Neonates and Infants” under Special Situations and Controversies.

Continuous Cardioplegia

**Cold Perfusion**

Continuous antegrade cold blood cardioplegia has been used as an alternative to single-dose and multidose intermittent cold cardioplegia. Khuri and colleagues have reported data from measurement of myocardial pH indicating that, at least in hypertrophied hearts, the myocardial milieu is more normal, although not completely normal, with this method than with intermittent cold cardioplegia. Clinical experiences suggest that retrograde continuous cold cardioplegic perfusion through the coronary sinus also provides an excellent method of myocardial management during cardiac surgery. Some have used this method after giving an initial antegrade dose of cold cardioplegia. Under experimental conditions, cold retrograde blood cardioplegia after initial antegrade cold blood cardioplegia has been found to maintain optimal myocardial pH.[15]

**Warm Perfusion**

Continuous warm blood cardioplegia, administered by antegrade infusion or by retrograde coronary sinus infusion after an initial antegrade dose, has also been used for CABG and other cardiac operations.[17,52,53] Some groups have found recovery of ventricular function better with use of warm continuous blood cardioplegia than with intermittent cold cardioplegia.[17] Others have found similar efficacy between warm and cold.[57] Although continuous warm blood cardioplegia provides good protection of the myocardium, it is surgically inconvenient for certain operations.

Cold Cardioplegia, Controlled Aortic Root Reperfusion, and (When Needed) Warm Cardioplegic Induction

In the belief that control of all aspects of the reperfusion may be even more important than details of cold cardioplegia, and that acutely ill patients coming to the operating room require a special form of myocardial management, the technique described in this section may be used. During reperfusion the heart is separated from the ongoing events in the remainder of the body for a brief time. The technique is surgically convenient, prolongs the operation only mildly, is essentially devoid of ventricular fibrillation, minimizes myocardial stunning and myocardial necrosis, and appears to result in better postoperative cardiac performance than methods previously used.[19,39] Yet the proof of its advantages has remained as difficult to obtain as for other techniques, which probably accounts for the fact that it is not, as yet, widely used in its entirety.

Some may wish to use simpler methods for routine operations and to restrict the use of this method for more complex high-risk operations. The problems with such a plan are the usual operational disadvantages of a surgical method that is used infrequently rather than routinely (see “Human Error” in Chapter 6), and the fact that even routine operations have a small mortality and occasionally considerable morbidity, which may be nearly eliminated by more perfect myocardial management.

**Circuitry**

A small, separate system on the pump-oxygenator, with its own miniaturized heat exchanger[9] and two pumps, manages aortic root infusions, retrograde infusions, or both. It enables the solution of choice to be infused at controlled temperature and pressure. Although the circuitry seems complex, from the surgeon’s standpoint its use is simple and extremely flexible. Perfusionists have demonstrated their ability to manage it both effectively and efficiently.

**Technique for Elective Surgery**

After the operation is completed, using cardioplegic myocardial management and with the aortic clamp still in place, controlled aortic root reperfusion is begun, initially using warm, hyperkalemic, modified, and enriched blood cardioplegia. The aortic root pressure is kept at 30 mmHg for the first 60 to 120 seconds of the reperfusion, for the reasons discussed earlier. The flow is then increased until the aortic root pressure is 50 to 75 mmHg in adults (or to the normal systemic arterial diastolic pressure in infants and children whose body surface area is <1 m²). A total of 500 mL of the modified blood reperfusate is administered. For patients with a body surface area of less than 1.5 m², the reperfusate volume = 500 × BSA + 1.5. Once that has been infused, the perfusionist continues the controlled aortic root reperfusion by arranging the circuit so aortic root perfusion continues with normothermic, normokalemic, unmodified blood.

During the controlled aortic root reperfusion, the surgeon must concentrate on avoiding ventricular distention, the adverse effects of which have been fully documented.[39,84] The heart remains flaccid and electromechanically quiescent for 2 to 10 minutes after the onset of the controlled aortic root reperfusion. During this time, the coronary resistance may rise, requiring the perfusionist to reduce the flow rate to maintain a constant aortic root pressure. Should that occur, boluses of 5 mL of nitroglycerin[5] may be administered into the line by the surgeon, although the value of this is uncertain.

When the period of quiescence passes and cardiac action begins, the initial rhythm frequently is AV dissociation. Very rarely, it is ventricular fibrillation.[19] The controlled aortic root perfusion continues. Small-volume pulmonary ventilation is begun, because the right ventricle pumps some blood through the lungs. Even the vented left ventricle will eject some blood into the isolated aortic root. The perfusionist must be alert to the need to reduce the aortic root perfusion flow rate to keep the aortic root pressure from becoming excessively high (>120 mmHg). At times, the perfusionist may need to place suction on the aortic root pressure catheter to prevent this problem. Controlled aortic root perfusion is continued until sinus rhythm has returned and ventricular contractions are strong. The interval between the beginning of the controlled aortic root reperfusion and the reaching of these end points

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1Bentley (surface, stainless steel; priming volume, 120 mL; efficiency 0.8) or Shiley (surface, anodized aluminum; priming volume, 150 mL; efficiency 0.6).

2One milligram of nitroglycerin in 5 mL of a balanced salt solution.
is usually 10 to 25 minutes. When the end points cannot be reached, myocardial management was in some way imperfect, and the patient almost certainly will require pharmacologic or mechanical support after CPB.

When the end points are reached, the perfusionist places strong suction (rather than perfusion) on the aortic root catheter and partly occludes the venous line so that some blood passes into the right ventricle and through the lungs; the anesthesiologist intermittently inflates the lung to assist in moving any air that is present out of the pulmonary veins and left atrium into the left ventricle, which ejects it into the aortic root. The suction on the aortic root catheter evacuates any mobilized boluses of air as the surgeon ballots the left atrium and pulmonary veins. These procedures are repeated several times. Although strong suction continues on the aortic root catheter, the aortic clamp is released. As the clamp is released, the patient’s blood volume is rapidly augmented to bring left atrial or pulmonary artery wedge pressure to 6 to 10 mmHg so that the heart’s ejection will continue to maintain a good systemic arterial pressure and a good coronary perfusion pressure. Thereafter, the usual detailed de-airing procedure is followed (see “De-Airing the Heart” in Section III of Chapter 2). CPB is then discontinued; usually nothing remains but to establish hemostasis and close the chest.

**Technique for Energy-Depleted Hearts**

Patients who come to operation in acute cardiac failure with hemodynamic instability or are severely cyanotic have energy-depleted hearts. Specific efforts to improve the energy charge of the heart before submitting it to the period of global myocardial ischemia probably result in better cardiac structure and function postoperatively. Survival should thereby be enhanced.

After making the median sternotomy, CPB at 35°C is established as expeditiously as possible. The aortic root catheter is inserted. The aorta is clamped, and warm hyperkalemic, modified and enriched blood infusion is begun. The infusion is given at the usual flow rate for induction of cardioplegia and continued for 5 minutes. The perfusionist then makes the cardioplegic solution as cold as possible while the aortic root infusion of the same cardioplegic solution continues for another 3 minutes.

Subsequent cold infusions are given every 20 to 30 minutes as usual, except with a potassium concentration of about 10 mmol · L⁻¹. After completing the cardiac procedure, warm reperfusion is performed in the standard manner. (See Special Situations and Controversies in this chapter for details on myocardial management when an acute coronary occlusion immediately precedes the operation.)

**ANCILLARY MEASURES FOR PREVENTING MYOCARDIAL DAMAGE**

Important myocardial necrosis can develop between induction of anesthesia and start of CPB in as many as 30% to 40% of patients undergoing CABG when anesthetic and supportive management is suboptimal (Roe CR: unpublished data, 1976). Lell and colleagues have shown that this proportion can fall to almost 3% under optimal circumstances.¹⁶ No doubt patients other than those undergoing CABG are also at risk of developing myocardial damage during this period, particularly those with marked ventricular hypertrophy or reduced myocardial energy charge. Proper intraoperative management before and after CPB avoids increased myocardial oxygen demand (which can be caused by arterial hypertension, tachycardia, and increased endogenous catecholamine secretion from anxiety and excitement). It avoids high ventricular end-diastolic pressures and the concomitant detrimental effect on perfusion of the subendocardium.²¹¹ Good management maintains an optimal myocardial oxygen supply by maintaining adequate arterial oxygen levels and arterial blood pressure and adjusts ventricular preload and afterload to achieve a reasonable compromise between adequacy of cardiac output and avoidance of deleterious effects (see Chapter 4 for details).

Important perioperative myocardial necrosis can develop because of events occurring after CPB, either before or after the patient leaves the operating room. These may be events that produce imbalances between myocardial oxygen demand and supply. Use of catecholamines for treating low cardiac output early after CPB can result in myocardial necrosis.²¹¹,²³²

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Species and Model Differences**

Possible species and experimental model differences pose a major problem in generating inferences regarding myocardial management during cardiac surgery in human subjects. For example, extensive myocardial edema is frequently observed after ischemia and reperfusion in experimental studies of many different types in many different animal models. Yet in clinical experience it has been rarely evident, except for instances of prolonged and severe damage and of some operations in young patients. In support of this, a careful study in humans using two-dimensional echocardiography failed to disclose any increase in left ventricular mass (a reasonably sensitive indicator of increased myocardial water) after ischemia and reperfusion in experimental studies of certain cardiac events begin at birth and change the characteristics of the neonatal heart into those of a mature heart. The time frame of many of these events is not known. As a result, the rather noncompliant neonatal heart gradually becomes more compliant and proceeds from having little functional reserve to having that of the mature heart. Coronary reserve may be greater in immature hearts.¹¹¹

**Neonates and Infants**

Certain cardiac events begin at birth and change the characteristics of the neonatal heart into those of a mature heart. The time frame of many of these events is not known. As a result, the rather noncompliant neonatal heart gradually becomes more compliant and proceeds from having little functional reserve to having that of the mature heart. Coronary reserve may be greater in immature hearts.¹¹¹
In general, the normal neonatal and infant heart is believed to be more resistant to ischemic and reperfusion damage than is the normal adult heart, even when both are protected by hypothermia during the ischemic period. This greater resistance is not necessarily present in hearts of cyanotic neonates and children or those in acute or chronic heart failure.

**Ischemic Damage**

The cell membrane (sarcolemma) of myocytes from immature hearts is generally believed to be more resistant to the calcium paradox and other forms of calcium damage than that of myocytes from mature hearts. Related to this is the finding that the sarcolemma of immature hearts binds calcium more effectively than that of mature hearts. All this points to greater stability of the sarcolemma of immature hearts and tighter glycolylyc junction, and consequently to greater resistance to the intracellular influx of calcium during and after ischemia. (However, some data suggest less membrane stability and less resistance to calcium influx in the newborn, in contrast to the neonatal heart.) By contrast, immature hearts do not have as good a capacity to sequester (immobilize) intracellular calcium as do mature hearts, making them more vulnerable to damage once calcium has entered the cell.

The adult myocardium normally relies primarily on fatty acids to produce energy for myocardial contraction and cell survival. This is also true in the neonatal heart; in contrast to the adult heart, the neonatal heart has relatively large glycogen stores and thus a relatively large capacity for anaerobic glycolysis. This feature begins to disappear shortly after birth and has disappeared completely by about 2 months of age. ATP utilization appears to be slower in immature hearts because of lower contractile energy requirements. These mechanisms and perhaps others probably provide to both neonatal and immature but otherwise normal infant hearts a higher tolerance to ischemia than that possessed by adult hearts.

Larger stores of amino acids in neonatal hearts also contribute to their increased capacity for anaerobic metabolism, including ATP production, and this persists throughout infancy. This anaerobic ATP production appears to be for the transamination and substrate level phosphorylation of glutamate and pyruvate. This may be expected to result in better maintenance of cellular integrity during ischemia and thereby better functional recovery after ischemia than experienced by adult hearts. These considerations also help explain the demonstrated value of amino acid supplementation for improving tolerance of the immature heart to ischemia and hypoxia. However, some have found the immature myocardium (less than about 18 months old) to be deficient in cytosolic 5'-nucleotidase and thereby less able than mature myocardium to convert cyclic AMP and inosine back to ATP.

**Reperfusion Damage**

Complement activation and leukocyte infiltration play as important a role in reperfusion injury in immature hearts as they do in mature hearts. Other than this, little is known about possible differences in susceptibility of immature hearts to reperfusion (as compared with ischemic) injury, compared with mature hearts.

**Abnormal Immature Hearts**

These characteristics of normal neonatal and infant myocardium may or may not be characteristic of abnormal neonatal or infant hearts. Neonates and infants who come to cardiac surgery are unlikely to have normal myocardium, because they are usually either cyanotic or in heart failure, or both. Julia and colleagues have shown that immature hearts in acute cardiac failure or recently subjected to hypoxia develop profound functional depression after periods of ischemia well tolerated by normal immature hearts. Thus, neonates and infants who come to open heart surgery probably have hearts that are not unusually resistant to the damaging effects of global myocardial ischemia. Cyanosis, both acute and chronic, accelerates these damaging effects and lessens posts ischemic recovery, probably as a result of its effect on myocardial metabolism.

Buckberg has demonstrated experimentally that cyanotic neonates and infants may suffer myocardial injury simply by exposure to reoxygenation during CPB, particularly the initial stages of CPB. This hypoxic/reoxygenation injury may be avoidable by beginning CPB at the ambient oxygen tension of the hypoxic subject. Reoxygenation injury is linked to oxidant damage and a lack of antioxidant reserve capacity in cyanotic immature myocardium. Reoxygenation is associated with elevation of conjugated dienes, generation of hydroxyl radicals causing lipid peroxidation, and release of nitric oxide. Buckberg's studies further suggest that adding desferrioxamine and antioxidants (N-[2-mercaptopropionyl]-glycine, catalase, and coenzyme Q10) to the CPB prime might limit in vivo oxidant damage and improve myocardial functional reserve. The importance of these observations made in animal preparations has yet to be clarified in human neonatal myocardial management.

**Methods of Myocardial Management**

The effectiveness of cold cardioplegia in the immature heart is arguable. A paper by Bull and colleagues is often cited in the introduction to experimental papers on the subject, in support of the idea that cold cardioplegia as used in adults is not effective in young patients. However, these investigators found the “safe” ischemic time to be 65 minutes when intermittent aortic clamping was used and 85 minutes when cold cardioplegia was used. Another early experience found cold crystalloid cardioplegia advantageous in neonates and infants, as did Schachner and colleagues in a small randomized trial.

From experimental models, many different and sometimes conflicting inferences have been derived. In one experimental study, cold cardioplegia was found to reduce ischemic injury in immature hearts. Multidose administration of cardioplegic solutions was shown to be disadvantageous in immature hearts. Various crystalloid solutions have been found experimentally to be superior to others for use in immature hearts. At least one study detected superior myocardial protection in infants and young children with cardiac surgery using cold blood cardioplegia rather than crystalloid St. Thomas solution. Other experimental studies have shown that including glutamate and aspartate in the warm induction of cardioplegia and in the reperfusion provides additional benefit.

One point of view, compatible with all available evidence but not with the opinions of some, is that the basic methodology for myocardial management in neonates, infants, and
Buffers crystalloid solution closer to a pH of 7.4

Lidocaine 1% 13 mL
KCl 2 mEq · mL⁻¹ 13 mL

Plasma-Lyte A Electrolyte-balanced and pH-adjusted carrier solution
Sodium bicarbonate Buffers crystalloid solution closer to a pH of 7.4
Mannitol Used to decrease myocardial edema and serve as an oxygen free radical scavenger

From del Nido and colleagues.⁹⁴

Ca²⁺ concentration is lower to address the evidence of protective calcium overload.⁴²,⁶,⁷,⁸

The del Nido cardioplegic solution (Baxter) is combined with blood in a ratio of four parts solution to one part blood. The accumulated clinical experience with del Nido solution in neonates, infants, and children has been very favorable, with most surgeons noting more rapid return of sinus rhythm and excellent cardiac function despite longer recommended periods between cardioplegia administration (30-45 minutes vs. 20-30 minutes) compared with Buckberg cardioplegia.

When using the technique of cold cardioplegia, controlled aortic root reperfusion, and (when needed) warm cardioplegic induction, all catheters, cannulae, doses, flow rates, and pressures should be scaled appropriately to small patients, as has been described.

Aortic Valve Surgery

When aortic regurgitation is mild in patients requiring aortic valve replacement or other operations, the initial cardioplegic induction may be administered antegradely in the usual way through the unopened aortic root or retrogradely via the previously placed coronary sinus cannula. If the aortic root infusion maintains an adequate pressure in the aortic root, and thus confirms that runoff is minimal, the left atrial vent line is clamped, the infusion continued, and the left ventricle gently massaged manually during the infusion period. This prevents left ventricular distention and assists in perfusing the coronary arteries. If runoff is excessive, an aortotomy is made and the cold cardioplegic infusion is given directly into the coronary ostia (see “Perfusion of Individual Coronary Arteries” earlier in this chapter).

Unless the aortic valve is completely competent, which is uncommon, induction of cold cardioplegia for aortic valve repair or replacement is best accomplished by direct infusion of the solution into the coronary ostia, preceded by retrograde induction via the coronary sinus. The apparently complex sequence about to be described is unnecessary for cardioplegia with the capability for retrograde delivery, but is needed until retrograde reperfusion is established as a useful modality.

The circuit is modified at the operating table in such cases by placing a Y connector in the antegrade cardioplegia tubing, one distal arm of which connects to the aortic root infusion catheter and the other to a second Y, to each arm of which an O-ring direct coronary perfusion cannula is connected. A clamp is placed just beyond the first Y on the tubing leading to the second Y and the direct coronary perfusion cannula. After CPB has been established and the aortic root catheter has been inserted, properly connected, de-aired, and the line leading to it clamped and the line to the second Y unclamped, the aorta is clamped, and the aortic root is opened transversely but not completely. One of the O-ring cannulae is inserted into the left coronary ostium and about three fifths of the initial cardioplegic infusion given. A second O-ring cannula is similarly placed in the right coronary ostium and the remaining two fifths of the cardioplegic infusion given. Ideally, and when easily accomplished, both infusions are given simultaneously. A 5-0 or 6-0 polypropylene suture is placed around each of the cannulae, brought out of the

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Table 3-2 del Nido Cardioplegic Solution

<table>
<thead>
<tr>
<th>Crystalloid Components</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plasma-Lyte A</td>
<td>1000 mL</td>
</tr>
<tr>
<td>Mannitol 20%</td>
<td>16.3 mL</td>
</tr>
<tr>
<td>Mg sulfate 50%</td>
<td>4.0 mL</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>13 mL</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>13 mL</td>
</tr>
<tr>
<td>Plasma-Lyte A</td>
<td>Electrolyte-balanced and pH-adjusted carrier solution</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>Buffers crystalloid solution closer to a pH of 7.4</td>
</tr>
<tr>
<td>Mannitol</td>
<td>Used to decrease myocardial edema and serve as an oxygen free radical scavenger</td>
</tr>
</tbody>
</table>

Arresting Agents

Potassium chloride Depolarizes cell membrane
Lidocaine Sodium channel blocker; serves to maintain arrest in a hyperpolarized state, counteracting negative effects of potassium
Magnesium Used as a calcium channel blocker and competitive inhibitor of calcium interaction with contractile proteins, preventing contractile activation

From del Nido and colleagues.⁵⁴

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children should be similar to that in adults. Little concerted effort has been made to overcome the technical difficulty of accomplishing this in very small hearts. For example, in many operations in neonates, the procedure is done largely through the right atrium; retrograde infusion of the sanguinous cardioplegic solution into the coronary sinus should be particularly convenient. In fact, the feasibility, safety, and efficiency of retrograde coronary sinus infusion of blood cardioplegic solution as maintenance cardioplegia has been demonstrated in the arterial switch operation and in complex arch reconstruction.⁶⁵

Despite the general point of view expressed earlier (that the methodology of myocardial management in infants should be similar to that in older and larger patients), there is considerable interest in and increasing experience with a cardioplegic solution that has a focused application in neonates, infants, and children. The del Nido cardioplegic solution (Table 3-2)⁵⁴ has undergone several modifications at various pediatric centers but contains the basic extracellular composition used in the Buckberg solutions, with the following major differences:

- Calcium concentration is lower to address the evidence that pediatric myocardium relies more on calcium flux for excitation-contraction and is less tolerant of postischemic calcium overload.
- Magnesium is increased to further depress cell excitability (and therefore cellular metabolism and ATP utilization) during the ischemic period.
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adjacent aortic wall, and secured with a “snugger.” Subsequent cardioplegic infusions may be given in this manner or retrogradely via the coronary sinus (see “Technique of Retrograde Infusion” earlier in this chapter).

A major reason for preferring this arrangement for the induction and maintenance of cardioplegia lies in the reperfusion phase. All devices for aortic valve replacement, except the allograft, autograft, and stentless xenograft valve inserted free hand or as an aortic root replacement, leak a variable but usually considerable amount of blood from the aortic root back through the sewing ring, at least, into the left ventricle. The left ventricular vent can keep the vent decompressed, but maintaining desired aortic root pressure frequently becomes impossible during reperfusion via the aortic root. Therefore, the usually warm and initially hyperkalemic modified blood reperfusion after aortic valve surgery is infused through the direct coronary perfusion cannulae. Many surgeons use simultaneous retrograde coronary sinus infusion as an adjunct to this reperfusion phase, beginning with substrate-enhanced hyperkalemic blood, then switching to normothermic normokalemic blood. While this is proceeding, closure of the aortotomy begins. The left ventricular vent keeps the operative field dry even after cardiac action begins. The last few sutures of the aortotomy closure are placed but left loose.

When the heart is beating well and the criteria previously described for ceasing the controlled aortic root reperfusion are met, suction on the left ventricular vent is reduced to a low level or stopped. If necessary, the venous tubing is occluded briefly to drive a little blood through the lungs and back into the left ventricle. Blood ejected by the left ventricle now essentially fills the aortic root and escapes through the loose part of the suture line. An assistant clamps the tubing leading to the Y connector with its direct coronary perfusion cannulae and unclamps the line to the aortic root catheter, the perfusionist places mild suction on the aortic root catheter, and the surgeon removes the “snuggers” on the sutures around the coronary cannulae; the sutures and then the cannulae are removed, and the aortotomy sutures are snuggled and tied. Because the heart is beating well, aortic root pressure (being monitored by the aortic root cannula as usual) may tend to rise, but the perfusionist controls this by increasing suction on the aortic root pressure monitoring catheter as needed. The aortic clamp is still in place, so systemic air embolization is not possible.

By slightly occluding the venous line, the perfusionist causes the left ventricle to receive sufficient blood so that its ejection maintains an aortic root pressure of about 100 mmHg systolic. Suction continues on the aortic root catheter with minimal or no suction on the left ventricular vent, and usual de-airing procedures are accomplished (see Chapter 2). The aortic clamp is then removed, and the entire de-airing procedure is repeated. The remainder of the operation proceeds in the usual manner.

Coexisting Mild Aortic Regurgitation

Some cardiac operations are complicated by the presence of aortic regurgitation, too mild to justify aortic valve replacement (or repair) but sufficient to complicate myocardial management. If an appropriate aortic root pressure can be maintained during induction of cold cardioplegia and reperfusion, standard aortic root infusions are used.

If the regurgitation is such that an appropriate aortic root pressure cannot be achieved during administration of the cold cardioplegic solution or during reperfusion, cold cardioplegic solution is administered retrogradely through the coronary sinus. In the reperfusion phase, the heart can be carried through the initially warm hyperkalemic reperfusion and then the normokalemic reperfusion until cardiac action fully resumes, using exclusively retrograde perfusion through the coronary sinus.

Alternatively, the aortic valve can be made surgically competent for subsequent multidose aortic root cardioplegia administration. With or without an initial antegrade cardioplegia dose into each coronary ostium, a 5-0 or 6-0 polypropylene suture is placed through the midpart of each cusp’s free edge (Frater stitch). The suture is pulled up to verify good leaflet apposition, after which the aortotomy is closed, bringing the polypropylene suture out through the suture line. With a now competent aortic valve, subsequent doses of cardioplegia can be administered through the aortic root. During reperfusion, the polypropylene suture is removed when cardiac contraction resumes.

Acute Occlusion of the Left Anterior Descending Coronary Artery

Patients brought to the operating room shortly after acute occlusion of the left anterior descending coronary artery (LAD) are usually hemodynamically unstable or in cardiogenic shock. Because of both the acute occlusion and the hemodynamic state, these patients present a special challenge. The principles set down and tested by Allen and Buckberg and colleagues form the basis for the management program described here.\(^8\) These principles include:

- Initial controlled administration of warm cardioplegic solution (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” earlier in this chapter), administered antegrade for 2.5 minutes and retrogradely (through the coronary sinus) for 2.5 minutes
- Use of at least a vein graft to the LAD (or another coronary vessel if it is responsible for the acute infarction)
- Prolonged (20 minutes) controlled reperfusion with hyperkalemic modified blood of the LAD (or another coronary artery if it was the culprit responsible for the area of acute ischemia)

The general plan of the operation is as described under Technique of Operation in Chapter 7. Initial warm cardioplegia (administered as just described) followed by usual cold cardioplegia produces cardiac quiescence. During the grafting procedure, it is supplemented in the usual manner by additional intermittent infusions of the cold cardioplegic solutions. Antegrade and retrograde routes of infusion are used alternately, or as dictated by ease of delivery, or by number of grafts in place.

Large Noncoronary Collateral Flow

Occasionally in patients with long-standing severe coronary artery disease, noncoronary collateral blood flow may be large and, under the usual circumstances of the coronary operation, can actually restart cardiac electromechanical activity by
washing out the cardioplegic solution, despite cardiac venting and multidose cardioplegia. Clinical experience indicates that under these circumstances, risk of important myocardial damage is increased. Therefore, at the first sign of this development, the whole-body perfusate temperature is made as cold as possible until the patient’s temperature reaches 20°C; the perfusate temperature is then set at 20°C and CPB flow is reduced to about 1 L · min⁻¹ · m⁻². Another dose of cold cardioplegia is then administered.

**Active Rheumatic Pericarditis Necessitating Multiple Valve Surgery**

Patients with active rheumatic pericarditis necessitating multiple valve surgery present special problems because of their extensive and vascular pericardial adhesions. If divided, these adhesions cause excessive bleeding and contribute an excessive collateral coronary flow. Such patients are critically ill, usually with aortic and mitral regurgitation. If cold cardioplegia is used, low-flow hypothermic perfusion and repeated cardioplegic infusions are necessary.

**Reoperative Surgery**

Reoperative CABG also may present special issues for myocardial management. In general, cardioplegic myocardial protection should be established early in the procedure—usually before mobilization of the cardiac mass. Antegrade and retrograde infusions are complementary; it is thus imperative that the retrograde catheter be placed accurately in the coronary sinus. This can be accomplished by minimal sharp dissection over the acute margin of the right ventricle followed by accurate posterior freeing dissection. In most cases, a patent internal thoracic artery graft should be identified by careful dissection, partially mobilized, and occluded during aortic inflow. Whether patent vein grafts should remain in situ is controversial; however, for induction of cardioplegia, aortic root is clamped. This can be accomplished by minimal sharp dissection over the acute margin of the right ventricle followed by accurate posterior freeing dissection. In most cases, a patent internal thoracic artery graft should be identified by careful dissection, partially mobilized, and occluded during the cardioplegic period. Alternatively, it can be left open and CPB conducted at 20°C to 25°C with frequent cardioplegia administration and intermittent fibrillation.

Because of adhesions, the myocardium tends to rewarm more quickly than usual. More frequent cardioplegia infusion, low systemic perfusion temperature, or both are appropriate.

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C


D


E


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Section I  Anesthetic Consultation for Adult Cardiovascular Surgery

The principal tasks of the anesthesiologist are to provide relief from pain for patients during operation and to provide optimal operative conditions for surgeons, both in the safest manner possible. To do this, the anesthesiologist must be a competent physician and a clinical pharmacologist, with a broad knowledge of surgery and the ability to utilize and interpret correctly a variety of monitoring devices.

— Dripps, Eckenhoff, and Vandam

Introduction to Anesthesia: The Principles of Safe Practice

Anesthetic management specifically for adult cardiovascular surgery is differentiated from management for general surgery by the high-risk profile and unique perioperative needs of the patient. Despite increasing age and comorbidity, operative mortality has been decreasing in these patients, likely reflective of advances in surgical technique, better management of comorbidity, and advances in monitoring and care by dedicated cardiothoracic anesthesiologists. Furthermore, implementation of evidence-based medical practice to better justify clinical decisions continues to favorably influence patient outcomes.

PREOPERATIVE PREPARATION AND EVALUATION

Consultation with a cardiothoracic anesthesiologist is essential to optimal preoperative evaluation and management. A thorough history, physical examination, and understanding of the presenting cardiac pathology and proposed surgical procedures are critical. Particular focus should be on areas that may affect perioperative management, such as concomitant patient comorbidity, potential for drug interactions, challenges to airway management and invasive monitoring, as well as acuity of presenting clinical status.

Management of Preoperative Medications

Cardiovascular Medications

Medical management of cardiovascular comorbidity often necessitates extensive pharmacologic support. In general, most anti hypertensive and antianginal cardiac medications are continued preoperatively. Whether to continue or when to withhold preoperative antihypertensive therapy requires careful consideration of patient risk/benefit. Acute withdrawal of particular antihypertensive medications such as β-blockers or clonidine may result in considerable perioperative hemodynamic instability; conversely, their continuation results in better hemodynamic stability, antiarrhythmic properties, and improved patient outcome.

Preoperative management decisions to continue angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor subtype I antagonists (ARA) are controversial. Patients in whom ACE therapy was maintained until the morning of surgery had increased probability of hypotension at anesthesia induction. ARA-treated patients had more postinduction hypotension refractory to conventional vaspressors than those on other antihypertensive therapy (β-blockers, calcium channel blockers, or ACE inhibitors), thus, some recommend discontinuing ARA before surgery.

Comfere and colleagues examined the relationship between timing of discontinuing chronic ACE inhibitors and ARA and development of hypotension after induction of general anesthesia. Patients receiving chronic ACE inhibitors or ARA therapy less than 10 hours prior to general anesthesia were at elevated risk of developing moderate hypotension within 30 minutes of induction. However, this responded to conventional therapy and was not associated with increased occurrence of postoperative complications.

Hemodynamic instability with continuation of ACE or ARA therapy is not consistent. Licker and colleagues reported that patients treated long term with ACE inhibitors and who had normal left ventricular function did not have altered endocrine response or hemodynamic instability during cardiac surgery. Furthermore, continuing therapy has beneficial effects on the myocardium and kidneys. If it is elected to continue these drugs on the day of surgery, one should recognize that episodic hypotension necessitating vasopressor support may occur.

Thus in general, continuation of preoperative cardiovascular medications is recommended.

Statins

Beyond lipid-lowering properties, statins possess pleiotropic effects that have been reported to reduce postoperative morbidity and mortality. Among patients undergoing percutaneous coronary interventions, Pascual and colleagues reported that statin pretreatment was associated with reduced early ischemic events, primarily in those with high levels of inflammatory markers. Pretreatment with fluvastatin of patients undergoing coronary artery bypass grafting (CABG) reduced P-selectin levels, an adhesion molecule that plays a role in the pathogenesis of arteriosclerosis, below those of patients given a placebo. Berk and colleagues reported less use of inotropic agents among patients treated with fluvastatin, speculating that myocardial injury caused by cardiopulmonary bypass–induced inflammatory changes was reduced. Others have reported a protective effect of statin pretreatment in reducing myocardial damage after CABG. Based on these beneficial pleiotropic effects, statin therapy should be continued routinely in the perioperative period.

Medications Affecting Hemostasis

Preoperative antiplatelet therapy affects perioperative hemostasis and may contribute to excess bleeding and increased blood product requirements.

Aspirin

In a meta-analysis of preoperative aspirin (ASA) use, Alghamdi and colleagues reported more blood loss and red blood cell (RBC) transfusion, yet similar platelet transfusion and reexploration for bleeding, among patients who received ASA preoperatively. Patients stopping ASA 2 days or less before surgery had higher RBC transfusion requirements than those stopping it more than 7 days preoperatively, patients discontinuing ASA 3 to 7 days before surgery had little increased requirement for RBC transfusion.
Discontinuing ASA 2 to 3 days preoperatively may be sufficient for return of adequate platelet function. Thus, there is little evidence to recommend a preoperative 7-day ASA-free interval.\textsuperscript{3,6} There are, however, reported benefits to continuing ASA therapy perioperatively. Dacey and colleagues reported that continuation of ASA therapy in isolated CABG was associated with reduced mortality without substantial risk of hemorrhage or blood product requirement.\textsuperscript{3,1} Similarly, Bybee and colleagues reported that preoperative ASA was used within 5 days of CABG was associated with lower in-hospital mortality and similar risk of reoperation for bleeding and blood product requirements as in those not receiving preoperative ASA.\textsuperscript{1,9}

Practice guidelines from the Society of Thoracic Surgeons (STS) state that although evidence indicates ASA is beneficial, recent ingestion has been associated with perioperative bleeding.\textsuperscript{3} Guideline recommendations are as follows: class IIA recommendation to discontinue ASA 3 to 5 days before elective CABG to reduce bleeding risk; class IIA recommendation for continuation of ASA in urgent and emergency CABG, recognizing that benefits of ASA outweigh the small bleeding risk; and class I to start ASA early postoperatively to take advantage of improved graft patency and mortality benefits.\textsuperscript{3,5}

**Clopidogrel** Clopidogrel, an inhibitor of platelet aggregation, works by irreversibly blocking adenosine diphosphate (ADP)-mediated platelet activation. Clopidogrel reduces thrombotic complications following coronary stenting and improves outcomes after acute coronary syndromes. Patients who undergo CABG within 3 to 5 days of clopidogrel treatment are at increased risk for bleeding, RBC requirement, and need for reoperation.\textsuperscript{8,10,26,21} (Fig. 4–1). Reichert and colleagues examined the effects of a waiting period after clopidogrel treatment before CABG. Patients who received clopidogrel treatment within 72 hours of operation vs. those delayed at least 5 days after clopidogrel treatment had higher transfusion requirements (95% vs. 52%).\textsuperscript{26}

Others, however, have reported no increase in bleeding, RBC transfusion, or reexploration for bleeding in CABG patients receiving clopidogrel.\textsuperscript{6,2} Ebrahimi and colleagues examined the effect of clopidogrel in patients with non-ST-segment elevation acute coronary syndromes (NSTE-ACS) requiring CABG in the Acute Catheterization and Urgent Intervention Triage strategy (ACUITY) trial.\textsuperscript{31} The trial enrolled 13,819 patients with NSTE-ACS undergoing early invasive management; 11.1% underwent CABG before discharge. Clopidogrel-exposed patients had longer median duration of hospitalization than nonexposed patients, but experienced fewer ischemic events within 30 days and had similar occurrence of non-CABG-related major bleeding and post-CABG major bleeding. Multivariable analysis demonstrated that clopidogrel use before CABG was a predictor of reduced 30-day composite ischemia.

**Combination Antiplatelet Therapy** Cannon and colleagues reported dual antiplatelet therapy within 5 days of CABG was associated with a moderate increase in bleeding; however, combined therapy conferred no appreciable risk for bleeding if discontinued more than 5 days before CABG.\textsuperscript{51} ASA and clopidogrel taken together until 2 days before operation is associated with higher postoperative blood loss, but not increased occurrence of reoperation for bleeding.\textsuperscript{70} Others report increased blood product requirement with preoperative dual antiplatelet therapy.\textsuperscript{34} For patients undergoing off-pump CABG, Shim and colleagues reported that preoperative ASA and clopidogrel exposure even within 2 days of operation did not increase perioperative blood loss and blood transfusion requirements.\textsuperscript{39} Of note, the authors used strict transfusion guidelines and intraoperative blood salvage techniques.

**Glycoprotein IIb/IIIa Inhibitors** Both short- and long-acting glycoprotein IIb/IIIa inhibitors cause profound platelet dysfunction. In patients requiring emergency operation, they are associated with increased risk for bleeding. Recommendations for discontinuation prior to surgery vary, depending on whether the agent used is a short- or long-acting inhibitor (4 to 6 hours for short acting; 12 to 24 hours for long)\textsuperscript{15} (Table 4–1). Lee and colleagues recommend delaying surgery for the appropriate time interval and transfusing platelets as needed rather than prophylactically.\textsuperscript{12} De Carlo and colleagues state that emergency surgery can be performed safely in patients treated with all glycoprotein (GP)IIb/IIIa inhibitors, and similarly note that platelet transfusion should be for clinically relevant bleeding.\textsuperscript{10} Lincoff and colleagues report that urgent CABG can be performed for abciximab-treated patients without excess mortality or important morbidity.\textsuperscript{6,6}

![Figure 4-1](image-url)  
**Figure 4-1** Prevalence of composite outcome (reoperation or major bleeding) by number of days clopidogrel was stopped before surgery. Denominator for points on curve is the total number of patients who were exposed to clopidogrel ≤7 days before surgery (n = 329); 89 patients experienced the composite outcome. Red line = clopidogrel exposure. CABG, Coronary artery bypass grafting. (From Berger and colleagues.)\textsuperscript{15}

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**Table 4-1 Platelet Inhibitors, Mechanism, and Half-Life**

<table>
<thead>
<tr>
<th>Platelet Inhibitor</th>
<th>Mechanism</th>
<th>Half-Life</th>
<th>Minimum Wait</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clopidogrel</td>
<td>ADP-platelet aggregation</td>
<td>8 hours</td>
<td>5–7 days</td>
</tr>
<tr>
<td>Abciximab</td>
<td>GP IIb/IIIa</td>
<td>30 minutes</td>
<td>12 hours</td>
</tr>
<tr>
<td>Tirofiban</td>
<td>GP IIb/IIIa</td>
<td>2.2 hours</td>
<td>4 hours</td>
</tr>
<tr>
<td>Eptifibatide</td>
<td>GP IIb/IIIa</td>
<td>2.5 hours</td>
<td>4 hours</td>
</tr>
</tbody>
</table>

Modified from Lee and colleagues.\textsuperscript{12}  
Key: ADP, Adenosine 5′-diphosphate; GP, glycoprotein.
**Table 4-2** Commonly Used Herbal Supplements, Relevant Pharmacologic Effects, and Perioperative Considerations

<table>
<thead>
<tr>
<th>Herbal Supplement</th>
<th>Relevant Pharmacologic Effects</th>
<th>Perioperative Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echinacea</td>
<td>Activation of cell-mediated immunity</td>
<td>Allergic reactions; decreased effectiveness of immunosuppressants; potential for immunosuppression with long-term use</td>
</tr>
<tr>
<td>Ephedra (&quot;ma huang&quot;)</td>
<td>Increase in heart rate and blood pressure through direct and indirect sympathomimetic effects</td>
<td>Risk of myocardial infarction and stroke from tachycardia and hypertension; ventricular arrhythmias with halothane; long-term use depletes endogenous catecholamines and may cause intraoperative hemodynamic instability</td>
</tr>
<tr>
<td>Garlic</td>
<td>Inhibition of platelet aggregation (may be irreversible); increased fibrinolysis; equivocal antihypertensive activity</td>
<td>Potential to increase risk of bleeding, especially when combined with other medications that inhibit platelet aggregation</td>
</tr>
<tr>
<td>Ginkgo</td>
<td>Inhibition of platelet activating factor</td>
<td>Potential to increase risk for bleeding, especially when combined with other medications that inhibit platelet aggregation</td>
</tr>
<tr>
<td>Ginseng</td>
<td>Lowers blood glucose; inhibition of platelet aggregation (may be irreversible); increased PT and PTT in animals</td>
<td>Hypoglycemia; potential to increase risk of bleeding</td>
</tr>
<tr>
<td>Kava</td>
<td>Sedation; anxiolysis</td>
<td>Potential to increase sedative effect of anesthetics; potential for addiction, tolerance, and withdrawal after abstinence unstudied</td>
</tr>
<tr>
<td>St. John’s wort</td>
<td>Inhibition of neurotransmitter reuptake</td>
<td>Induction of cytochrome P450 enzymes, affecting cyclosporine, warfarin, steroids, protease inhibitors, possibly benzodiazepines; decreased serum digoxin levels</td>
</tr>
<tr>
<td>Valerian</td>
<td>Sedation</td>
<td>Potential to increase sedative effect of anesthetics; benzodiazepine-like acute withdrawal; potential to increase anesthetic requirements with long-term use</td>
</tr>
</tbody>
</table>

Modified from Ang-Lee and colleagues.\(^{A9}\)
Key: PT, Prothrombin time; PTT, partial thromboplastin time.

**Herbal Supplements**

Complementary medicine is growing, with 32% to 37% of Americans using herbal supplements in a given year.\(^{B18,317}\) Herbal supplements are frequently underreported and taken in conjunction with conventional drugs. This results in the potential for herb-drug interactions that may affect absorption and metabolism and/or potentiate or antagonize cardiovascular medications.\(^{A2,A5,A9,A12}\)

There are no clear data on specific herbal-anesthetic interactions, but increased bleeding tendency, cardiovascular instability, and sedation have been associated with their use.\(^{A17}\) Garlic, ginkgo biloba, and ginger possess antiplatelet activity that may increase bleeding risk, particularly for patients on ASA therapy.\(^{A2,A9,317,F3}\) Garlic inhibits platelet aggregation in a dose-dependent manner. Ginkgo inhibits platelet activating factor; based on pharmacokinetic data and bleeding risk, patients should discontinue ginkgo at least 36 hours preoperatively.\(^{A9}\) Coumarin-containing medications such as chamomile, horse chestnut, motherwort, and tamarind also enhance bleeding risk.\(^{A2}\) In addition to increased bleeding risk, ginkgo biloba has been associated with elevated blood pressure when combined with thiazide diuretics.\(^{H12}\)

Prolongation of anesthesia may result from kava, valerian, and St. John’s wort. Kava, an anxiolytic and sedative, may prolong benzodiazepine sedation secondary to its ability to potentiate central nervous system depressants.\(^{A9,317,F3}\) Concomitant use of opioids with valerian and kava may lead to increased central nervous system depression. Valerian produces dose-dependent sedation, which appears to be mediated through modulation of \(\gamma\)-aminobutyric acid (GABA) neurotransmission.\(^{A9}\) Ginseng may inhibit the analgesic effect of opioids.\(^{A2}\)

Other direct effects of herbal medicines in the operative setting include cardiovascular instability from ephedra ("ma huang") and hypoglycemia from ginseng.\(^{A9}\) Ephedra contains alkaloids, including ephedrine and pseudoephedrine, that can increase blood pressure and heart rate. Tachyphylaxis may result from long-term use secondary to depletion of endogenous catecholamine stores, which may necessitate use of direct-acting sympathomimetic agents for hypotension.\(^{A9}\) Ginseng may lower postprandial glucose, resulting in hypoglycemia, particularly in fasting patients.\(^{A9}\) Immunosuppressant properties of echinacea theoretically increase risk for poor wound healing and infection.\(^{B15,H8,317}\) Short-term use of echinacea has immunostimulatory effects that may diminish effectiveness of immunosuppressive medications in the perioperative period.\(^{A9}\)

In general, current recommendations are for patients to discontinue herbal medicines at least 2 weeks before surgery.\(^{A9,317,F1,F2}\) (Tables 4-2 and 4-3).

**MONITORING**

**Cannulae**

In addition to standard American Society of Anesthesiologists monitoring, large-bore intravenous (IV) and brachial or radial arterial cannulae are placed prior to induction of anesthesia. Central venous access is commonly obtained following induction of anesthesia. Decisions about whether to use a central venous triple-lumen catheter vs. a pulmonary artery flotation catheter are case and surgeon/anesthesiologist specific, as is use of ultrasound guidance for placement.
Table 4-3 Herbal Supplements and Interactions with Cardiovascular Medicines

<table>
<thead>
<tr>
<th>Conventional Medicine</th>
<th>Herbal Supplement</th>
<th>Result of Interaction</th>
<th>Possible Mechanism of Interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Interaction with:</strong></td>
<td><strong>Digoxin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guar gum</td>
<td>Decreased plasma digoxin levels</td>
<td>Reduced absorption; guar gum reduces gastric emptying, which results in transient delayed digoxin absorption</td>
<td></td>
</tr>
<tr>
<td>St. John’s wort</td>
<td>Decreased plasma digoxin concentration</td>
<td>Induction of P-glycoprotein; digoxin is a substrate of P-glycoprotein, which is induced by St. John’s wort</td>
<td></td>
</tr>
<tr>
<td>Siberian ginseng</td>
<td>Increased plasma digoxin levels</td>
<td>Some component of Siberian ginseng might impair digoxin elimination or interfere with digoxin assay</td>
<td></td>
</tr>
<tr>
<td>Wheat bran</td>
<td>Decreased plasma digoxin levels</td>
<td>Reduced absorption; bran contains fibers that can trap digoxin</td>
<td></td>
</tr>
<tr>
<td><strong>Interactions with:</strong></td>
<td><strong>Antihypertensive drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ginkgo</td>
<td>Increased blood pressure</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Licorice</td>
<td>Hypokalemia</td>
<td>Additive effect on potassium excretion; licorice has mineralocorticoid effects that may cause potassium excretion</td>
<td></td>
</tr>
<tr>
<td><strong>Interactions with:</strong></td>
<td><strong>Antiplatelet drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ginkgo</td>
<td>Spontaneous hyphema</td>
<td>Additive inhibition of platelet aggregation; ginkgolides have antiplatelet activities and are platelet activating factor receptor antagonists</td>
<td></td>
</tr>
<tr>
<td><strong>Interactions with:</strong></td>
<td><strong>Anticoagulants</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boldo/fenugreek</td>
<td>Increased anticoagulant effect</td>
<td>Additive effect on coagulation mechanism; boldo and fenugreek contain anticoagulant coumarin</td>
<td></td>
</tr>
<tr>
<td>Devil’s claw</td>
<td>Increased anticoagulant effect, purpura</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Garlic</td>
<td>Increased anticoagulant effect; increased clotting time</td>
<td>Additive effect on coagulation mechanisms; garlic has antiplatelet activity</td>
<td></td>
</tr>
<tr>
<td>Ginkgo</td>
<td>Reports of intracerebral hemorrhage</td>
<td>Additive effect on coagulation mechanism; ginkgolides from ginkgo have antiplatelet activity and are platelet activating factor receptor antagonists</td>
<td></td>
</tr>
<tr>
<td>Green tea</td>
<td>Decreased anticoagulant effect</td>
<td>Pharmacologic antagonism; warfarin produces anticoagulation by inhibiting production of vitamin K–dependent clotting factors; green tea contains vitamin K and thus antagonizes effect of warfarin</td>
<td></td>
</tr>
<tr>
<td>St. John’s wort</td>
<td>Decreased anticoagulant effect</td>
<td>Hepatic enzyme induction; warfarin is metabolized by CYP1A2 in the liver, which is induced by St. John’s wort</td>
<td></td>
</tr>
<tr>
<td><strong>Interactions with:</strong></td>
<td><strong>Antilipidemic drugs</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>Decreased plasma levels simvastatin concentration</td>
<td>Hepatic enzyme induction; simvastatin is extensively metabolized by CYP3A4 in the intestinal wall and liver, which is induced by St. John’s wort</td>
<td></td>
</tr>
<tr>
<td>Lovastatin</td>
<td>Decreased lovastatin absorption</td>
<td>Decreased absorption of lovastatin resulted in an increase in LDL levels that led to abortion of trial. Lovastatin pharmacokinetics and LDL returned to normal after bran discontinuation</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Izzo and colleagues.\textsuperscript{25}

Transesophageal Echocardiography

Transesophageal echocardiography (TEE) is integral to monitoring cardiovascular patients.\textsuperscript{23,31,12,33} It is useful in identifying and determining the mechanism of cardiac pathology, can assist with separation from cardiopulmonary bypass (CPB), and may identify unsatisfactory surgical results. In 12,566 consecutive cardiac surgical patients, Eltzschig and colleagues found that TEE influenced surgical decision making in 7% of patients pre-CPB and 2.2% post-CPB.\textsuperscript{33} Minhaj and colleagues recommended that TEE be used routinely in all patients undergoing cardiac surgery, because the information provided substantially influences subsequent patient management. They found that TEE demonstrated new cardiac pathology in one of every three patients, and in 3% of patients, it influenced decisions regarding use of CPB.\textsuperscript{11} Similarly, Qaddoura and colleagues support use of TEE in primary CABG, noting that it provided new findings pre- and post-CPB in 13% of patients.\textsuperscript{23} Early work by Leung and colleagues revealed an association between new and
persistent post-CPB wall motion abnormalities and increased risk for postoperative mortality and myocardial infarction.\(^4\)\(^,\)\(^5\)

TEE Doppler-derived hemodynamic indices can provide noninvasive quantitative information on intracardiac velocities, pressure gradients, and valve area.\(^6\)\(^,\)\(^7\) Estimates of forward flow (stroke volume and cardiac output) provide useful information, particularly in cases in which a pulmonary artery flotation catheter is not used (Fig. 4-2). Pulmonary artery systolic pressure can be estimated with use of the modified Bernoulli equation (Box 4-1), which converts instantaneous velocities to pressure gradients.\(^6\) Stroke volume can be calculated as the product of the cross-sectional area and time velocity integral using two-dimensional and Doppler measurements.\(^6\) Figure 4-3 and Box 4-2 illustrate TEE-derived noninvasive calculation of aortic valve area.

Intraoperative TEE has particular utility and is considered standard of care for patients undergoing mitral valve repair. It allows immediate assessment of reconstructed mitral valves, revealing residual or de novo regurgitation. Whether to intervene for residual mitral regurgitation following repair is controversial. Gillham and colleagues suggest not returning to CPB for a second attempt at mitral valve repair for mild mitral regurgitation based on TEE findings alone.\(^6\) In their

---

**Box 4-1** Modified Bernoulli Equation for Calculating Intracardiac Pressure, and an Example

\[
\Delta P = 4 V^2
\]

\[P_{PA} \text{ (systolic) pressure} = 4 V^2_{TR} + P_{RA}\]

**Example:**

\[P = 4 (2.3 \text{ m} \cdot \text{s}^{-1})^2 + 10 \text{ mmHg} \]

\[P_{PA} \text{ (systolic) pressure} = 31 \text{ mmHg}\]

---

**Figure 4-2** Transesophageal echocardiographic image depicting peak tricuspid regurgitant velocity in m \(\cdot\) s\(^{-1}\). Key: CW, Continuous wave; HR, heart rate; PG, pressure gradient; V, velocity.

**Figure 4-3** Use of transesophageal echocardiography (TEE) for noninvasive calculation of aortic valve area. **A,** Midesophageal imaging plane for left ventricular outflow tract diameter measurement (2.98 cm). **B,** Continuous-wave Doppler velocity time integral (VTI) of aortic valve (1.43 m). **C,** Pulsed-wave Doppler of left ventricular outflow tract (0.232 m).
investigation, 61% of patients with mild mitral regurgitation identified by intraoperative TEE had zero to trace regurgitation at follow-up transthoracic echocardiography. On the other hand, others have reported a trend toward increased need for reoperation when TEE identifies residual mitral regurgitation following mitral valvuloplasty. TEE is critical in assessing and detecting patients at risk for a rare complication following mitral valve repair: left ventricular outflow obstruction secondary to systolic anterior motion of the anterior mitral valve (Table 4-4). Advances in ultrasound technology with real-time three-dimensional TEE will enhance the ability to image and add to the utility of intraoperative echocardiography in cardiac surgery.

**Cerebral Oximetry**

Use of noninvasive measures of regional cerebral oxygen saturation in adult cardiac surgical patients is controversial because there are conflicting data regarding the ability of cerebral oximetry to predict outcomes following cardiac surgery. Hong and colleagues reported cerebral oximetry was not predictive of cognitive decline following heart surgery; however, patients who exhibited intraoperative desaturation required longer postoperative hospitalization. Similarly, Reents and colleagues reported that use of cerebral oximetry was not predictive of postoperative cognitive performance. In contrast, Slater and colleagues reported that intraoperative cerebral oxygen desaturation was associated with increased risk for cognitive decline and prolonged hospital stay after CABG. More data are clearly needed to demonstrate whether complications associated with modifications in patient care are reduced by noninvasive monitoring of regional cerebral oxygenation.

**MEDICATIONS**

**Premedication**

With a majority of patients being admitted the same day as their surgical procedure, preoperative medications for anxiolyis are commonly administered in the preoperative holding area or operating room once the IV cannula is placed. A short-acting sedative such as midazolam is administered in doses of 1 to 2 mg and is preferred over longer-acting agents.

**Induction Agents**

Propofol (substituted isopropylphenol) and etomidate (a carboxylated imidazole-containing compound) are commonly used induction agents in combination with a low-dose opioid and muscle relaxant, with the goal of facilitated recovery (Table 4-5). Propofol has several properties that make it an advantageous induction agent, particularly for procedures of short duration. It facilitates more rapid awakening compared with other induction drugs, and its antiemetic effects minimize postoperative nausea. Etomidate possesses minimal cardiovascular side effects, making it an ideal agent for induction in hemodynamically unstable patients and those with impaired ventricular function. However, it has a number of side effects, including pain on injection and transient adrenocortical suppression through inhibition of 11-β-hydroxylase. Use of etomidate, particularly in the critical care setting, is controversial because of its adrenal suppression side effects. Ketamine (a phencyclidine derivative) is less commonly used as an induction agent, primarily because of cardiovascular side effects including increases in heart rate and blood pressure, myocardial depression, and episodic emergence delirium. Thiopental is also less commonly used for induction of general anesthesia in cardiac surgery because of less favorable properties. Some centers use high-dose narcotics for induction of anesthesia in cardiovascular patients.

**Maintenance of Anesthesia**

The goal of maintenance anesthesia is to maintain stable hemodynamics while allowing for facilitated recovery in a majority of patients. Maintenance of general anesthesia

---

**Box 4-2 Use of Transesophageal Echocardiography for Noninvasive Calculation of Aortic Valve Area, and an Example**

<table>
<thead>
<tr>
<th>Continuity Equation</th>
<th>CSA(LVOT) × TVI(LVOT)</th>
<th>CSA(aortic valve) × TVI(aortic valve)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve area</td>
<td>CSA(LVOT) × TVI(LVOT)</td>
<td>CSA(aortic valve) × TVI(aortic valve)</td>
</tr>
</tbody>
</table>

Example:

\[
\text{Example:} = 0.785 \times (2.98)^2 \times (23 \text{ cm}) / (143 \text{ cm}) \\
= 7.06 \times 23 / 143 \\
= 1.13 \text{ cm}^2
\]

Modified from Oh and colleagues. Key: CSA, Cross-sectional area; LVOT, left ventricular outflow tract; TVI, time velocity integral.

---

**Table 4-4 Echocardiographic Factors Related to Poor Outcome after Mitral Valve Repair for Degenerative Mitral Regurgitation**

<table>
<thead>
<tr>
<th>Pre-CPB</th>
<th>Post-CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posterior leaflet height (&gt;15 mm)</td>
<td>Residual mitral regurgitation &gt; mild</td>
</tr>
<tr>
<td>Anterior leaflet height (&gt;45 mm)</td>
<td>Persistent prolapse</td>
</tr>
<tr>
<td>Anterior leaflet to posterior leaflet &gt; 1.5</td>
<td>Increased mean MV pressure gradient</td>
</tr>
<tr>
<td>Coaptation point of MV leaflets to septum (C-septal) distance &lt; 15 mm</td>
<td></td>
</tr>
<tr>
<td>Bileaflet prolapse</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Iglesias. Key: CPB, Cardiopulmonary bypass; MV, mitral valve.

---

**Epiaortic Scanning**

Epiaortic scanning may aid surgical decision making. Djaiani and colleagues modify their surgical management in one third of patients based on its results in CABG. Similarly, Rosenberger and colleagues report that it changed epiaortic surgical decision making in 4.1% of patients, including using cardiac arrest, performing aortic atherectomy or replacement, using off-pump support; avoiding aortic clamping; using ventricular fibrillatory arrest; changing arterial cannulation site; and avoiding aortic cannulation.
Table 4-5 Induction Agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Mechanism of Action</th>
<th>Systolic Blood Pressure Response</th>
<th>Heart Rate Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propofol</td>
<td>1.5-2.5 mg · kg⁻¹ IV</td>
<td>Interaction with GABA</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Etomidate</td>
<td>0.2-0.4 mg · kg⁻¹ IV</td>
<td>Interaction with GABA</td>
<td>No change to decreased</td>
<td>No change</td>
</tr>
<tr>
<td>Ketamine</td>
<td>1-2 mg · kg⁻¹ IV</td>
<td>Interaction with NMDA, opioid, monoaminergic, muscarinic receptors and voltage-sensitive calcium channels</td>
<td>Increased</td>
<td>Increased</td>
</tr>
<tr>
<td>Thiopental</td>
<td>3-5 mg · kg⁻¹ IV</td>
<td>Interaction with GABA</td>
<td>Decreased</td>
<td>Increased</td>
</tr>
</tbody>
</table>

Modified from Stoelting (p. 141). Key: GABA, γ-Aminobutyric acid; IV, intravenous; NMDA, N-methyl-D-aspartate.

Table 4-6 Commonly Used Opioids

<table>
<thead>
<tr>
<th>Opioid</th>
<th>Elimination Half-Time (hours)</th>
<th>Effect-Site (Blood-Brain Equilibration [minutes])</th>
<th>Analgesic Potency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl</td>
<td>3.1-6.6</td>
<td>6.8</td>
<td>75-125 times more potent than morphine</td>
</tr>
<tr>
<td>Sufentanil</td>
<td>2.2-4.6</td>
<td>6.2</td>
<td>5-10 times more potent than fentanyl</td>
</tr>
<tr>
<td>Alfentanil</td>
<td>1.4-1.5</td>
<td>1.4</td>
<td>1/10-1/5 as potent as fentanyl</td>
</tr>
<tr>
<td>Remifentanil</td>
<td>0.17-0.33</td>
<td>1.1</td>
<td>Similar potency to fentanyl</td>
</tr>
</tbody>
</table>

Modified from Stoelting (p. 83).

Table typically consists of a balanced anesthetic technique employing low-dose opioid in combination with a volatile inhalational anesthetic agent or IV agent. The specific choice of opioid, inhalational agent, and muscle relaxant depends on the surgical procedure and patient hemodynamics.

No specific anesthetic maintenance regimen is more advantageous than another in terms of patient outcomes, but evidence supports the potential role of inhalational anesthetic agents in myocardial preconditioning. In a double-blind randomized controlled trial of patients undergoing CABG, Meco and colleagues reported beneficial preconditioning effects of desflurane on myocardial injury (lower troponin I) and myocardial functional recovery following surgery.

Regional anesthesia with or without a general anesthetic has produced mixed patient outcomes. There have been reports of regional anesthetic techniques using epidural blockade in off- and on-pump cardiac surgical patients, however, regional anesthetic techniques have not been generally adopted.

Opioids

Semisynthetic opioids—fentanyl, sufentanil, and remifentanil—are differentiated by potency, onset, and duration of action. All have demonstrated safety and effectiveness for use in cardiac surgery (Table 4-6). Cheng and colleagues conducted a multicenter randomized controlled trial on the efficacy and resource utilization of remifentanil and fentanyl in fast-track recovery from cardiac surgery. Both anesthetic techniques permitted early and similar times to tracheal extubation, less intense monitoring, and reduced resource utilization after CABG. Similarly, Howie and colleagues compared remifentanil to fentanyl combined with isoflurane/profentanil for early extubation following CABG. Both allowed for fast-track cardiac anesthesia. In a randomized clinical trial, Mollhoff and colleagues demonstrated the efficacy and safety of remifentanil and fentanyl for fast-track CABG. Time to extubation was longer, and occurrence of shivering and hypertension were higher in the remifentanil group. However, the groups had similar intensive care unit (ICU) and hospital lengths of stay. Engoren and colleagues compared three opioids used for fast-track cardiac anesthesia: fentanyl, sufentanil, and remifentanil. Exubation times and costs were equivalent. Shorter duration of action of remifentanil allowed for faster recovery, but it is more expensive than fentanyl, and trachal extubation times were similar.

Antifibrinolytic Drugs

e-Aminocaproic acid inhibits conversion of plasminogen to plasmin by binding to the lysine binding sites on the plasminogen molecule; tranexamic acid is an alternative antifibrinolytic agent. Lysine analogs have class IA level of evidence indication for use in cardiac surgery to reduce blood loss and transfusion requirements. These drugs play an important role in blood conservation practices in cardiac surgery.

Heparin Management

Monitoring

Several automated devices are available for anticoagulation management following heparin administration; the activated clotting time (ACT) monitor is the most common. Unfractionated heparin is commonly administered on a weight-based protocol (300-400 units per kilogram) with the goal of achieving an ACT greater than 480 seconds prior to initiation of CPB. In general, if an ACT of 480 or greater has not been achieved with doses of heparin (up to 600 units · kg⁻¹), one should suspect heparin resistance.

Heparin Resistance

Reports of heparin resistance in cardiac surgical patients requiring CPB range between 4% and 22%. Chan and colleagues statistically modeled predictors of heparin resistance in 400 patients for elective cardiac surgery. Eight percent met predefined criteria for heparin resistance, defined as a
Table 4-7 Alternative Anticoagulants in Patients with Heparin-Induced Thrombocytopenia Requiring Anticoagulation for Cardiopulmonary Bypass

<table>
<thead>
<tr>
<th>Drug</th>
<th>Half-Life</th>
<th>Reversal</th>
<th>Metabolism</th>
<th>Monitoring</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bivalirudin</td>
<td>25 minutes</td>
<td>None</td>
<td>Metabolic &gt; renal</td>
<td>ACT, ECT</td>
<td>1.5 mg · kg⁻¹, 50 mg in pump, 2.5 mg · kg⁻¹ · h⁻¹ infusion</td>
</tr>
<tr>
<td>Lepirudin</td>
<td>80 minutes</td>
<td>None</td>
<td>Renal</td>
<td>PTT, ECT</td>
<td>0.25 mg·kg⁻¹, 0.2 mg·kg⁻¹ in pump prime, 0.5 mg·min⁻¹ infusion</td>
</tr>
<tr>
<td>Argatroban</td>
<td>30 minutes</td>
<td>None</td>
<td>Hepatic &gt; renal</td>
<td>PTT, ACT</td>
<td>0.1 mg·kg⁻¹ bolus, 5-10 µg·kg⁻¹·min⁻¹ infusion</td>
</tr>
<tr>
<td>Danaparoid</td>
<td>20 hours</td>
<td>None</td>
<td>Renal</td>
<td>Factor Xa levels</td>
<td>125 units·kg⁻¹, 3 units·kg⁻¹ in pump prime, 7 units·kg⁻¹·h⁻¹ infusion</td>
</tr>
</tbody>
</table>

Data from Bojar.¹¹⁴

Key: ACT, Activated clotting time; ECT, ecarin clotting time; PTT, partial thromboplastin time.

Heparin requirement greater than 5 mg · kg⁻¹ to achieve a pre-CPB ACT greater than 400 seconds. Preoperative use of heparin, low-molecular-weight heparin, a platelet count of 300,000 or more, and albumin plasma concentration of 35 g · dL⁻¹ or less were risk factors for heparin resistance.

Treatment options for heparin resistance include fresh frozen plasma administration and antithrombin III therapy, but few randomized clinical trials have addressed the merits of these therapies for treating heparin resistance.¹¹⁵ In one of the few randomized clinical trials, Avidan and colleagues concluded that antithrombin III was effective in restoring heparin responsiveness for a majority of patients exhibiting heparin resistance prior to CPB (the authors defined heparin resistance as an ACT < 480 seconds after 400 units · kg⁻¹ of heparin).¹¹¹ Interestingly, among the 52 patients randomized to antithrombin III, 21% also required fresh frozen plasma.

**Heparin-Induced Thrombocytopenia**

Heparin-induced thrombocytopenia (HIT) is an immune reaction occurring in 1% to 3% of patients following cardiac surgery.²⁰² HIT is the most frequent antibody-mediated drug-induced thrombocytopenic disorder.³ It develops as a result of platelet factor 4–heparin complexes, subsequent platelet activation, and thrombocytopenia following heparin exposure, and is induced by immunoglobulin (Ig)G antibody production.¹⁶⁶ Paradoxically, heparin-induced antibody-mediated activation of platelets and the coagulation system may result in thrombosis.²⁰² Clinical features may include thrombocytopenia, defined as a 50% or greater reduction in platelet count or decrease to less than 100,000 · dL⁻¹, thrombosis (50%-70% of patients), and heparin-induced skin lesions (5%-10% of patients). Diagnosis rests on one or more clinical features of thrombocytopenia and thrombosis as well as detection of HIT antibodies.²⁰²

Guidelines recommend use of unfractionated heparin for patients with a history of HIT who require cardiac surgery and are HIT antibody negative. Repeat exposure to heparin is an option if the prior HIT episode occurs more than 100 days before surgery, because HIT antibodies are transient and generally not regenerative during the brief heparin reexposure. Guidelines also recommend that heparin be restricted to CPB and that alternative anticoagulants be used pre- and postoperatively. For patients with acute HIT—thrombocytopenia and HIT antibody positive—requiring surgery, it is recommended that surgery be delayed until HIT is resolved and antibodies are negative. Alternatively, a non-heparin anticoagulant such as bivalirudin can be used (Table 4-7).

**Heparin Reversal**

Following discontinuation of CPB and decannulation, heparin is reversed with protamine sulfate (typically 1 mg of protamine for every 100 units of heparin). Heparin-protamine titration may also be used to provide a more precise amount of protamine to be administered. Protamine administration has well-recognized adverse side effects, from hypotension with rapid administration to anaphylactic and anaphylactoid reactions.⁶⁶

**WEANING FROM CARDIOPULMONARY BYPASS**

A number of factors require attention before CPB separation: achieving normothermia, proper electrolyte balance (potassium, glucose, ionized calcium), adequate hemoglobin, anticipation of inotropic and vasopressor support, reestablishing ventilatory support, heart rhythm, and need for pacing. TEE plays an integral role in weaning from CPB, particularly for patients who have undergone valve repair or who have compromised ventricular function. TEE permits rapid recognition in the partial bypass period of circumstances that could complicate separation from CPB, such as persistent valvar regurgitation, intracardiac air, or regional wall motion abnormalities related to graft failure.

**Inotropic and Vasopressor Support**

Muller and colleagues examined clinical, surgical procedure, and intraoperative factors related to the need for inotropic support following CPB, including previous myocardial infarction, heart failure, higher New York Heart Association functional class, and aortic clamp time.⁵⁴⁶ McKinlay and colleagues incorporated information from the intraoperative TEE examination along with demographic and clinical factors to predict the need for inotropic use following separation from CPB.⁶⁸ Reoperation, wall motion score index, combined CABG and valve repair or replacement, left ventricular ejection fraction less than 35%, moderate to severe mitral regurgitation, and longer aortic clamp time were risk factors. Ahmed and colleagues added laboratory and hemodynamic factors and identified four risk factors for inotropic requirement: low cardiac index, left ventricular end-diastolic pressure 20 mmHg or higher, left ventricular ejection fraction 40% or lower, and chronic kidney disease stage 3 to 5.⁵⁴

Table 4-8 lists the mechanism of action for commonly used sympathomimetic and vasopressor agents. In addition, milrinone, an inodilator, acts by inhibiting phosphodiesterase III to increase intracellular cyclic adenosine monophosphate levels. Levosimendan, a new calcium sensitizer, possesses...
vasodilatory and inotropic properties without increasing intracellular calcium concentrations or increasing myocardial oxygen consumption. It acts by inducing a calcium-dependent conformational change of troponin C and enhances both rate and extent of cardiac contraction.\textsuperscript{55,51,110} Levosimendan has demonstrated utility in facilitating weaning from CPB.\textsuperscript{55}

### SPECIFIC MANAGEMENT ISSUES

**Fast-Track Anesthesia**

Early work by Cheng and colleagues was instrumental in establishing a new standard of care for recovery from cardiac surgery by demonstrating the safety and feasibility of facilitated recovery.\textsuperscript{67} They tested extubation within 1 to 6 hours vs. conventional tracheal extubation within 12 to 22 hours after CABG in a randomized clinical trial. Post-extubation intrapulmonary shunt fraction improved and ICU and hospital lengths of stay were shorter, without increased morbidity.\textsuperscript{67} Similarly, Reis and colleagues reported that fast-track and ultra–fast-track (extubated on ICU arrival) anesthesia were not associated with increased patient morbidity and mortality following CABG.\textsuperscript{87} In off-pump CABG, Djaiani and colleagues reported facilitated operating room extubation, lower nurse-to-patient ratio, and earlier patient discharge without need for reintubation with ultra–fast-track anesthetic techniques.\textsuperscript{88} Risk factors for delayed extubation of patients planned for fast-track anesthesia are advanced age, female gender, postoperative use of intraaortic balloon pumping, inotropes, and postoperative bleeding and atrial arrhythmias.\textsuperscript{81,111}

**Perioperative Glucose Control**

Poor control of perioperative glucose is associated with adverse outcomes following cardiac surgery.\textsuperscript{52} Ouattara and colleagues reported a 7.2 increased odds of morbidity in patients with poor intraoperative glucose control (four consecutive blood glucose concentrations $> 200$ mg · dL$^{-1}$ without any decrease despite insulin therapy).\textsuperscript{52} Lipshutz and Gropper performed an evidence-based review of perioperative glycemic control, noting that hyperglycemia in the perioperative period is a risk factor for morbidity.\textsuperscript{127} An appropriate glucose target and specific populations who might benefit from intensive insulin therapy have yet to be identified. van den Berghe and colleagues reported that intensive insulin therapy to maintain blood glucose at or below 110 mg · dL$^{-1}$ reduced morbidity and mortality among surgical ICU patients.\textsuperscript{52} However, there are conflicting results about whether intensive insulin therapy to normalize glucose perioperatively improved outcomes. Gandhi and colleagues examined the effect of intensive intraoperative insulin therapy vs. conventional glucose management on morbidity after cardiac surgery and found increased morbidity with glucose levels at normoglycemia.\textsuperscript{52} Target glucose range at Cleveland Clinic is 70 to 150 mg · dL$^{-1}$. Cleveland Clinic’s intraoperative insulin management protocol and adjustment schedule are described in Appendix 4A and Table 4A-1.

**Blood Management**

RBC transfusion practices vary considerably throughout the world, despite published transfusion guidelines.\textsuperscript{81,122} This variability reflects insufficient information on risk-to-benefit ratio of anemia vs. transfusion and lack of randomized controlled trials examining RBC transfusion and patient outcomes. Hence, transfusion decisions tend to be based on opinion rather than evidence.\textsuperscript{81} There have been a number of investigations demonstrating a strong association between RBC transfusion and morbidity following cardiac surgery.\textsuperscript{10,99,118,114} RBC transfusion has been associated with excess risk of cardiac and serious infectious complications, renal failure, neurologic complications, prolonged

### Table 4-8: Sympathomimetics

<table>
<thead>
<tr>
<th>Sympathomimetics</th>
<th>α-Receptor</th>
<th>β$_1$-Receptor</th>
<th>β$_2$-Receptor</th>
<th>Mechanism of Action</th>
<th>Cardiac Output</th>
<th>Heart Rate</th>
<th>Dysrhythmias</th>
<th>Pao</th>
<th>Peripheral Vascular Resistance</th>
<th>Renal Blood Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Natural Catecholamine</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epinephrine</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>Direct</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>+</td>
<td>+/−</td>
<td>−</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>+++</td>
<td>++</td>
<td>0</td>
<td>Direct</td>
<td>−</td>
<td>−</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>−</td>
</tr>
<tr>
<td>Dopamine</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>Direct</td>
<td>+++</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Synthetic Catecholamine</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Isoproterenol</td>
<td>0</td>
<td>+++</td>
<td>+++</td>
<td></td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+/−</td>
<td>−</td>
<td>−</td>
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<tr>
<td>Dobutamine</td>
<td>0</td>
<td>+++</td>
<td>0</td>
<td></td>
<td>+++</td>
<td>+</td>
<td>+/−</td>
<td>+</td>
<td>NC</td>
<td>++</td>
</tr>
<tr>
<td><strong>Synthetic Noncatecholamine</strong></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Indirect acting:</td>
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</tr>
<tr>
<td>Ephedrine</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>Indirect, some direct</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>−</td>
</tr>
<tr>
<td>Direct acting:</td>
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<td></td>
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<tr>
<td>Phenylephrine</td>
<td>+++</td>
<td>0</td>
<td>0</td>
<td>Direct</td>
<td>−</td>
<td>−</td>
<td>NC</td>
<td>+++</td>
<td>+++</td>
<td>−</td>
</tr>
</tbody>
</table>

Modified from Stolting\textsuperscript{114} (p. 260).

Key: NC, No change; Pao, mean arterial pressure.
ventilatory support, in-hospital mortality, and increased resource utilization and cost. Infectious complications such as sepsis, bacteremia, and superficial and deep sternal wound infections are higher for transfused patients. Possibly this is related to immunomodulatory effects known as transfusion-associated immunomodulation (TRIM). Additional evidence supports persistent and increased late risk related to perioperative RBC transfusion, including a higher hazard for death and lower functional health-related quality of life.

Structural and functional changes occurring during RBC storage may partially account for complications associated with transfusion. Many of these changes are time dependent and include decreases in pH, 2,3-diphosphoglycerate, and adenosine triphosphate (ATP), and increases in free hemoglobin, potassium, and lactate. Reduced deformability is also time dependent and begins at 2 weeks and progresses throughout the storage period. These time-dependent changes have been demonstrated in both the laboratory and clinical arena to contribute to adverse consequences.

Laboratory investigation demonstrates increased thrombin generation for RBC products with longer storage duration. Centrifuged supernatant of stored RBC demonstrates that some RBC microvesicles express phosphatidylserine that is capable of facilitating thrombin generation. This may be a mechanism for adverse thrombotic effects for RBC with increased storage duration that has been observed in clinical investigations. Concern about complications related to length of RBC storage requires further investigation to determine whether patients undergoing cardiac surgery are adversely affected by prolonged storage. The role of storage time on microcirculation, tissue oxygenation, and outcomes is currently under debate.

The risk and benefit balance of anemia and RBC transfusion is complex and at this point unsettled. Although transfusion is beneficial in subsets of patients, there is uncertainty about whom to transfuse, and when; unrestricted liberal use of RBC transfusion requires closer scrutiny. Hebert and colleagues in the Transfusion Requirements in Critical Care trial reported that restrictive transfusion strategies for RBC were as effective as liberal ones. Blood conservation methods should be more widely applied and instituted, including optimization of preoperative hematocrit, use of intraoperative cell salvage, lower hemoglobin thresholds for transfusion, and use of antifibrinolytic agents. Evidence suggests that centers that have implemented evidence-based transfusion guidelines reduce use of RBC products without increasing patient morbidity.

### REOPERATION

Principles of anesthetic induction, maintenance, and facilitated recovery are similar for patients undergoing reoperation. Because of an increased risk for complications on sternal reentry, patients typically have additional IV access and RBC immediately available prior to sternotomy. Communication with the surgical team is essential before sternal reentry, particularly if alternative cannulation techniques (e.g., femoral or axillary artery cannulation) will be used. Surgical dissection can be challenging and lengthy, with a risk for excess bleeding, ischemia due to manipulation of prior grafts, and arrhythmias due to positioning of the heart.

### Off-Pump Coronary Artery Bypass Grafting

Revascularization without CPB has several reported benefits over on-pump surgery: fewer transfusions, less early neurocognitive dysfunction, and less renal insufficiency. Goals for anesthetic management are similar to those for on-pump surgery; however, a number of special considerations pertain specifically to case management for off-pump CABG (OPCAB). Invasive monitoring is similar, as is facilitated recovery with extubation in the operating room or soon after in the ICU. Heparin management is surgeon and institution specific, ranging from partial to full-dose heparinization. TEE is particularly useful for detecting regional wall motion abnormalities, accessing volume status, and determining the effect of lifting and retracting the heart and stabilizer devices on hemodynamics. OPCAB can be particularly challenging in managing acute changes in hemodynamics that occur with necessary positioning and stabilization of the heart to perform coronary artery anastomosis.

TEE monitoring for OPCAB typically identifies transient regional wall-motion abnormalities during vessel occlusion. Temporizing measures to maintain hemodynamic stability include the Trendelenburg position, vasopressors, and IV fluids. Couture and colleagues examined mechanisms of hemodynamic changes during OPCAB, noting that mobilization and stabilization of the heart or myocardial ischemia can produce important changes in hemodynamics. They report that suction- and compression-type stabilizers produce hemodynamic changes via different mechanisms. For suction-type stabilizers, hemodynamic changes are due to heart dislocation (90-degree anterior displacement) and right ventricular compression. Compression-type stabilizers compress the left ventricular outflow tract and produce abnormal diastolic expansion secondary to direct deformation of the left ventricular geometry. Depending on collateral flow, coronary occlusion during the anastomosis can variably affect the status of left ventricular function. Bainbridge and Cheng highlighted anesthetic considerations for both less invasive direct CABG and OPCAB procedures, noting goals similar to those for conventional CABG but with some key differences, including use of regional techniques for postoperative pain (unilateral paravertebral blocks or intercostal blocks).

### Heart Transplantation

The approach to anesthetic management for heart transplant recipients follows principles similar to those for heart failure patients, recognizing, however, that transplant recipients often have ingested food or drink within hours of surgery. Potential heart transplant recipients typically have IV and arterial access prior to rapid-sequence or modified rapid-sequence anesthetic induction. Although alternative induction agents may be used successfully, etomidate and succinylcholine with small doses of narcotic are effective agents for this, recognizing that circulation time is longer and important hemodynamic instability secondary to reduced ejection fraction may occur. Central venous access is obtained following anesthetic induction. Maintenance of anesthesia is similar to that for other cardiovascular procedures, using a balanced technique of narcotic, muscle relaxation, and low-dose inhalation agent. Similar to other procedures, anesthetic goals are to maintain hemodynamic stability and facilitate recovery following surgery.
The newly implanted heart is denervated without vagal tone. In general, post-implantation, agents with direct-acting catecholamines are preferred; agents with indirect activity (e.g., ephedrine) may have diminished effect. Similarly, medications such as atropine and glycopyrrolate will not provide typical heart rate responses. B13, M17

TEE has particular utility in heart transplantation as a guide for separating the patient from CPB, detecting presence of intracardiac air, and evaluating ventricular function. It is particularly useful for detecting right ventricular dysfunction that may ensue, especially in patients with pulmonary hypertension.

Lung Transplantation

Similar to heart transplant recipients, lung transplant recipients typically have eaten within hours of surgery. A special consideration for anesthetic induction of lung transplant recipients is avoiding prolonged positive pressure with mask ventilation, which may lead to important hypotension. Central venous access is obtained following anesthetic induction. Some centers use a pulmonary artery flotation catheter pre-transplant and pull it back into the pulmonary trunk before clamping the pulmonary artery. Lung isolation is commonly achieved with a left-sided double-lumen endotracheal tube. However, use of a single-lumen endotracheal tube with a bronchial blocker for lung isolation is also an option. Ability to tolerate one-lung ventilation is assessed early, because failure to do so necessitates use of CPB. TEE may guide in assessing ventricular function during transplantation, right ventricular function upon pulmonary artery clamping, and pulmonary vein stenosis, and also in detecting intracardiac air.

Feltracco and colleagues report that lung transplantation for severe pulmonary hypertension has distinct challenges compared with other etiologies. F11 Common echocardiographic features of patients with severe pulmonary hypertension include right ventricular enlargement, tricuspid regurgitation, and diastolic dysfunction. The authors recommend ventilation strategies that include avoiding excessively increased intrathoracic pressure, moderate hypercapnia, and optimal positive end-expiratory pressure to prevent increases in pulmonary vascular resistance. They recommend CPB support in the following circumstances: intractable hypoxemia, greater than 30% reduction in cardiac output during trial of pulmonary artery clamping, doubling of pulmonary vascular resistance, an increase in systolic pulmonary artery pressure to greater than 80% of systemic systolic pressure, surgical manipulation that severely compromises cardiac function, and severe ventricular wall motion abnormalities. F11

Baez and colleagues similarly noted that hemodynamic instability may ensue from myocardial depressant effects of induction agents, with excessive positive pressure ventilation on anesthetic induction, and with surgical retraction to gain exposure while removing the lungs. B1 They recommend reducing lung hyperinflation, such as by decreased tidal volumes, lowering respiratory rate to maximize expiratory time, and permissive hypercapnia. TEE can be used to assess presence and degree of right ventricular dysfunction, which may necessitate use of pulmonary vaso dilators. Those available vary in selectivity for pulmonary vasculature and cost. Agents used include milrinone, inhaled nitric oxide (preferred, because of greater selectivity for the pulmonary vasculature vs. systemic vasculature), and inhaled epoprostenol (similarly efficacious and less costly). B11

If risk from CPB is low, some centers place epidural catheters prior to anesthetic induction. M13 Goals of ventilation management include prolonging expiratory time to allow for more complete emptying of the lungs, along with permissive hypercapnia, with the thought that hypoventilation reduces hemodynamic effects of dynamic hyperinflation and auto positive-end-expiratory pressure. Miranda and colleagues list various methods to decrease pulmonary vascular resistance, such as use of vasodilators and induction with 100% fraction of inspired oxygen to reverse hypoxic pulmonary vasoconstriction. M13

Descending Thoracic Artery Aneurysm

Open repair of descending thoracic aorta aneurysm requires considerable anesthetic preparation. Monitoring typically necessitates large-bore IV access, right-sided brachial and femoral arterial catheter placement, central access with a large French introducer and pulmonary artery flotation catheter, a cerebro spinal fluid drainage catheter, and TEE. Depending on extent of the disease, repair may require use of CPB and circulatory arrest. OPCAB procedures employ a double-lumen endotracheal tube or single-lumen endotracheal tube with an endobronchial blocker for lung isolation. Additional venous access, if needed, is obtained via the right femoral vein, because the surgeon may choose to use left atrial–to–left femoral artery bypass. If partial bypass is used, the perfusionist can adjust flow to maintain upper-extremity mean blood pressure typically greater than 80 mmHg, and lower mean greater than 70 mmHg. Intrathecal preservative-free papaverine may be requested prior to clamping as a spinal cord protective measure. Additional neuroprotective measures include maintaining cerebrospinal fluid (CSF) pressure at less than 10 mmHg and passive cooling. Estrera and colleagues recommend early management using free CSF drainage to maintain CSF pressure at less than 10 mmHg, but later limiting cerebrospinal drainage unless neurologic deficit occurs. E16

In addition to hypothermia and CSF drainage for spinal protective measures, monitoring of somatosensory (SSEP) or motor-evoked potentials (MEP) has been reported to provide additional protection. K11 Keyhani and colleagues note that MEPs and SSEPs are highly correlated only when intraoperative changes are irreversible, and these irreversible changes are associated with immediate neurologic deficit. E5 Normal SSEP and MEP findings have strong negative predictive value, indicating that patients without signal loss were likely to be without a neurologic deficit. E5 Some centers have used epidural cooling with epidural catheters placed at thoracic (T) T-12 to lumbar (L) L-1 and a 4F intrathecal thermistor catheter placed at L-3–L-4. G14

Jacobs and colleagues reported that MEP is a highly reliable technique to assess spinal cord ischemia and is useful in reducing paraplegia during thoracoabdominal aneurysm repair. G2 Their protocol includes CSF drainage, moderate hypothermia, and left heart bypass with selective organ perfusion. MEP was used to monitor spinal cord function, and when important decreases occurred, hemodynamic (raising distal aortic and mean arterial pressure) and surgical (realignment of visible intercostal arteries) strategies were employed. G2
Endovascular stenting of thoracic aortic aneurysms is a less invasive approach to repair. Anesthetic management may be regional (spinal or epidural) or general. Disadvantages of regional anesthesia include patient movement, inability to use TEE as a monitoring tool, potential for hypotension with sympathectomy, and difficulty establishing an airway should complications occur during the procedure.\textsuperscript{69}

Transcatheter Aortic Valve Replacement

Transcatheter aortic valve replacement (TAVR) is currently used for patients with aortic stenosis who have important comorbidity and are not surgical candidates because of high operative risk. Cheung and Ree summarized the procedure’s four key steps: surgical access (via femoral vein or artery, or left ventricular apex), native aortic valvuloplasty (predilatation by balloon valvuloplasty), positioning and deployment of the prosthesis, and surgical closure.\textsuperscript{69} TEE can assist with proper sizing by providing measurement of aortic annular dimension, guidewire advancement, and valve prosthesis positioning. TEE has particular utility in identifying complications with placement, such as device embolization, tamponade, perivalvar regurgitation, and coronary ostial obstruction with resultant regional wall-motion abnormalities.\textsuperscript{69} Pharmacologic agents (adenosine or β-blockers) or, more commonly, rapid ventricular pacing are used for device deployment to attenuate left ventricular ejection. The procedure is performed under general anesthesia, which is beneficial for patient immobility, tolerance of rapid ventricular pacing, and better management of complications.\textsuperscript{69}

Ventricular Assist Devices

Anesthetic management for placing left ventricular assist devices (LVAD) focuses on considerations similar to those for severe heart failure, recognizing that these patients are critically ill with limited cardiac reserve and may have considerable hemodynamic instability on anesthetic induction.\textsuperscript{610} TEE is a critical monitoring tool (Table 4-9). Identifying intracardiac shunts, such as a patent foramen ovale (PFO), has implications post implantation. An unrecognized PFO may lead to hypoxemia because unloading of the left ventricle leads to decreased left atrial pressure, which may result in substantial right-to-left shunting. TEE detection of aortic regurgitation is also critical, because this will reduce forward flow from the LVAD. In addition, TEE is useful for identifying right ventricular dysfunction, position of the inflow cannula, and de-airing.\textsuperscript{611}

Bleeding is not uncommon following LVAD insertion and is often multifactorial, with hepatic dysfunction, preoperative anticoagulation, and excessive fibrinolysis.\textsuperscript{62} Patients with severe right ventricular dysfunction may need a right ventricular assist device, use of pulmonary vasodilators (nitric oxide), or both.\textsuperscript{66}

**CONCLUSION**

Practice of contemporary cardiothoracic anesthesia requires expertise in monitoring, coagulation, and pharmacology. Continued advances in perioperative monitoring, more selective pharmacologic agents, and focused research supporting evidence-based care will further advance the specialty and ultimately contribute to improved patient outcomes.

### Table 4-9 Utility of Transesophageal Echocardiography for Left Ventricular Assist Device Placement

<table>
<thead>
<tr>
<th>Pre-CPB</th>
<th>On CPB</th>
<th>Post-CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimize left ventricular filling</td>
<td>Appropriate inlet cannula orientation (oriented to mitral valve)</td>
<td>Monitor cannula position</td>
</tr>
<tr>
<td>Exclude patent foramen ovale, aortic regurgitation, mitral stenosis</td>
<td>Verify device is functioning</td>
<td>Right ventricular function and tricuspid regurgitation</td>
</tr>
<tr>
<td>Monitor right ventricular function and assess tricuspid regurgitation</td>
<td>Exclude right-to-left shunting</td>
<td>Decompression of left ventricle and left atrium</td>
</tr>
<tr>
<td>Monitor decompression of left ventricle and left atrium</td>
<td>Possible air entrainment if left ventricle collapses and subatmospheric intradevice pressures occur</td>
<td></td>
</tr>
<tr>
<td>Exclude aortic insufficiency</td>
<td>Doppler-determined LVAD flows</td>
<td></td>
</tr>
<tr>
<td>De-airing</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Modified from Mets.\textsuperscript{610} Key: CPB, Cardiopulmonary bypass; LVAD, left ventricular assist device.
Physiologic monitoring includes routine noninvasive monitoring as well as an arterial catheter, central venous catheter, and temperature probes. In term newborns, a 22-gauge radial arterial catheter is preferred. In small babies or premature infants, a 24-gauge catheter is used. Posterior tibial and dorsalis pedis arterial catheters should be avoided because of their tendency to function poorly after CPB. Femoral artery catheters may be used, but because of future need for cardiac catheterizations, they are not preferred. In extremely low-birth-weight babies, a 22-gauge axillary arterial line can be placed. Use of an umbilical artery catheter for up to 7 days is appropriate for newborns.

Many centers employ percutaneous central venous catheters as a standard monitoring tool. When available, these catheters must be placed under ultrasound guidance to increase safety and decrease risk of complications. Placing percutaneous central catheters should be carefully considered in infants with single-ventricle physiology, because thrombosis of upper-extremity vessels could preclude or complicate a future bidirectional Glenn procedure. Size and length of central venous catheters placed percutaneously should be based on age and weight of the patient. Others rely on directly placed transthoracic catheters placed before or after repair of the malformation to obtain information for separation from CPB. However, these do not allow central venous pressure monitoring in the prebypass period or effective monitoring of superior vena cava (SVC) pressure during CPB. Although not universally employed, direct measurement of left atrial, right atrial, and pulmonary artery pressures via small indwelling catheters provides more accurate assessment of central pressures than other methods used to guide treatment in the postbypass and postoperative periods.

Temperature

Thermistor probes are placed for measuring rectal (core) and either nasopharyngeal or tympanic membrane temperatures. Nasopharyngeal and tympanic membrane temperatures provide a reasonable estimate of brain temperature. Large gradients between rectal and nasopharyngeal or tympanic membrane temperature may reflect inadequate total-body cooling and may predispose the patient to unanticipated warming during periods of circulatory arrest or low-flow CPB.

Intraoperative Echocardiography

Intraoperative TEE is important for monitoring myocardial function and detecting air emboli, in addition to providing a morphologic map for surgical repair. In the postinduction period, TEE provides an opportunity to assess the anatomy and revise the operative plan if necessary. It permits assessment of systolic and diastolic function, identification of valvar dysfunction, and estimation of pulmonary artery pressure. These observations may lead to modifying the anesthetic plan. After CPB, previously unidentified malformations and residual defects can be identified and corrected in the same operative setting, which may reduce morbidity and mortality. In patients weighing less than 2.5 kg, the TEE probe should be placed with caution because of risk of esophageal injury and airway obstruction. In such instances, use of an intracardiac echocardiography (ICE) probe should be considered. To do this, a 4.0 uncuffed endotracheal tube is placed in the esophagus and taped to the angle of the mouth. The ICE probe is passed through this esophageal tube for the TEE exam; following the exam, it is withdrawn and placed in cold water to cool the end of the probe.

Neurologic Monitoring

The ICE probe is passed through this esophageal tube for the TEE exam; following the exam, it is withdrawn and placed in cold water to cool the end of the probe.
Although not yet standard of care, near-infrared spectroscopy (NIRS) monitoring, either alone or with transcranial Doppler (TCD) and some form of electroencephalography (EEG), is used in several children’s heart surgery programs. It is our practice to routinely monitor NIRS during heart surgery, on or off CPB. TCD is valuable in detecting emboli and during antegrade cerebral perfusion to determine optimal flow. However, the angle of insonation is important, and changing this will change the velocity of flow measured. Positioning the TCD probe in infants is challenging. TEE is also an invaluable monitor of emboli, a use that must not be overlooked. Of the modalities, EEG is least useful in the operative setting, because it is susceptible to changes in intraoperative temperature and the type of anesthetic agents used.

Near-Infrared Spectroscopy

Light in the near-infrared (700-1300 nm) range has three important physical properties that make it useful for diagnostic assessment:

- It penetrates tissue.
- It is non-ionizing.
- It is absorbed differentially by relevant chromophores depending on their oxygen-binding state.

When near-infrared light is emitted across a tissue (e.g., brain) and detected at its exit, absorption of the light can be used to calculate chromophore concentration using variants of the Beer-Lambert equation. All optical spectrometers consist of the same basic components: a light source of known intensity and wavelength, a light detector to measure the intensity of the light exiting the tissue, and a computer to translate the changes in light intensity into clinically useful information such as the concentrations of HbO₂, hemoglobin, or oxidized cytochrome aa₃.

When photons impinge on biological materials, their transmission depends on a combination of reflectance, scattering, and absorption effects. A light source (light-emitting diode or laser source) emits near-infrared light that passes through a “banana-shaped” reflectance path in the frontal cerebral cortex to two to three detectors placed 3 to 5 cm from the emitter. Absorption occurs at specific wavelengths, determined by the molecular properties of the material in the light path. Optical path length for reflected light is linearly related to spacing between transmission and receiving sites, so many NIRS measurement instruments place the transmitting and light detector several centimeters apart on the head. Although this spacing results in a measurable signal intensity, it affects the amount and depth of tissue monitored.

On a practical level, the available instruments space their transmitting and receiving sites differently, thus measuring different quantities and depths of tissue, which makes comparisons between instruments difficult.

Shallow arcs of light travel across skin and skull but do not penetrate the cerebral tissue. Deep arcs of light cross skin, skull, dura, and cortex. Subtracting the absorbance measured in the narrow arc from that measured in the deep arc leaves absorbance that is due to intracerebral chromophores. This is one of the distinguishing characteristics of cerebral oximeters compared with pulse oximeters. Cerebral oximeters use spatial resolution techniques to differentiate cortical from extracranial blood, whereas pulse oximeters differentiate pulsatile (arterial) from nonpulsatile (venous/capillary) blood. Cerebral oximetry measures predominantly venous saturation (75:25 or 85:15, depending on age and model used). NIRS could be a surrogate for jugular venous oxygen saturation (SjvO₂) monitoring without being invasive. It does not depend on pulse, blood pressure, or body temperature. This makes the technique ideally suited for monitoring oxygenation during CPB, hypothermic circulatory arrest, shock, or cardiovascular collapse.

Validation of NIRS

Studies in humans have focused on measuring SjvO₂ under controlled experimental and clinical conditions and determining its correlation with cerebral oximetry. NIRS correlates well with SjvO₂ as well as with superior vena cava oxygen saturation (ScvO₂). NIRS values also have been validated in piglet studies that correlate regional oxygen saturation (rSO₂) values and metabolic markers of cerebral oxygenation, such as cerebral ATP, phosphocreatine (PCr), and brain lactate concentrations. Human and animal data support the ischemic threshold value of approximately 45%. Prolonged periods of NIRS values in this range have been correlated with adverse postoperative neurologic magnetic resonance imaging (MRI) findings in newborns undergoing surgery for hypoplastic left heart physiology. In piglets, increasing lactates and decreasing ATP concentrations were noted at cerebral oxygen saturation (ScO₂) values of 33% to 44%.

Clinical Applications

To use the device, one or two cerebral oximeter probes are placed on the forehead below the hairline. Andropoulos and colleagues reported that during antegrade cerebral perfusion, left-sided cerebral saturation was substantially lower than the right (92%-94% right and 60%-65% left). However, the left-sided values were well within normal limits, and the right-sided values suggest luxury perfusion. Such large differences have not been our observation in more than a decade of neuromonitoring (unpublished), suggesting that the circle of Willis is intact in most neonates, and blood flow is adequate to both hemispheres during antegrade cerebral perfusion. However, with ongoing miniaturization of oximetry probes, it may be possible to place bilateral NIRS oximeters (Table 4-10).

The landmark Austin and colleagues observational study using multimodality neurologic monitoring must be credited with the interest in NIRS for pediatric open heart surgery. These authors reported a 26% postoperative adverse neurologic outcome when intraoperative desaturations were not treated vs. only 6% when the changes were treated. ScO₂ is a balance between oxygen delivery and utilization. If the latter remains unchanged, then any decrements in cerebral saturation must be due to decreased cerebral oxygen delivery. This could be due to decrease in arterial saturation, hemoglobin, or cerebral blood flow. Hence, if ScO₂ decreases in the face of normal pulse oximetry (SpO₂), it is important to decide why cerebral oxygen delivery has changed. Conditions of increased utilization include hyperthermia, seizures, and change in level of arousal; these must be treated. During initiation of CPB, one of the common causes for decreased rSO₂ is arterial cannula malposition or occlusion to venous drainage, which decreases cerebral perfusion pressure and reduces cerebral blood flow. Moreover, cerebral oximetry could be a guide to hypothermic circulatory arrest and intermittent perfusion, making circulatory arrest safer.

Outcomes after Heart Surgery and NIRS Monitoring

The Austin study was a retrospective cohort study; no
Table 4-10  Currently Available Near-Infrared Spectrometry Devices

<table>
<thead>
<tr>
<th>Device/Manufacturer</th>
<th>Light Source</th>
<th>Wavelengths Used</th>
<th>Readout</th>
<th>FDA Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>INVOS Covidien (United States)</td>
<td>LED</td>
<td>2</td>
<td>rSo₂, %</td>
<td>Approved for pediatric use</td>
</tr>
<tr>
<td>Niro Hamamatsu (Japan)</td>
<td>LED</td>
<td>3</td>
<td>c-TOI</td>
<td>Not FDA approved</td>
</tr>
<tr>
<td>Foresight Casmed (United States)*</td>
<td>Laser</td>
<td>4</td>
<td>SctO₂</td>
<td>Approved for pediatric use</td>
</tr>
<tr>
<td>Equinox 7600°</td>
<td>LED</td>
<td>3</td>
<td>rSo₂, %</td>
<td>Approved for pediatric use &gt;40 kg</td>
</tr>
</tbody>
</table>

*Measures “absolute” cerebral saturation. All other devices are marketed as trend monitors.

Key: c-TOI, Cerebral tissue oxygenation index; FDA, U.S. Food and Drug Administration; LED, light-emitting diode; rSo₂, regional cerebral oxygen saturation index; SctO₂, cerebral tissue oxygen saturation.

randomized trial of NIRS has been conducted in children. Recently, Hunaid and colleagues\textsuperscript{55} addressed the issue of whether intraoperative cerebral oximetry during cardiac surgery could lead to improved clinical outcomes. They reviewed nearly 500 papers, of which 8 were included in the best-evidence topic analysis. The only study that included children was the one by Austin and colleagues (class 1b level of evidence); the other seven were studies of adults undergoing coronary artery bypass grafting or valve surgery. In all of these, the authors noted reduced postoperative neurocognitive deficits (class 1b to 2b level of evidence) and concluded that judicious use of cerebral oximetry reduced major organ morbidity and mortality; despite the moderate cost associated with its use, all support using the device routinely during open heart surgery.

Although Dent and colleagues\textsuperscript{56} showed a correlation between prolonged low rSo₂ (<45% rSo₂ for ≥180 minutes) and new MRI abnormalities in a group of neonates who underwent the Norwood procedure with ACP, more recently in a prospective study of neonates with either single- or two-ventricle physiology undergoing surgery with CPB and ACP,\textsuperscript{57} they were unable to show an association between new white matter injury on postoperative MRI and prolonged low perioperative rSo₂.\textsuperscript{58} However, it is important to note that in this study, 50% of patients in the single-ventricle group had prolonged low rSo₂ (<45% for 240 minutes), a third of whom had new white matter injury in the postoperative period. No patients in the two-ventricle group had prolonged rSo₂% below 45% for 120 minutes. Although stroke and chorea are obvious neurologic abnormalities, subtle neurocognitive changes are difficult and expensive to establish. Thus, despite lack of level 1A evidence that NIRS improves neurocognitive outcomes, we recommend intraoperative cerebral oximetry as a tool to optimize anesthesia (ventilation, oxygenation), perfusion (alpha-stat, pH-stat, hemoglobin, flow, temperature) and surgical techniques (cannulation). Figure 4-4 shows the Stanford management strategy for maintaining rSo₂ within 20% of baseline.

Anesthetic Agents

A wide variety of anesthetic drugs have been used successfully and safely, including inhalation agents such as sevoflurane, and IV agents such as propofol, fentanyl, midazolam, thiopental, and ketamine (IV or intramuscular).\textsuperscript{10,19} For critically ill neonates, opioid drugs with or without benzodiazepeine are generally preferred. Fentanyl is most often used, titrated in 5 to 10 μg · kg⁻¹ increments with or without midazolam (0.1 mg · kg⁻¹ per increment) until the patient is no longer responsive. A nondepolarizing muscle relaxant is then administered (e.g., vecuronium, rocuronium, pancuronium). Alternatively, combined infusions of opioids and benzodiazepeine may be used.\textsuperscript{64} Pancuronium causes a mild vagal blockade and an increase in heart rate. This effect—which is undesirable in adults with coronary artery disease—is appropriate in infants and children, who have a greater dependence on heart rate for augmenting cardiac output. Additionally, use of an opioid tends to reduce heart rate, and pancuronium will prevent this reduction. Ketamine in doses of 1 to 2 mg · kg⁻¹ is an IV agent, has minimal effects on hemodynamics, and allows the concentration of inhalation agent to be reduced or turned off altogether. Regardless of the anesthetic used, 80% of children with poor myocardial function experience hypotension requiring treatment.\textsuperscript{37}

Presence of intracardiac shunts affects anesthetic induction. Presence of right-to-left shunt leads to rapid IV induction but can slow inhalational induction with a volatile anesthetic because of decreased pulmonary blood flow.\textsuperscript{514} Left-to-right shunts generally do not affect speed of induction. These physiologic effects must be considered when choosing an anesthetic. This also makes de-bubbling all medications and IV fluid mandatory.

Intubation and Ventilation

Endotracheal intubation can be performed orally or nasally; the preference is based less on science and more on institutional choice. An orotracheal or nasotracheal tube of proper diameter and length is introduced and fixed in position.\textsuperscript{515} Cuffed endotracheal tubes (ETTs) have traditionally been avoided in children younger than 8 years of age. A recent multicenter randomized trial in patients younger than age 5, including neonates, found cuffed ETTs to be reliable in infants and children.\textsuperscript{517} In fact, the number of attempts at tube changes to place the correct-sized tube was reduced, and cuffed tubes did not increase the risk of post-extubation stridor. It is important to measure ETT cuff pressure and maintain it below 20 cm H₂O to minimize risk of tracheal mucosal ischemia. In neonates and extremely low-birth-weight infants, it is prudent to obtain an intraoperative chest radiograph to confirm ETT position.

Traditional anesthesia ventilators have limitations that make accurately ventilating pediatric patients challenging.\textsuperscript{514} If indicated, an intensive care ventilator is set up in the operating room.

High fractional concentration of inspired oxygen (FIO₂) is avoided in children with shunt physiology or a nonrestrictive ventricular septal defect. Oxygen is a potent pulmonary vasodilator, and use of high concentrations can reduce systemic cardiac output (Qs) by diverting more of the cardiac output
through the shunt into the pulmonary circulation (Qp). Similarly, a low partial pressure of arterial carbon dioxide (PaCO₂) can reduce pulmonary vascular resistance (Rp), increase Qp, and reduce Qs. Increased PaCO₂ increases Rp and thus also may be hazardous in patients with intracardiac or extracardiac shunts. Therefore, induction with reduced FiO₂ and a normal or slightly elevated PaCO₂ is helpful in balancing blood flow between the systemic and pulmonary circulations.

**Maintenance of Anesthesia**

A combination of an opioid, usually fentanyl, and an inhalation anesthetic, usually isoflurane, is used for anesthesia maintenance. In general, children with limited cardiac reserve are maintained primarily on an opioid anesthetic, with low concentrations of inhalation agent as a supplement when tolerated. Historically, use of high-dose opioids has been advocated to blunt the stress response in neonates and infants. More recently, lower doses of opioids have proved to be equally effective, with less release of inflammatory mediators and a lesser degree of endothelial injury.

In patients in whom early extubation is planned, anesthesia in the postbypass period is maintained with an inhalation anesthetic, and use of fentanyl is limited. Remifentanil is a synthetic ultra–short-acting narcotic metabolized by plasma cholinesterase, with a half-life of 3 to 5 minutes, and has been used for fast-track anesthesia in children. Onset of CPB affects plasma levels of anesthetic drugs because of dilution and drug binding to oxygenator, and additional dosing is necessary adjustments made.

In combination with general anesthesia, both epidural and spinal anesthesia have been safely used in children undergoing open heart surgery. Maintenance of anesthesia is accomplished with inhalation of isoflurane and supplemental IV midazolam. This technique facilitates early extubation and provides excellent postoperative pain control.

**INFANTS AND CHILDREN UNDERGOING HYPOThERMIA WITH OR WITHOUT CIRCULATORY ARREST**

In neonates and infants who require complex operative repairs, hypothermic low-flow CPB or hypothermic circulatory arrest may be used. During the prebypass period, the patient’s temperature should be maintained above 30°C to 32°C to minimize the effects of hypothermia on cardiac output and prevent dysrhythmias. Using CPB, the patient is cooled to between 15°C and 20°C nasopharyngeal or tympanic membrane temperature and rectal temperature. The goal is to achieve optimal uniform cooling through a combination of core cooling using CPB and surface cooling using a cooling blanket beneath the patient. Room temperature is lowered after arterial and venous catheter placement. When circulatory arrest is planned, ice packs are placed around the child’s head after initiating CPB.

**Cardiopulmonary Bypass**

With initiation of CPB, cooling is started. In neonates and infants undergoing hypothermia, the pump prime may be maintained at a temperature of 18°C to 22°C (cold), 30°C (moderate), or 37°C (warm). Duration of cooling before reducing flow to low levels or initiating circulatory arrest is generally 20 to 25 minutes. Cooling should proceed at a controlled rate so that temperature does not fall more than 1°C per minute (see Chapter 2). A reduced rate of head or rectal cooling may indicate suboptimal tissue perfusion or a malpositioned temperature probe. If pump flow is inadequate, vasodilators (e.g., phentolamine, phenoxybenzamine) can be added directly to the CPB circuit. During cooling and before circulatory arrest, arterial blood gases and hematocrit are measured and necessary adjustments made.

In children, the appropriate arterial blood gas management strategy during hypothermia is the pH-stat technique. This technique is favored more in children than adults. The reason is that pH-stat management leads to more cerebral emboli, the primary etiology for postoperative cognitive dysfunction in adults; in children, it is hypoxic ischemia. During cooling and rewarming periods, pH-stat provides better cerebral blood flow, particularly in patients with aortopulmonary collaterals and is also useful during antegrade cerebral perfusion, because the increased cerebral blood flow allows for rapid cooling. Data are unclear but suggest overall that pH stat is useful in most pediatric patients; however, crossover strategies may be another option (see Chapter 2).

**Separation from Cardiopulmonary Bypass**

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Figure 4-4: Stanford’s approach to maintaining cerebral oxygen saturation (ScO₂) within 20% of baseline in children undergoing heart surgery. On cardiopulmonary bypass (CPB), if ScO₂ decreases 20% below baseline and persists for more than a minute, intervene. Transient decreases with cannulation usually resolve, but if they do not, cannulae should be repositioned. Decreases are most often seen during normothermic beating heart surgery. Under these conditions, if anesthetic doses are adequate, cool further or liberalize the PaCO₂ on CPB, or both. Key: Hct, Hematocrit.
The patient is rewarmed to a core temperature of 35°C to 36°C, the heart is filled and allowed to eject, arterial blood gases are obtained to ensure adequate acid-base balance, and calcium level is corrected to normal values for neonates and infants. Pacing wires are applied to the heart and tested, and the heart rate is maintained at an age-appropriate level using atrial or atrioventricular sequential pacing if needed. In most patients, low-dose dopamine (5 µg · kg⁻¹ · min⁻¹) is begun prior to weaning from CPB.

If high doses of inotropic agents are required despite adequate preload and ventilatory support, presence of a residual anatomic defect or poor adaptation to new loading conditions resulting from the operative repair may be contributing factors. TEE is helpful for determining the cause of the low output state.

Rationale for Specific Therapies

Right Ventricular (Pulmonary Ventricle) Dysfunction

Primary right ventricular (RV) dysfunction may occur after intracardiac surgery in neonates, infants, and children. Diagnosis of RV dysfunction is suggested by high right-sided filling pressures, liver distention, hypotension, tachycardia, reduced cardiac output, and systemic venous desaturation (low mixed-venous saturation).

Treatment of RV dysfunction is directed toward improving oxygen delivery by increasing preload, augmenting contractility directly or indirectly, enhancing coronary perfusion, and reducing afterload.

The RV is generally less responsive to inotropic support than the left ventricle and therefore may require higher doses of inotropic agents. Epinephrine enhances RV contractility. By improving systemic arterial pressure, epinephrine can augment RV coronary blood flow. Maintaining a normal to slightly elevated systolic arterial pressure will maximize coronary perfusion and augment RV contractility. Milrinone, a phosphodiesterase-3 inhibitor, is a useful inotrope with pulmonary vasodilation properties. In a randomized controlled trial of infants and children after heart surgery, a bolus of 75 µg · kg⁻¹ followed by a 0.75 µg · kg⁻¹ · min⁻¹ infusion reduced the occurrence of low cardiac output syndrome by 55%. Stanford’s institutional preference is a bolus of 25 to 50 µg · kg⁻¹ · min⁻¹ during rewarming, followed by an infusion of 0.5 µg · kg⁻¹ · min⁻¹. Communication with the surgeon is important prior to administering the bolus even on CPB, because some surgeons are concerned with the hypotension that could result.

RV afterload can be decreased by mechanical ventilation with or without nitric oxide (NO). Mechanical ventilation should be adjusted to optimize preload and decrease afterload. The RV is extremely sensitive to alterations in intrathoracic pressure; therefore, ventilation that enables the lowest possible mean airway pressure should be the goal. Increased mean intrathoracic pressure increases RV afterload by direct compression of alveolar and extra-alveolar pulmonary vessels.

NO is an endothelium-derived smooth muscle relaxant. It has been used in neonates with persistent pulmonary hypertension and in pulmonary hypertension related to congenital heart disease. NO decreases RVp and reduces intrapulmonary shunting, which may improve oxygenation. However, results of its use in the postoperative period are conflicting. In a randomized controlled trial of more than 100 infants at high risk for pulmonary hypertension, 20 ppm not only failed to show any benefit but did not prevent pulmonary hypertensive crisis in children after congenital heart surgery. However, in a similar population, others have shown it to be effective even at lower doses. If NO is used, NO2 levels should be monitored and NO should not be abruptly withdrawn, because rebound pulmonary hypertension can occur.

If these measures are unsuccessful, extracorporeal membrane oxygenation (ECMO) should be implemented (see Chapter 5). ECMO unloads the RV and favorably shifts the oxygen supply-demand ratio, often allowing the injured myocardium to recover.

Left Ventricular (Systemic Ventricle) Dysfunction

After separation from CPB, the contractile state of the systemic ventricle may be depressed. Contributing factors include preoperative condition of the myocardium (myocardial hypertrophy, elevated end-diastolic pressure, systolic dysfunction), response of the myocardium to the new loading conditions imposed by the operative repair, effects of hypothermia on myocardial compliance, suboptimal myocardial management, and residual anatomic problems.

Systemic ventricular dysfunction is managed by optimizing preload, afterload, and heart rate (see Chapter 5). Tachycardia (>180-190 beats · min⁻¹) may impair ventricular function in newborns and infants and should be treated with β-adrenergic blocking agents and, if necessary, vasopressors. When the heart rate is less than 120 to 130 beats · min⁻¹, atrial or atrioventricular sequential pacing is appropriate.

If inotropic support is necessary, it is usually initiated with dopamine (5-10 µg · kg⁻¹ · min⁻¹) (see Table 4-8). Infusion of calcium intravenously is an important step to augment ventricular contractility in pediatric patients (20 mg · kg⁻¹ · h⁻¹). Epinephrine is also a potent inotropic agent and is particularly useful in patients with important systemic ventricular dysfunction.

Clinical studies of the effects of milrinone in pediatric patients have shown considerable benefit, especially in those whose myocardium is afterload sensitive, such as patients who have had an arterial switch operation. Other trials suggest a different dosing regimen.

Management of Hypoplastic Left Heart Physiology

In the preinduction period, ductal patency must be maintained with prostaglandins to ensure systemic cardiac output. Management depends on optimizing systemic oxygen delivery (by increasing cardiac output) and restricting Qp.

In patients with hypoplastic left heart physiology, Rp decreases within hours of delivery, thereby redistributing blood flow away from the systemic circulation. Excessive Qp can be reduced by hypoxia or hypercarbia, because both raise Rp. In the preoperative period, 3% CO2 mixture compared with a 17% hypoxic gas mixture improved not only ScvO2 but also cardiac output. During administration of CO2, the patient must be sedated or given a muscle relaxant to eliminate increased respiratory effort. When transporting patients with single-ventricle physiology to the operating room, monitoring of hemodynamic state and arterial oxygen saturation is essential.

Before discontinuing CPB, ionized calcium levels and hematocrit must be optimized to ensure adequate
oxygen-carrying capacity. Myocardial function is supported by judicious use of inotropes. Tidal volume is increased to account for a reduction in lung compliance, and minute ventilation is adjusted to maintain normocarbia. After separation from CPB, FiO₂ is adjusted to maintain SaO₂ between 75% and 85% and an arterial PaO₂ of 40 to 50 mmHg.

Modified ultrafiltration has been shown to improve myocardial function, decrease lung water, and remove inflammatory mediators in patients with hypoplastic left heart physiology as well as other complex malformations (see Chapter 2).

Excessive Qp is less common in the immediate postbypass period. After modified ultrafiltration and before chest closure, the anesthesiologist should estimate Qp/Qs and attempt to adjust FiO₂ and minute ventilation accordingly.

Chest closure can markedly reduce lung compliance and worsen hemodynamics. Leaving the chest open may improve Qp and heart filling by reducing mean airway pressure.

Rationale for Managing Fontan, Hemi-Fontan, and Bidirectional Glenn Procedures

Patients undergoing a bidirectional Glenn or hemi-Fontan procedure usually have had either a pulmonary trunk band or a systemic–pulmonary artery shunt in the neonatal period. Cardiac performance may be impaired by either a small non-compliant ventricle or a large dilated ventricle, the latter resulting from excessive aortopulmonary shunt flow. Inotropic support may therefore be necessary in the prebypass period as well as postoperatively.

After the bidirectional Glenn or hemi-Fontan procedure, cardiac output is generally well maintained because inferior vena cava flow mixes with pulmonary venous blood in the physiologic left atrium. Low systemic arterial saturation and reduced Qp, however, are problems in the postoperative period. A marked discrepancy between end-tidal carbon dioxide (PETCO₂) and PaCO₂ is an early sign of reduced Qp. If Qp is reduced with no residual cardiac abnormalities, cardiac output should be optimized and interventions to lower Rp employed. To optimize cardiopulmonary interactions, children undergoing bidirectional Glenn or Fontan operations should be considered for fast-track anesthesia.

INFANTS AND CHILDREN NOT UNDERGOING CARDIOPULMONARY BYPASS (CLOSED PROCEDURES)

The most common procedures that do not involve CPB are palliative (systemic–pulmonary artery shunting and pulmonary trunk banding) or corrective (ligation of patent ductus arteriosus or repair of coarctation of the aorta).

Palliative Procedures

Palliative procedures are performed under general anesthesia with monitoring of systemic arterial pressure. Measurement of arterial pressure, SaO₂, and PETCO₂ are necessary to assess the procedure’s adequacy. Important reduction in PETCO₂ after pulmonary trunk banding indicates that Qp may be excessively reduced. This is followed by a precipitous drop in SaO₂. If the banding procedure is optimal, systemic arterial blood pressure should increase by approximately 10 to 15 mmHg. The gradient between PETCO₂ and PaCO₂ should be about 6 to 10 mmHg. SaO₂ should be no lower than 75% to 80%, and pulmonary arterial pressure should decrease to about 50% of systemic pressure.

Closure of Patent Ductus Arteriosus

Anesthetic considerations for patent ductus arteriosus (PDA) closure depend on the ductus size and clinical condition and age of the patient. Babies with a large PDA and low Rp generally present with excessive Qp and heart failure. Neonates and premature infants also may have left ventricular dysfunction from coronary ischemia due to substantial diastolic runoff to the pulmonary circuit. Thus, patients range from the relatively healthy young child to the sick ventilator-dependent premature infant on inotropic agents. Healthy children can tolerate a variety of anesthetic techniques with extubation in the operating room and use of epidural/caudal analgesia. Symptomatic neonates and premature infants require a carefully controlled anesthetic and fluid management plan.

Most preterm infants who fail medical management consisting of indomethacin, diuretics, and fluid restriction require admission to a neonatal ICU. A common finding is sepsis, so it is important to ascertain a history of medical treatment and verify negative blood cultures before surgical intervention. Premature neonates with ductal patency are operated on in the neonatal ICU, thereby avoiding transport hazards such as hypothermia, multiple transfers to and from infant incubators, inadvertent extubation, and venous access disruption.

In the neonatal ICU, the patient is positioned on a warmer, and access to the patient must be shared among the anesthesiologist, surgeon, surgical assistant, and scrub nurse. Careful positioning of an IV catheter and rapid access to a manual resuscitator or equivalent should be established before the baby is draped. Anesthesia is induced with fentanyl (usually in 1- to 5-µg aliquots) to maintain appropriate arterial pressure and perfusion. Muscle relaxation is obtained with pancuronium to prevent reduction in heart rate and preserve cardiac output. Hypotension following anesthesia induction should be anticipated, because these neonates are often on large doses of diuretics to manage their ventilation. The patient may temporarily require ventilation with 100% oxygen if SaO₂ drops below 90% or is associated with changes in heart rate and blood pressure. Oxygen is weaned once both lungs are allowed to expand after ductal closure. Manual ventilation is often necessary during retraction of the lung in small neonates or in those with preexisting increased oxygen requirements.

Complications include ligation of a pulmonary artery or the aorta. If SaO₂ remains low and PETCO₂ decreases, this alerts the perioperative team to possible pulmonary artery ligation. Similarly, placing a pulse oximeter on the foot ensures that aortic blood flow below the duct is maintained and can signal a possible aortic ligation.

In older children, PDAs are often closed in the interventional cardiac catheterization laboratory. Large PDAs or those with a short segment, however, often require intervention in the operating room under combined general and regional anesthesia. One-lung ventilation is seldom necessary because the procedure is brief.

Coarctation of the Aorta
Coarctation of the aorta is a common cardiac defect and in infants often is associated with anomalies of the mitral valve and left ventricular outflow tract, and with malformation of the great arteries. As with PDA, neonatal repairs are performed in critically ill patients. Coarctation in the newborn is typically associated with left ventricular dysfunction, and these patients may be receiving prostaglandins to ensure ductal patency. Usually they are also receiving mechanical ventilation and inotropic agents. Central IV, arterial, and peripheral IV catheters are normally placed for operation. Optimal placement of an arterial pressure catheter is in the right radial artery so that pressure can be monitored during aortic clamping. If right-sided arterial access is not achieved, a blood pressure cuff is placed on the right arm, and the arterial catheter in the left arm or lower extremity. Anesthesia is administered with a combination of fentanyl and an inhalation agent. During aortic clamping, proximal systemic arterial pressure is allowed to rise by 20% to 25% over baseline to optimize spinal cord perfusion. Intravascular volume loading with 10 to 20 mL · kg⁻¹ of crystalloid is given just before removal of the aortic clamp. The anesthetic concentration is decreased, and additional fluid is administered until arterial pressure rises. In inotrope-dependent neonates, 1 to 2 mL · kg⁻¹ of bicarbonate is administered before clamp release.

Avoidance of hyperthermia along with mild cooling is appropriate for patients undergoing aortic coarctation repair. Intraoperative hyperthermia has been associated with risk of spinal cord ischemia and paraplegia. A target core temperature of approximately 35°C is appropriate.

In older subjects, post-repair rebound hypertension caused by heightened baroreceptor reactivity often occurs and requires therapy. After aortic clamp release, systemic hypertension is most effectively lowered by institution of β-adrenergic blockade using esmolol or combined α and β blockade with labetalol. Sodium nitroprusside may be a necessary adjunct to control refractory hypertension; however, it increases calculated ventricular wall stress in the absence of β-adrenergic blockade by accelerating dP/dt. An effective alternative to nitroprusside is the calcium channel blocker nicardipine. Again, neonates are unlikely to require or tolerate lung isolation.

One-Lung Ventilation in Children

Lung isolation is helpful during thoracoscopic procedures or unifocalization via thoracotomy or coarctation repair in older children and adolescents. Lung isolation in infants and toddlers can be achieved with endobronchial intubation or bronchial blocker. The latter can be placed under fiberoptic or fluoroscopic guidance. It is Stanford’s institutional preference to use a bronchial blocker rather than endobronchial intubation for lung isolation in children. The former allows expansion of the surgical side, if necessary, by deflating the blocker to improve oxygenation. Both techniques are associated with complications and should be undertaken judiciously. Lung isolation in cyanotic pediatric patients requires close communication between surgeon and anesthesiologist, as further reductions in oxygen saturation may be associated with ischemic changes on the electrocardiogram or persistent declines of ScO₂.

Effects of Anesthetic Medications on the Developing Brain

In the last decade, interest has focused on the role anesthesia and sedation might play in affecting the developing brain and has been the subject of considerable debate and review. Studies in rat pups exposed to prolonged volatile anesthetic agents resulted in learning disabilities and associated histopathologic changes in the brain. In a retrospective population-based study, Wilder and colleagues examined the medical and school records of children born to mothers residing in Olmsted County, Minnesota, from 1976 to 1982 who still lived in the community at age 5 years. Of the 5357 children in this cohort, 593 received general anesthesia before age 4 years (years associated with rapid synaptogenesis) and 4764 did not (controls). A single exposure to anesthesia (n = 449) was not associated with learning disabilities. However, children receiving two or more anesthetics were twice as likely as controls to have learning disabilities. The risk for learning disabilities increased with longer cumulative duration of anesthesia exposure (≥120 minutes)—a dose-response relationship. Complete anesthesia records were available, and anesthetic techniques were consistent, with most children (88%) receiving halothane as a primary anesthetic. In addition, those with learning disabilities had a lower birth weight, were of younger gestational age, and were more likely to be male. Although from this study one cannot answer whether anesthesia caused learning disabilities, the repeated need for anesthesia could be a marker for them. Prospective multicenter studies are currently underway to answer whether anesthesia affects the developing brain. The findings could affect timing of complex neonatal heart surgery and should therefore be a concern for healthcare providers involved in caring for children with heart disease.

Blood Glucose Management in the Perioperative Period

Among infants undergoing the arterial switch operation, those who spent more than 50% of the time in a 24-hour period with blood glucose levels in the 80 to 110 mg · dL⁻¹ range were at higher risk for postoperative adverse events than hyperglycemic infants with blood sugars greater than 200 mg · dL⁻¹ 50% of the time. A study in infants had similar results. Among infants undergoing the arterial switch operation, those who spent more than 50% of the time in a 24-hour period with blood glucose levels in the 80 to 110 mg · dL⁻¹ range were at higher risk for postoperative adverse events than hyperglycemic infants with blood sugars greater than 200 mg · dL⁻¹ 50% of the time. A study in infants had similar results. On the other hand, Polito and colleagues reported that pediatric patients with blood glucose greater than 126 mg · dL⁻¹ in a 72-hour period had a longer ICU stay following surgery, suggesting that hyperglycemia could be detrimental in infants as well. However, all these studies were retrospective.

A placebo-controlled prospective study of 700 patients in a pediatric ICU reported that tight glycemic control resulted in shorter ICU length of stay, reduced lactate levels, decreased C-reactive protein, and reduced occurrence of infections. However, occurrence of hypoglycemia (blood glucose < 40 mg · dL⁻¹) was higher in the intensive insulin treatment group (25%) vs. the conventional group (1%), for whom insulin was administered only if blood glucose exceeded 200 mg · dL⁻¹ on at least two occasions. The majority (80%) of patients who had hypoglycemia were infants, but those who developed hypoglycemia did not have a
substantially increased risk of mortality. No early neurologic abnormalities were detected related to either hyper- or hypoglycemia. More studies of this nature with long-term follow-up are required before insulin infusion and tight glycemic control can be recommended routinely in children during and after heart surgery.

4A

Intraoperative Insulin Management Protocol (Cleveland Clinic)

Starting insulin: Start if pre-CPB blood glucose > 120 mg · dL⁻¹ and if on-pump or post-pump blood glucose > 150 mg · dL⁻¹.

Bolus dose: 0.03 units · kg⁻¹ (maximum bolus is 3 units). Initiate continuous infusion: initial rate 0.03 units · kg⁻¹ · h⁻¹ (maximum initial rate is 3 units · h⁻¹). See Table 4A-1 (Insulin Infusion Adjustment) for adjustment of insulin rate.

1. Blood glucose monitoring
   Measure blood glucose every 30 to 60 minutes.

2. Hypoglycemia protocol
   If blood glucose ≤ 60 mg · dL⁻¹: stop insulin infusion, give 25-50 mL of 50% dextrose solution, obtain blood glucose level every 30 minutes until blood glucose >

### Appendix Table 4A-1 Insulin Infusion Adjustment (Cleveland Clinic)*

<table>
<thead>
<tr>
<th>Blood Glucose</th>
<th>If Blood Glucose Decreases ≥ 30 mg · dL⁻¹ Since Last Level</th>
<th>If Blood Glucose Is Stable (change &lt; 30 mg · dL⁻¹) Since Last Level</th>
<th>If Blood Glucose Increases ≥ 30 mg · dL⁻¹ Since Last Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤60</td>
<td>Stop insulin infusion See Hypoglycemia protocol</td>
<td>Stop insulin infusion See Hypoglycemia protocol</td>
<td>—</td>
</tr>
<tr>
<td>61-70</td>
<td>Stop insulin infusion See Hypoglycemia protocol</td>
<td>Stop insulin infusion See Hypoglycemia protocol</td>
<td>—</td>
</tr>
<tr>
<td>71-85</td>
<td>Stop insulin infusion See Hypoglycemia protocol</td>
<td>Decrease rate by 50%</td>
<td>—</td>
</tr>
<tr>
<td>86-100</td>
<td>Decrease rate by 50%</td>
<td>Decrease rate by 50%</td>
<td>—</td>
</tr>
<tr>
<td>101-115</td>
<td>Decrease rate by 50%</td>
<td>Continue current rate</td>
<td>—</td>
</tr>
<tr>
<td>116-150</td>
<td>Decrease rate by 50%</td>
<td>Increase rate by 25%</td>
<td>Increase rate by 25%</td>
</tr>
<tr>
<td>151-200</td>
<td>Decrease rate by 25%</td>
<td>Increase rate by 25%</td>
<td>Bolus 2 units/Increase rate by 25%</td>
</tr>
<tr>
<td>201-250</td>
<td>Continue current rate</td>
<td>Bolus 2 units/Increase rate by 25%</td>
<td>Bolus 4 units/Increase rate by 25%</td>
</tr>
<tr>
<td>251-300</td>
<td>Continue current rate</td>
<td>Bolus 4 units/Increase rate by 50%</td>
<td>Bolus 6 units/Increase rate by 50%</td>
</tr>
<tr>
<td>301-350</td>
<td>Continue current rate</td>
<td>Bolus 6 units/Increase rate by 50%</td>
<td>Bolus 8 units/Increase rate by 50%</td>
</tr>
<tr>
<td>351-400</td>
<td>Continue current rate</td>
<td>Bolus 8 units/Increase rate by 50%</td>
<td>Bolus 10 units/Increase rate by 50%</td>
</tr>
<tr>
<td>&gt;400</td>
<td>Notify staff anesthesiologist*</td>
<td>Notify staff anesthesiologist*</td>
<td>Notify staff anesthesiologist*</td>
</tr>
</tbody>
</table>

Note: If insulin rate is ≥30 units · h⁻¹, notify staff anesthesiologist.
*Do not adjust insulin rate every hour; make adjustments every 2 hours.
*Severe hyperglycemia is treated per anesthesiologist’s discretion.

Key: CPB, Cardiopulmonary bypass.
80 mg · dL⁻¹ for three consecutive levels, then check blood glucose every 30-60 minutes.

If blood glucose 60-70 mg · dL⁻¹, or 71-85 mg · dL⁻¹ and decreasing: stop insulin infusion, obtain blood glucose level every 30 minutes until blood glucose > 85 mg · dL⁻¹ for three consecutive measurements, then check blood glucose every hour.

3. Resuming insulin infusion

Restart at half the previous rate when blood glucose rises above 150 mg · dL⁻¹.

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PART I General Considerations


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### Section I: Subsystems during Early Convalescence after Cardiac Surgery

#### Cardiovascular Subsystem

- **Cardiac Reserve**
- **Adequacy**
  - Cardiac Index
  - Arterial Blood Pressure
  - Pedal Pulses
  - Skin Temperature
  - Whole Body Oxygen Consumption
  - Mixed Venous Oxygen Level
  - Urine Flow and Serum Potassium
  - Metabolic Acidosis
- **Cardiac Output and Its Determinants**
  - Ventricular Preload
  - Ventricular Afterload
  - Myocardial Contractility
  - Relative Performance of Left and Right Ventricles
- **Heart Rate**
- **Cardiac Rhythm**

#### Pulmonary Subsystem

- **Adequacy**
- **Causes of Acute Dysfunction (Low Cardiac Output) after Cardiac Surgery**
  - Inadequate Operation
  - Myocardial Dysfunction
  - Reduced Preload
  - Hypovolemia
  - Diastolic Dysfunction
  - Acute Cardiac Tamponade
  - Increased Ventricular Afterload
- **Risk Factors for Low Cardiac Output**
  - Patient-Specific
  - Procedural
  - Postoperative
- **Course of Dysfunction After Cardiac Surgery**

#### Renal Subsystem

- **Adequacy**
- **Causes of Acute Dysfunction After Cardiac Surgery**
- **Risk Factors for Acute Dysfunction**
  - Patient-Specific
  - Procedural
  - Postoperative
- **Course of Dysfunction After Cardiac Surgery**

#### Neuropsychological Subsystem

- **Generalized (Diffuse) Neuropsychological Function**
  - Adequacy
  - Causes of Dysfunction
  - Risk Factors for Acute Dysfunction
  - Course of Dysfunction
  - Management and Treatment
- **Mood State**
  - Adequacy
  - Causes and Risk Factors for Acute Dysfunction
  - Course of Dysfunction
  - Management and Treatment
- **Localized Neuropsychological Function**
  - Adequacy
  - Causes and Risk Factors for Acute Dysfunction
  - Management
The primary determinants of a cardiac operation’s success are events in the operating room (OR), but even patients who are seriously ill when they leave the OR can survive and have a good long-term result when postoperative care is appropriate and intensive. Conversely, ill-advised or overly energetic interventions early after operation can put a patient at risk. Generally, they have adequate function of all subsystems, as uncomplicated convalescence devoid of findings or events that increase the probability of hospital death, complications, or a suboptimal late result is what patients can now expect. Generally, they have adequate function of all subsystems, as determined by standard criteria. So long as this pattern of normal convalescence continues, testing and intervention can be safely minimized. In these situations, expeditious discharge from the intensive care unit (ICU) can be accomplished and a short subsequent hospital stay anticipated.

But alertness to deviations from the pattern of an uncomplicated convalescence is mandatory; deviations are an indication for closer observation and possibly more intensive testing and treatment. Analysis of early convalescence can place the patient into one of three categories: optimal, suboptimal but in control, and critically ill. Each category carries therapeutic implications.

- Optimal: routine care; no change or important modification is currently necessary or foreseeable.
- Suboptimal but in control: careful consideration is given to a change in therapy, and a new modality is likely (e.g., additional catecholamine support for low cardiac output...
or lidocaine drip for frequent premature ventricular contractions [PVCs]).

- Critically ill: a modification, change, or new intervention is necessary and urgent (e.g., treatment of oliguria or metabolic acidosis; return to the OR for bleeding).

Both the suboptimal and critically ill categories define abnormal convalescence.

The patient convalescing normally and without complications after cardiac surgery usually appears at a glance to be doing well. Although there is always pain, varying in intensity from patient to patient, there is no restlessness, agitation, or anxiety. Eyes and skin look normal, and the pulse is full but may be rapid. Breathing is neither labored nor excessively rapid. The patient is oriented and lucid and—whether a neonate, infant, or adult—exhibits generally appropriate behavior. Few tests and interventions are needed.

When convalescence is abnormal, observations and interventions must be intensive and at times complex. In these situations in particular, care must be well organized and follow specific patient-management protocols that allow all members of the intensive care team to be clear about details of management.

Use of protocols is facilitated by considering the patient to be a complex, integrated system composed of a number of separate but interrelated subsystems (i.e., cardiovascular, pulmonary, renal, nervous, gastrointestinal). Care of such a patient can be accomplished effectively using a “subsystems analysis” approach. This analysis begins in the OR as CPB is discontinued (see Chapters 2 and 4) and continues into the early and late postoperative period. This is not to say that care can be carried out in an automatic fashion. Optimal postoperative care requires overall direction by a knowledgeable and experienced physician using, when indicated, specialized methods of securing information and the skills of personnel in a dedicated cardiovascular ICU.

Management of patients after cardiac surgery has become in some institutions a specialty of its own. Literature on the subject abounds. Around the world, numerous institutions with extensive experience in the surgery of both congenital and acquired heart disease have developed their own protocols and specific systems of management. These include “fast track” protocols and critical pathways that integrate the goals of all caregivers and other interested parties. Within the context of these developments, this chapter discusses general principles, along with enough specific details to be helpful to those desiring to change or develop their own protocols.

Section I Subsystems during Early Convalescence after Cardiac Surgery

CARDIOVASCULAR SUBSYSTEM

Cardiac Reserve

Cardiac reserve is the capacity to increase (or at least maintain) cardiac output as a response to a variety of stressful sudden developments, including increased total body oxygen consumption (\(\text{VO}_2\)), increased ventricular afterload, and decreased ventricular preload. Providing that capacity are all the cardiac and extracardiac mechanisms for maintaining and increasing the force of ventricular contraction and cardiac output. Most of these reside in myocardial contractility and coronary blood flow. In patients convalescing from cardiac surgery, adequacy of cardiac performance alone is insufficient for a high probability of normal convalescence and survival. There must, in addition, be adequacy of cardiac reserve.

Inadequacy of cardiac reserve may become apparent only during periods of increased \(\text{VO}_2\) (from struggling or hyperthermia), suddenly increased ventricular afterload (from paroxysmal pulmonary arterial hypertension in a neonate), or acute reduction in ventricular preload (from sudden blood loss). Such inadequacies of cardiac reserve probably explain “sudden death” occurring early after cardiac surgery.

Cardiac reserve is highly dependent on the preoperative condition of the patient. When, because of disease, reserves are being nearly fully utilized to maintain adequate cardiac performance in nonstressful situations, that which remains may be insufficient to successfully meet the stresses of the intraoperative and postoperative period. Reserves probably cannot be increased before the operation unless they are acutely impaired by a reduced myocardial energy charge. Energy charge may be increased by the cardioplegic technique used in the OR (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” under Methods of Myocardial Management during Cardiac Surgery in Chapter 3).

Limited cardiac reserves are specifically compensated for by many features of early postoperative care.

Adequacy

Although not often conceptualized and not specifically measurable, adequacy of blood flow (cardiac output) in meeting the patient’s needs during recovery from cardiac surgery is the central issue with respect to the cardiovascular subsystem. Arteries and veins are infrequently the primary limiting factors, so emphasis is on adequacy of performance of the heart itself in providing adequate blood flow to the body.

Cardiac Index

Cardiac index (cardiac output expressed as L \(\cdot\) min\(^{-1}\) \(\cdot\) m\(^{-2}\)) is one measure of adequacy of the cardiovascular subsystem, as evidenced by the oft-demonstrated relation between cardiac index and survival (described by Dietzman and colleagues in 1969\(^{11,12}\)). In adults, a cardiac index of at least 2.0 L \(\cdot\) min\(^{-1}\) \(\cdot\) m\(^{-2}\) during the first few hours in the ICU and one of at least 2.4 on the morning after operation are required for normal convalescence (Fig. 5-1). This is at the lower end of the range of normal, which is 2.2 to 4.4.\(^{82}\) Infants and small children appear, in general, to require a somewhat higher cardiac index for normal convalescence (Fig. 5-2). Also, in young patients, cardiac index tends to be lower about 4 hours after operation than it was soon after discontinuing CPB, and then begins to rise after 9 to 12 hours.\(^{11}\)

Cardiac indices below these values are usually inadequate for maintaining a normal convalescence; this can be formalized in the inverse relation between cardiac index early

\(^{11}\)The familiar exercise stress test is a test for cardiac reserve.
postoperatively and the probability of hospital death. This relation can be refined by considering not only cardiac output but also mixed venous oxygen levels, with lower levels worsening prognosis at any given value of cardiac output.\textsuperscript{2}

**Arterial Blood Pressure**

Arterial blood pressure is an insensitive method of estimating adequacy of cardiac output early postoperatively, primarily because systemic vascular resistance (Rs) is usually elevated.\textsuperscript{112}

This may be related to increased levels of circulating catecholamines,\textsuperscript{114} plasma renin,\textsuperscript{110} angiotensin II, or other mechanisms. This high resistance may result in a normal or high arterial blood pressure even when cardiac output is low.

Some patients tend early postoperatively to have low Rs and arterial blood pressure, even when cardiac performance is good. This may occur more frequently in children with cyanotic heart disease, adults with diabetes, and patients with sepsis or drug interactions (especially preoperative use of angiotensin-converting enzyme [ACE] inhibitors).\textsuperscript{13,M20} Arterial hypotension is an indication for thoughtful evaluation. Children cannot be considered to be convalescing normally when mean arterial blood pressure is lower than about 10% below normal for the patient’s age (Table 5-1). For adults, particularly the elderly, arterial blood pressure may mandate maintenance at or above commonly accepted normal values to ensure adequate perfusion of various organs like the brain, viscera, and kidneys.

**Pedal Pulses**

Simple observation of pedal pulses is a commonly used, useful, but not infallible method of estimating adequacy of cardiac output in children and young adults. Normal (grade 4) pedal pulses early postoperatively are highly but not perfectly correlated with adequate cardiac output and a high probability of survival.\textsuperscript{K15,K16} In older adults, estimation of the adequacy of perfusion by amplitude of pedal pulses is often confounded by the presence of peripheral arterial occlusive disease.

**Skin Temperature**

Skin temperature in the foot is another indirect but reasonably reliable estimator of adequacy of cardiac output. A study of cardiac surgery in infants younger than 3 months of age indicated that pedal pulses and skin temperature predicted probability of hospital death from cardiac causes and thus were reasonably good estimators of adequacy of cardiac output.\textsuperscript{K15} As with assessment of pedal pulse amplitude, in older adults skin temperature offers guidance but not solid evidence for adequacy of perfusion.

### Table 5-1 Normal Values for Blood Pressure According to Age

<table>
<thead>
<tr>
<th>Age</th>
<th>Systolic Pressure/ Diastolic Pressure (mmHg)</th>
<th>Mean\textsuperscript{a} (mmHg)</th>
<th>10% &gt; Mean Normal Value (mmHg)</th>
<th>10% &lt; Mean Normal Value (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤Years</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.5</td>
<td>0.5</td>
<td>80/46</td>
<td>57</td>
<td>63</td>
</tr>
<tr>
<td>1.0</td>
<td>1.0</td>
<td>89/60</td>
<td>70</td>
<td>77</td>
</tr>
<tr>
<td>2.0</td>
<td>2.0</td>
<td>99/64</td>
<td>76</td>
<td>84</td>
</tr>
<tr>
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<td>4.0</td>
<td>105/65</td>
<td>77</td>
<td>85</td>
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<tr>
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<td>12.0</td>
<td>118/68</td>
<td>85</td>
<td>94</td>
</tr>
<tr>
<td>15.0</td>
<td>15.0</td>
<td>120/70</td>
<td>87</td>
<td>96</td>
</tr>
</tbody>
</table>

Data from Nadas and Fyler.\textsuperscript{K11}

\textsuperscript{a}Mean arterial blood pressure has been calculated as the diastolic pressure plus one third of the pulse pressure.

\textsuperscript{b}40 mmHg in infants <1 month of age.

\textsuperscript{1}Although dye dilution or thermodilution is the standard for measuring cardiac output, caution is required in interpreting measurement values. In small individuals, confidence intervals around the measurement may be large; low core temperature may diminish accuracy; and tricuspid regurgitation, absence of an adequate mixing chamber, lack of steady state, and intracardiac shunts (as originally articulated by Stewart and Hamilton\textsuperscript{112,K15}) invalidate the measurement.
**Whole Body Oxygen Consumption**

Whole body VO\textsubscript{2} is infrequently calculated, but knowledge of it is useful, in some circumstances, it is a better basis for prognostic and therapeutic inferences than cardiac output or mixed venous oxygen levels. Whole body VO\textsubscript{2} can be calculated by a rearranged Fick equation,\(^3\) which states:

\[
\text{VO}_2 (\text{mL} \cdot \text{min}^{-1} \cdot \text{m}^{-2}) = Q \cdot (\text{CaO}_2 - \text{CvO}_2) \quad (5-1)
\]

The normal value for VO\textsubscript{2} at 37°C is 155 mL \cdot min\(^{-1} \cdot \text{m}^{-2}\). The value for whole body VO\textsubscript{2} in the patient recovering from cardiac surgery must be interpreted in light of his or her body temperature; residual hypothermia is the most common explanation for the somewhat low VO\textsubscript{2} usually present within the first few hours after open heart surgery. This reduced VO\textsubscript{2} is in part due to reduced capillary density (reduced area of capillary flow) and increased heterogeneity of capillary flow through the muscle mass and other tissues of the body in the early hours after CPB.\(^{28}\) Normally convalescing patients operated on with hypothermic CPB generally require 4 to 8 hours for this to disappear and their peripheral perfusion to return to normal.\(^{29}\)

When VO\textsubscript{2} is appreciably reduced below the normal level for the existing body temperature, a hazardous condition exists; indeed, one useful definition of shock is “a condition characterized by an acute reduction in VO\textsubscript{2}.” Abnormally low VO\textsubscript{2} may result from reduction or extreme heterogeneity of capillary flow (of which “no reflow” is an extreme example) in one or more organs of the body (sometimes termed a *reduction in capillary density*), lengthening of the diffusion path between capillaries and cells, or intracellular metabolic derangement. One or all of these may exist in patients early after cardiac surgery. When important reduction in VO\textsubscript{2}, considering the temperature, persists for more than a few hours, probability of death increases.

**Mixed Venous Oxygen Level**

Mixed venous oxygen level, generally expressed as oxygen tension (\(\text{PvO}_2\)) or saturation (\(\text{SvO}_2\)), is a useful index of circulatory adequacy, because it reflects to some extent mean tissue oxygen levels.\(^{20}\) When \(\text{PvO}_2\) is less than 30 mmHg, cardiac output is likely to be inadequate; when it is below about 23 mmHg, the inadequacy is apt to be severe (Fig. 5-3). However, normal or near-normal venous oxygen levels are not reassuring as to the adequacy of cardiac output, unless it is known that VO\textsubscript{2} is approximately normal for the existing body temperature.

In a nonsurgical but critically ill ICU population, Jain and colleagues\(^{13}\) found a weak relationship between \(\text{SvO}_2\) and cardiac index. There was considerable variability among all patients in various conditions, but when normalized for VO\textsubscript{2} and hemoglobin concentration, the correlation coefficient improved (Fig. 5-4). Using indwelling fiberoptic reflectance oximetry,\(^{14}\) other investigators have found no or only a very weak relationship between \(\text{SvO}_2\) or \(\text{PvO}_2\) and measured cardiac index.\(^{28,29}\) Following CPB, changes in \(\text{SvO}_2\) may be useful in detecting low cardiac output, one of many causes of decreased oxygen delivery. Identifying decreases may be of particular value in patients coming to surgery with a high severity of illness index. Online continuous oximetry is useful in critically ill patients because it reflects unanticipated events or occasionally the usefulness (or nonusefulness) of therapeutic maneuvers.\(^{25}\) These aspects of postoperative care illustrate the need for uniformity in monitoring techniques and highlight the conflict between overreliance on devices and the ability to form accurate estimates (in this case, of cardiac performance) based on previous correlations.\(^{28}\) However, many surgeons rely on continuous \(\text{SvO}_2\) monitoring to detect deviations from normal convalescence early postoperatively. Catheters that allow measurement of both \(\text{SvO}_2\) and cardiac output are optimal.

**Urine Flow and Serum Potassium**

Urine flow and serum potassium levels are useful indirect guides to the adequacy of cardiac output. Early postoperative
oliguria suggests inadequate cardiac output and thus is often an indication for treatment of the cardiovascular subsystem. Hyperkalemia rising over a 4-hour period (with sampling every 2 hours) to a level of about 5 mEq·L⁻¹ is a sensitive indicator of a low or falling cardiac output in neonates and infants, and hence an indication for intensifying treatment. Hyperkalemia is usually accompanied by a fall in pedal skin temperature and a rise in esophageal temperature, but it often precedes the appearance of a base deficit or of arterial hypotension.

**Metabolic Acidosis**
A frequently used but somewhat nonspecific and insensitive indicator of the adequacy of cardiac output is the acid-base status of blood. Metabolic acidosis during and after cardiac surgery is almost always a result of lactic acidemia. Lactate production is a byproduct of anaerobic metabolism, which most often occurs under conditions in which cardiac output and oxygen consumption are suboptimal. Occasionally, excess lactate may occur with high measured cardiac output under conditions of high metabolic rate, diabetes, sepsis, or intestinal ischemia.

Concentration of lactic acid in blood may be measured directly. Normally, little or none is present, normal values in plasma being 0.7 to 2.1 mEq·L⁻¹. A concentration of about 5 mEq·L⁻¹ correlates in general with moderate metabolic acidosis, and one of 10 mEq·L⁻¹ with severe metabolic acidosis and usually markedly reduced cardiac output. Moderate elevation of lactic acid concentration is a common finding early after cardiac surgery, but in the normally convalescent patient, lactic acid gradually declines to normal values within 12 to 24 hours.

When arterial pH is less than about 7.4, acidosis is present but may be the result of retention of carbon dioxide; this is reflected in an arterial $P_{aCO_2}$ greater than 40 mmHg. Alternatively, acidosis may be “metabolic” and due primarily to accumulation of lactic acid. Quantification of metabolic acidosis is expressed by a derived value obtained from an equation after measuring arterial pH and $P_{aCO_2}$. Either the buffer base deficit or the standard bicarbonate is calculated. Most commercially available equipment calculates the buffer base deficit or excess (which takes account of the buffering capacity of blood as well as that of bicarbonate) after measuring $P_{aO_2}$, $P_{aCO_2}$, and pH of whole blood. The
normal buffer base is about 48 mEq \cdot L^{-1}, and the normal base excess or deficit is 0.

Cardiac Output and Its Determinants

The cardiac index in normally convalescing adults is often 2.5 to 3.5 L \cdot min^{-1} \cdot m^{-2} after cardiac surgery performed with modern methods of myocardial management. It is generally higher 4 to 6 hours after operation than it is in the OR and still higher the next day, although exceptions occur. Even in patients who convalesce well, some variability in cardiac output occurs.

Risk factors for low cardiac output seem primarily to be those that affect cardiac output in the OR, which in turn is strongly correlated with cardiac output 4 to 6 hours later and the next day.\textsuperscript{59} Cardiac output after operations using CPB is usually correlated with age of the patient (older patients have lower output), cardiac condition, functional state of the patient just before operation (the higher the New York Heart Association [NYHA] class, the lower the output), duration of CPB, and duration of global myocardial ischemia. During the early postoperative period, a heart rate within usual ranges correlates directly with cardiac output, and arterial blood pressure within usual ranges correlates inversely with it.\textsuperscript{411} Within the usual ranges, the higher the atrial pressures, the higher the cardiac output\textsuperscript{411} (Fig. 5-5).

Determinants of cardiac output are ventricular preload, afterload, myocardial contractility, and heart rate. Most normally convalescent patients require no special measures to adjust these fundamental determinants; patients with impaired or inadequate cardiac performance require at least adjustment of preload and afterload, and at times adjustment of heart rate and/or pharmacologic or interventional augmentation of contractility. In many patients who have undergone cardiac surgery, it is specifically either the left (LV) or the right ventricle (RV) that limits cardiac output, less commonly both (see “Relative Performance of Left and Right Ventricles” later in this section).

Ventricular Preload

Ventricular preload, which is correlated directly with the force of contraction, is equated with sarcomere length at end-diastole, and thus with change in ventricular volume between end-systole and end-diastole. This volume change is determined by transmural pressure during diastole, compliance and thickness of the ventricular wall, and curvature of the wall (La Place effect). Transmural geometric arrangement of fibers also plays a role but changes little during the postoperative period.

Transmural pressure is determined by intraventricular pressure and intrapericardial pressure. Intraventricular pressure at end-diastole (which is a determinant of the force of contraction) is related to phasic changes in atrial pressure, and these are affected by blood volume and systemic venous capacitance. The latter is decreased early after CPB.\textsuperscript{52} Because transmural pressure is affected by intrapericardial pressure, it is affected by closure of the pericardium and sternum, both of which increase intrapericardial pressure and decrease transmural pressure. Daughters and colleagues\textsuperscript{53} have demonstrated that pericardial closure in the setting of cardiac surgery, both itself and independent of sternal closure, increases intrapericardial pressure, decreases transmural pressure, and unfavorably affects cardiac performance. Changes in myocardial compliance during and after cardiac operations are due primarily to changes in myocardial water content.

After cardiac surgery in patients with normal atioventricular (AV) valves, most acute changes in preload are equated with acute changes in mean left (in the case of the LV) or right (in the case of the RV) atrial pressure. This is because in this setting, and when the atria are functioning normally as reservoirs,\textsuperscript{59} ventricular end-diastolic pressure is similar to the mean pressure in the corresponding atrium. Therefore, mean atrial pressure is measured in cardiac surgical patients to deduce ventricular end-diastolic pressure. Right atrial pressure is usually measured using a fine polyvinyl catheter introduced through the right atrial appendage or internal jugular vein. Left atrial pressure is measured through a fine catheter introduced through the right superior pulmonary vein (or the left atrial appendage in neonates and young infants). In the absence of pulmonary vascular disease and important pulmonary congestion or edema, pulmonary artery diastolic pressure is a reasonable approximation of left atrial pressure. In most adult patients following CPB, pulmonary capillary wedge pressure exceeds left atrial pressure, and this discrepancy increases through the twelfth postoperative hour. It is thought this difference is due to accumulation of interstitial lung water\textsuperscript{544} (Fig. 5-6).

Ventricular Afterload

In the intact ventricle, afterload is defined as systolic wall stress. This is the analog of the load that resists shortening in the isolated papillary muscle. Other things being equal, increased afterload results in decreased stroke volume. In the intact ventricle, afterload is related to (1) ventricular transmural pressure during systole, (2) ventricular wall curvature as determined by ventricular volume (La Place effect), (3) ventricular wall thickness, and (4) shape of the ventricle.
Ventricular wall determinants of afterload change little during and early after operations. Instead, acute changes in afterloads of the LV and RV are usually produced by changes in intraventricular pressures during systole. These changes are equated with changes in proximal aortic and pulmonary arterial systolic pressures. During and early after operation, proximal pulmonary arterial pressures may be monitored directly, but proximal aortic pressures are not. They must be inferred from measured radial (or femoral) artery pressures. Because of the many determinants of the magnitude of systolic amplification, systolic blood pressure at the radial artery is usually higher than in the ascending aorta, except in the situation of peripheral vasoconstriction secondary to low cardiac output or high-dose α-adrenergic agents. In most instances, systolic pressure variability between the aorta and peripheral arteries is not clinically important, but an awareness of it is advantageous in some situations. Mean pressures are similar in the two areas.

A tendency toward arterial hypertension is present in many adult patients early postoperatively, related to increased systemic arteriolar resistance. This complication (1) increases ventricular afterload and thereby decreases stroke volume, (2) increases aortic wall tension and thereby increases the likelihood of tearing the aortic purge-string sutures and suture lines, and (3) increases LV metabolic demands that exacerbate any latent myocardial ischemia. An appropriate criterion for treatment to lower arterial blood pressure in this setting is a mean arterial blood pressure of 10% above the normal value. Mean arterial blood pressure, not systolic pressure, is monitored for this purpose because of the interrelations between peripheral and central arterial pressures discussed earlier. However, the patient’s preoperative blood pressure must be taken into account, and to avoid cerebral complications, markedly hypertensive patients must not be rendered hypotensive. In the ICU, sodium nitroprusside is generally used for this purpose (see Appendix 5A), but nitroglycerin may be preferred when myocardial ischemia is present, because it decreases coronary resistance. Negative intrathoracic pressure also increases LV load resisting shortening by increasing LV transmural pressure. Positive-pressure ventilation negates this effect, but labored spontaneous ventilation may augment afterload, and this may decrease cardiac output.

Myocardial Contractility
When a change in stroke volume cannot be explained by a change in end-diastolic fiber length (preload) or load resisting shortening (afterload), it is considered to result from a change in the contractile state. Contractility in a given ventricle can be acutely depressed or increased. When an attempt is made to compare ventricular contractility from patient to patient, and from time to time in the same patient, problems arise. A papillary muscle that is twice as thick as others might appear to have twice the contractility when studied in the usual way. In the ventricle, and at least theoretically in papillary muscle, data interpreted in terms of contractility must be normalized according to muscle thickness and length.

In vivo assessment of myocardial contractility and the resultant quantification of ventricular pump function are desirable goals postoperatively. The simplest representation of the capacity of the heart as a pump is a determination of any of several modifications of the Frank-Starling mechanism. For instance, the measured change in cardiac output (or stroke volume) with aliquot infusions of blood or blood substitute serves as a surrogate for assessment of contractile function. Clearly this is not reflective of intrinsic contractile properties of the myocardium, because the pressure-volume relationship is affected not only by preload but also by load resisting shortening, myocardial compliance, and intact vagal and sympathetic reflex activity. Changes in the instantaneous ventricular pressure (or aortic pressure) over time, dp/dt, may reflect myocardial contractility, but this quantity is exquisitely sensitive to afterload and preload and cannot be assumed to be an index of contractility that can be transferred from one patient to another or within the same patient over a period of time.

The relationship between ventricular pressure and volume (pressure-volume loop) is currently the nearest approximation to an in vivo assessment of contractility. Additionally, the area within the loop represents stroke work. The end-systolic pressure and the pressure at end-diastole of several different loops allow an expression of contractility and stiffness, respectively. The loops are composed of four segments: isovolumic contraction, ejection, isovolumic relaxation, and filling (Fig. 5-7). When ventricular volume or resistance is altered, a group of points at end-systole fall along a line, the slope of which Suga and colleagues called Emax. Emax is an index of contractility (Fig. 5-8). Changes of the slope in a steeper direction reflect increased inotropy. A shift in the rightward direction represents negative inotropy. With the use of catheters to measure LV pressure and transesophageal echocardiography (TEE) for instantaneous border detection, pressure-volume loops and Emax (contractility at zero volume) can be interpreted online in the ICU. It is paradoxical that the least clearly and directly defined determinant of the force of cardiac contraction is the one most discussed and treated. Its specific treatment is by the administration of inotropic drugs, usually catecholamines (see “Treatment of Low Cardiac Output” later in this section).
Chapter 5  Postoperative Care

**Figure 5-7** Diagrammatic representation of a pressure-dimension relationship of the left ventricle, on which events of the cardiac cycle have been indicated. (From Foex and Leone.25)

**Figure 5-8** When resistance to ejection is altered, pressure-dimension loops at end-systole extend to a straight line termed the *end-systolic pressure-dimension line*. Slope of this line is an index of contractility. Increase in inotropy causes an increase in the slope of the line. It can also be seen that an increase in inotropy causes widening of the loop as ejection shortening is increased. Extrapolation of end-systolic pressure-dimension line to zero pressure defines 

\[ V_0 \]  

(or \( D_0 \)), the dimension the ventricle would attain if intracavitary pressure became zero. (From Foex and Leone.25)

**Table 5-2** Ranges of Heart Rate during Sinus Rhythm in Normally Convalescing Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Heart Rate (beats · min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤Years</td>
<td>1/12</td>
</tr>
<tr>
<td>&gt;1/12</td>
<td>120⁻190</td>
</tr>
<tr>
<td>1/12</td>
<td>110⁻180</td>
</tr>
<tr>
<td>6/12</td>
<td>100⁻170</td>
</tr>
<tr>
<td>1</td>
<td>90⁻160</td>
</tr>
<tr>
<td>3</td>
<td>80⁻150</td>
</tr>
<tr>
<td>6</td>
<td>80⁻140</td>
</tr>
<tr>
<td>15</td>
<td>70⁻130</td>
</tr>
</tbody>
</table>

From Kirkin and colleagues.63

**Relative Performance of Left and Right Ventricles**

During and early after cardiac operations, one of the two ventricles is usually the factor limiting cardiac performance, not both. It is usually advantageous to consider and treat patients with this concept clearly in mind. The clue of greatest importance in this regard, when the AV valves are normal, is the relation between the left and right atrial pressures, because they represent the closest approximation available to ventricular end-diastolic pressure and, by implication, sarcomere length.514 When the cardiac valves are normal, the ventricle with the highest corresponding atrial pressure is the one limiting cardiac performance. Echocardiography can often provide supportive information.55

**Heart Rate**

Sinus rhythm is optimal postoperatively, and with this rhythm a wide range of heart rates at various ages is compatible with survival (Table 5-2). The normal compensatory response to increased \( \text{O}_2 \) demand is increased heart rate. Often in the elderly and also in patients with diseased myocardium, this response is absent. It is prudent to manipulate heart rate in otherwise normally convalescing patients with slow sinus (or junctional) rhythm to improve cardiac output. For this, atrial pacing via two temporary atrial leads placed at operation is used. In these situations, atrial pacing is also helpful to suppress premature beats (both atrial and ventricular) and may limit the onset of an established arrhythmia.

**Cardiac Rhythm**

Disturbances of cardiac rhythm may also contribute to low cardiac output. Junctional (AV nodal) rhythm reduces cardiac output by 10% to 15%. Junctional rhythm is less efficient than sinus rhythm because the atrial contribution to ventricular filling is absent in the former. Because junctional rhythm is usually transient and its effects are easily overcome by atrial pacing (unless the rate is rapid),106 its presence does not connote an added immediate risk.

Bradyarrhythmias due to damage to the AV node or His bundle, hypoxemia, or drugs can result in low cardiac output. Tachyarrhythmias in the form of atrial fibrillation or flutter or paroxysmal atrial tachycardia may result in hypotension. Risk of tachyarrhythmias increases during infusion of catecholamines. A complete discussion of postoperative rhythm...
disturbances and their treatment is found later in this section under “Cardiac Arrhythmias.”

Causes of Acute Dysfunction (Low Cardiac Output) after Cardiac Surgery

Inadequate Operation
The surgeon’s responsibility for obtaining an adequate operation demands that he or she continue to search for evidence of this postoperatively, particularly when the patient has low cardiac output. Using the methods described in this and other chapters, a search is made for residual intra- or extracardiac shunting, pathway obstructions, valvar regurgitation, graft or conduit dysfunction, or cardiac compression. If the operation is found to be inadequate in any of these respects, prompt reoperation is usually indicated.

Myocardial Dysfunction
Myocardial dysfunction was once thought to explain low cardiac output after cardiac surgery when atrial pressures were elevated above the usual postoperative values in the absence of any other explanation. The availability of two-dimensional echocardiography in the OR and ICU, particularly TEE, makes possible both direct demonstration of ventricular wall motion and assessment of end-diastolic and end-systolic volumes. These studies can lead more directly to the inference that low cardiac output is due to myocardial necrosis or stunning or to impaired cardiac reserve in the face of increased stress. This inference can be supported by the finding of increased creatine kinase (CK)-MB isoenzyme or troponin in the serum.

Reduced Preload
Hypovolemia. The most common cause of reduced preload is overlooked hypovolemia. This may be a relative intravascular loss secondary to vasodilatation, bleeding into undrained cavities (pleural spaces, retroperitoneum, or free peritoneal space), or uncharted chest tube drainage. The most obvious cause of hypovolemia, of course, is bleeding associated with cardiotomy or CPB, reflected by excessive chest tube output. Low cardiac output or low arterial blood pressure associated with low filling pressures (left or right atrial pressure, central venous pressure, or pulmonary capillary wedge pressure) is the sine qua non of hypovolemia. Echocardiography showing vigorous wall motion and small chamber size is simply confirmatory.

Occasionally there is a sympathetic response that supports blood pressure, but often this is blunted early after anesthesia. There may be reflex tachycardia, but ultimately cardiac output suffers.

Infrequently, excessive diuresis leads to relative hypovolemia and lowering of cardiac output. In this instance, the picture may be complicated by hypokalemia leading to arrhythmias.

Diastolic Dysfunction. In the presence of LV hypertrophy, fibrosis, or myocardial edema, filling pressures do not reflect ventricular volume. In this situation, ventricular compliance is diminished. The root problem is inadequate resting (diastolic) sarcomere length. In these situations, echocardiography is especially useful. The picture is characterized by a small ventricular chamber in the presence of high filling pressure, tachycardia, small stroke volume, low arterial blood pressure, and low cardiac output. Appropriate interventions should be aimed at decreasing heart rate, initiating β-blockade, and subsequent volume infusion. Some inotropic agents may be detrimental in this situation.

Acute Cardiac Tamponade. Acute pericardial tamponade (with its resultant acute decrease in ventricular preload in the face of elevated atrial pressures) must always be considered when low cardiac output is present early postoperatively. Undrained intrapericardial bleeding may cause acute cardiac tamponade. It may also occur as a result of marked myocardial edema and chamber dilatation inside the closed chest, because the pericardium can be constricting under these circumstances even when it has not been resutured. Acute dilatation of the RV during an acute pulmonary hypertensive crisis may result in acute atypical tamponade in neonates and infants. It is these phenomena that explain the advantage of leaving the sternum open and covering the mediastinum with an impermeable sheet sutured to the skin edges in critically ill patients, or of opening it in the ICU when this form of cardiac tamponade is limiting cardiac output.

After an early period of adequate and stable cardiac output, cardiac tamponade is a likely cause of rapid deterioration that cannot be easily explained otherwise. It is usually associated with rapidly rising right and left atrial pressures that often, but not always, equalize. Often, drainage from chest tubes is initially brisk and then ceases, and serial chest radiographs show progressive widening of the cardiac and superior mediastinal shadows. Arterial pressure falls, and a paradoxical pulse may be replaced by a narrow pulse pressure. Characteristically, arterial pressure shows a minimal response to a bolus injection of an inotrope. TEE examination is indicated as soon as cardiac tamponade from retained intrapericardial blood is suspected, and is often diagnostic.

Cardiac tamponade can also manifest in multiple atypical presentations that must always be considered when acute low cardiac output develops. For example, right and left atrial pressures may differ widely in the setting of impacted clot adjacent to the right atrium. Neither TEE nor transthoracic echocardiography (TTE) is reliable for detecting this impacted clot, creating the potential for misdiagnosing tamponade as acute RV failure secondary to other causes such as pulmonary hypertension. Therefore, when the diagnosis of cardiac tamponade is considered as a possible etiology of low cardiac output that does not promptly respond to nonsurgical intervention, emergent reoperation is advisable (or reopening the sternum at bedside, especially in infants).

Increased Ventricular Afterload
Increased RV afterload may appear quickly as a result of a sudden rise in pulmonary artery pressure and vascular resistance. Consequently, during an episode of paroxysmal pulmonary hypertension (often provoked by intratracheal suctioning), cardiac output may fall rapidly and apparently “sudden” death may occur, particularly in neonates and infants. These outcomes are probably not purely the result of increased RV afterload, because they reflect impaired RV reserve as well.

Increased LV afterload may result from a sudden elevation of systemic arterial pressure, such as may occur during suctioning, restlessness, or hypoxia. These result in a sudden increase in LV afterload that, combined with impaired LV reserves, can result in low cardiac output early postoperatively. Sustained increase in systemic vascular resistance and LV afterload is present early after cardiac operations in at least
half the adult patients operated on for acquired heart disease.\textsuperscript{E13,F13,W4}

Often, disturbances of afterload (afterload mismatch) and preload (preload reserve)\textsuperscript{E17} are neither independent nor isolated events. Increased RV afterload leads to decreased LV preload. Similarly, but not as important, increased LV afterload leads to decreased RV preload. A common situation in which a corrective operation leads to increased LV afterload is restoration of mitral valve competence or closure of a ventricular septal defect (VSD). In a physics analogy, mitral regurgitation or left-to-right flow through a VSD represents a pair of resistors in a parallel circuit in which $R_T = 1/r_1 + 1/r_2$, where $r_1$ and $r_2$ represent resistances in the two outflow streams and $R_T$ is total resistance. Closure of one outflow ($r$) increases downstream resistance to ventricular shortening; by inference, wall tension and myocardial oxygen consumption ($MVO_2$) increase.

### Risk Factors for Low Cardiac Output

A number of circumstances increase the probability of low cardiac output after cardiac surgery. These have been determined for the most part by numerous multivariable analyses of outcomes after surgery for specific conditions (see Chapters 7 through 58).

#### Patient-Specific

Chronic impairment of ventricular preload, afterload, and/or contractility by any mechanism (ventricular hypertrophy, stiffness, chronic heart failure) increases the risk of low cardiac output after the cardiac surgical procedure. These are for the most part immutable risk factors for low cardiac output, because they do not change quickly after the operation. However, when a patient who had been alive and ambulatory preoperatively has inadequate cardiac output postoperatively, the assumption must be that intraoperative damage has been superimposed on the chronic state. On the other hand, certain surgical procedures, such as ablation of the regurgitant volume of aortic regurgitation or closure of a defect with a large left-to-right shunt, have an immediately favorable impact on cardiac output. Thus, the cardiac surgical procedure itself often increases cardiac output; it is myocardial damage during the procedure that decreases it.

Acute reduction in ventricular contractility preoperatively can sometimes be ameliorated by intraoperative maneuvers. For the most part, these maneuvers are directed toward increasing an acutely reduced energy charge (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” under Methods of Myocardial Management during Cardiac Surgery in Chapter 3).

#### Procedural

The most important intraoperative risk factor for low cardiac output early postoperatively, other than an incomplete operation, is a discrepancy between the duration of any global myocardial ischemia and the efficacy of the measures used for myocardial management (see complete discussion in Chapter 3). This is often reflected in the finding of long global myocardial ischemic time as a risk factor for low cardiac output and for death after operation. Coronary air embolization during CPB is said to adversely affect cardiac performance after the operation, but most air entering the coronary arteries while the heart is not supporting the circulation passes quickly into the coronary sinus and may have little deleterious effect.

The extensiveness of the “whole body inflammatory response” to CPB affects the heart as well and relates to the probability of low cardiac output after operation. This is one aspect of the association of duration of CPB with death after operation; another is that long CPB duration is sometimes the result, rather than the cause, of poor cardiac performance.

Low cardiac output can be the result of (1) an incomplete or inadequate operation; (2) acute myocardial ischemia, with or without necrosis, from impaired coronary blood flow resulting from failure of some part of a coronary artery bypass operation (CABG); (3) incomplete relief of ventricular inflow or outflow obstruction; (4) important residual or created AV valve or semilunar valve regurgitation that may increase the stroke volume requirements of the ventricle; and (5) residual VSD and large left-to-right shunt that may similarly increase LV stroke volume requirements.

One of the reasons for placing temporary fine polyvinyl catheters in the left atrium, right atrium, occasionally the pulmonary trunk via the RV and uncommonly the LV, and for placing temporary epicardial atrial and ventricular wires, is that they can be helpful in intraoperative and early postoperative efforts to identify an inadequate or incomplete operation as the cause of low cardiac output. TEE with color flow Doppler imaging is also important in identifying an incomplete or inadequate operation. The possibility of residual left-to-right shunting contributing to low cardiac output must always be considered after repair of congenital heart disease. With the materials now used as patches for repair of VSDs, an appreciable left-to-right shunt ($Q_p/Q_s > 1.5$) early postoperatively must be assumed to represent an incomplete repair or an overlooked defect. The shunt can be quantified by double indicator dilution, a method rarely used in the current era.\textsuperscript{W29} Alternatively, the left-to-right shunt may be estimated in terms of the pulmonary (Q\textsubscript{p}) to systemic (Q\textsubscript{s}) flow ratio by simultaneously removing samples from the radial artery, right atrium, and pulmonary artery and solving the simplified shunt equation:

$$Q_p/Q_s = \frac{SaO_2 - SaO_2}{SaO_2 - SpO_2}$$

where $SaO_2$ is the percent oxygen saturation of arterial blood, $SaO_2$ that of blood withdrawn from the right atrium, and $SpO_2$ that of blood withdrawn from the pulmonary artery.

TEE with color flow Doppler imaging now can sometimes settle the issue simply, but without the desirable quantification. Intraoperative TEE has become standard of care for intracardiac repairs of congenital heart disease for patients 3 kg or larger. In one study, intraoperative TEE during post-repair evaluation led to surgical revision in 4% of cases.\textsuperscript{E11}

#### Course of Low Cardiac Output

The heart is in an especially vulnerable position early postoperatively, because its poor function adversely affects coronary blood flow; this in turn further worsens cardiac function. This explains the observation that low cardiac output early after cardiac operations rarely resolves spontaneously. Aggressive treatment is indicated.
With treatment, most patients with low cardiac output early postoperatively recover, and unless it was produced by a large area of myocardial necrosis, most patients have no demonstrable ill effects from it late postoperatively.

Treatment of Low Cardiac Output

Experience indicates that it is worthwhile to intensively treat patients with low or inadequate cardiac output early after cardiac surgery, because cardiac performance often improves after 1 or 2 days, followed by good recovery.

Many causes of low cardiac output are reversible. Investigating whether cardiac tamponade or compression is the cause is one of the first steps (see “Acute Cardiac Tamponade” earlier in this section). If tamponade is present and is caused by retained blood in the pericardium, emergency reoperation is indicated. If there is acute cardiac dilatation, such as may occur in a pulmonary hypertensive crisis, the sternum and pericardium should be rapidly opened (if they were closed). In patients at an increased risk of low cardiac output, this complication can be prevented by leaving the sternum open at operation and closing it 24 to 48 hours later. The pericardium should rarely be closed after cardiac operations, because this has a restrictive effect on the heart early postoperatively.

When cardiac constriction is believed not to be present, treatment is directed at increasing cardiac output by manipulating preload, afterload, contractile state, and heart rate and improving tissue oxygen levels. When these measures fail, use of devices to support the circulation must be considered (see “Intraaortic Balloon Pump” and “Temporary Ventricular Assistance” later in this section). All such devices have their own risks and imponderables; except for the intraaortic balloon pump, they are typically not used unless it seems likely the patient will not survive without them. The decision to use such devices is always made with concern for the possibility the patient may survive but be left seriously disabled, and with knowledge of the costs of such interventions.

Noninvasive Methods

When cardiac output is low, preload is manipulated by increasing blood volume with an appropriate fluid until the higher of the two atrial pressures is about 15 mmHg. If the wall thickness of the LV is unusually great or its contractility or compliance is decreased, it may be helpful to raise mean left atrial pressure to 20 mmHg. However, the tendency to pulmonary edema is increased when left atrial pressure is elevated to this level. When the RV is the limiting factor in cardiac performance, right atrial pressure usually can be raised advantageously only to about 18 mmHg. Above this, a descending limb on the Starling curve usually becomes apparent, and cardiac output falls. Also, the tendency to whole body fluid retention, pleural effusion, and ascites is increased by high right atrial pressure.

When LV performance is the limiting factor and systemic arterial blood pressure is more than 10% above normal (see Table 5-1), vasodilating agents should be used to reduce LV afterload to between normal and 10% above normal. Nitroprusside is generally the drug of choice because it is a potent arterial, and to a lesser extent venous, dilator with a short half-life (see Appendix 5A). The drug appears to be as safe in very young patients as it is in adults. Calcium channel antagonists (e.g., nifedipine, diltiazem) lead to similar arteriolar vasodilatation and may improve coronary perfusion in this setting. However, their longer half-life and depressive effect on ventricular contractility make nitroprusside the preferred drug.

Rarely in patients with severe long-standing mitral valve disease or congenital heart disease with pulmonary vascular obstructive changes, RV dysfunction associated with elevated pulmonary artery pressure may limit cardiac performance. Reduction of RV afterload with vasodilating agents is occasion-ally dramatic in its increase of RV, and thus stroke volume. Nitroprusside (0.5 to 3 μg · kg⁻¹ · min⁻¹), nitroglycerin (0.5 to 3 μg · kg⁻¹ · min⁻¹), or phenolamine (1.5 to 2 μg · kg⁻¹ · min⁻¹) may be effective in this setting. In infants, maintaining near-anesthesia for 24 to 48 hours with fentanyl or another intravenously administered agent may minimize paroxysms of pulmonary artery hypertension and the consequent increased RV afterload (see “Pulmonary Hypertensive Crises” later in this section).

Alternatively, management of neonates and infants may be based on use of the long-acting α-receptor blocking agent phenoxybenzamine (see Appendix 5A). It is administered first at the commencement of CPB (see “Other Additives” under Perfusate in Section II of Chapter 2). An additional dose is usually given about 12 hours after returning to the ICU.

Heart rate is adjusted to optimal levels when necessary by atrial pacing, by ventricular pacing when atrial fibrillation is present, or by AV sequential pacing when AV dysynchrony or dissociation is present. When tachyarrhythmias are present, pharmacologic means of control may be used (see text that follows).

If these relatively simple measures do not quickly bring cardiac performance to an adequate level, inotropic agents are begun (see Appendix 5B for details), although their disadvantages are recognized. There is no ideal inotropic agent, nor are there specific indications for specific agents. In their review, Doyle and colleagues classified inotropic drugs based on their effect on intracellular cyclic adenosine monophosphate (cAMP): cAMP-independent drugs include calcium, digoxin, and α-adrenergic agonists; cAMP-dependent agents include epinephrine (and levarterenol), dobutamine, and isoproterenol. These are β-adrenergic agonists that, coupled with dopaminergic drugs (dopamine), have variable effects on peripheral resistance. Phosphodiesterase inhibitors (aminidine, milrinone, enoximone) may enhance contractility while producing myocardial relaxation (lusitropism) and relaxation of vascular smooth muscle. They are not susceptible to receptor down-regulation.

Initially, dopamine may be infused at 2.5 μg · kg⁻¹ · min⁻¹. This dose can be increased to 15 or 20 μg · kg⁻¹ · min⁻¹ if needed, but if a favorable response is not obtained at 10 μg · kg⁻¹ · min⁻¹, it is not likely to be obtained at higher doses. Dopamine has the advantage of augmenting renal blood flow in addition to increasing cardiac contractility. Dopamine increases ventricular automaticity (hence the probability of ventricular arrhythmias), but to a lesser extent than isoproterenol. At low doses (2 to 4 μg · kg⁻¹ · min⁻¹), systemic peripheral vascular resistance is decreased or unchanged by dopamine, whereas higher doses (>6 μg · kg⁻¹ · min⁻¹) increase peripheral resistance. Tachycardia may limit the rate at which dopamine can be administered. When dopamine is ineffective, dobutamine is gradually added in similar doses. Dobutamine, although more expensive than dopamine, appears to augment myocardial blood flow more, in
general, its effectiveness is similar to dopamine.\textsuperscript{D15} Isoproterenol may be preferred initially and is probably superior in the presence of predominantly RV dysfunction and decreased or normal heart rate because of its favorable effect on pulmonary vascular resistance.

Occasionally, hypotension exists in the presence of normal and adequate cardiac output. Under that special circumstance, norepinephrine administered through a central venous catheter is rational treatment; a very low dose (0.01 µg · kg\(^{-1} \cdot \text{min}^{-1}\)) is often sufficient under these circumstances. Under more dire circumstances, larger doses can be used.

Epinephrine is the catecholamine of choice of some, but its powerful vasoconstricting effects make it less desirable than dopamine or dobutamine. When an insufficient response is obtained from other drugs, or excessive tachycardia develops, epinephrine is added or substituted. The drug is initially infused at a dose of 0.01 to 0.05 µg · kg\(^{-1} \cdot \text{min}^{-1}\), which may be increased as needed.

Milrinone also is useful in patients with low cardiac output after cardiac surgery, because it combines a peripheral vasodilator action with its inotropic effect.\textsuperscript{G12} This drug is different in structure and mode of action from catecholamines in that it is a phosphodiesterase enzyme inhibitor in cardiac and vascular tissue, not a β-adrenergic receptor agonist. Administration is usually initiated with a loading dose of 5 µg · kg\(^{-1}\) over 10 minutes, followed by a maintenance dose of 0.3 to 0.75 µg · kg\(^{-1} \cdot \text{min}^{-1}\). The drug is effective in neonates and infants as well as adults, but in small patients, particular care is necessary to maintain an adequate blood volume because of the vasodilatory effect of the drug.\textsuperscript{12} The indications for this drug vs. catecholamines remain arguable. However, it appears to cause less tachycardia and fewer atrial arrhythmias than catecholamines.\textsuperscript{R18}

Additionally, 10% calcium chloride is administered in a dose of 0.1 mmol · kg\(^{-1}\), with supplemental doses if the ionized serum calcium level is below 1.2 mmol · L\(^{-1}\).

Once the acute problems have subsided, some patients in sinus rhythm appear to require chronic augmentation of ventricular contractile function. Use of digitalis in this setting has long been argued, but there is evidence that it does increase contractility.\textsuperscript{G21} Digitalization appears to be useful, particularly in children (see “Atrial Arrhythmias” under Cardiac Arrhythmias later in this section), but it is not recommended in neonates because it may impair diastolic function.\textsuperscript{530}

**Intraaortic Balloon Pump**

The concept of intraaortic balloon pumping (IABP) to produce diastolic augmentation of coronary and systemic blood flow was elucidated by Moulopoulos, Topaz, and Kolff in 1962.\textsuperscript{M29} The procedure was first performed clinically by Kantrowitz and colleagues in 1968.\textsuperscript{K30} IABP uses the principle of diastolic counterpulsation, which augments diastolic coronary perfusion pressure, reduces systolic afterload, favorably affects the myocardial oxygen supply/demand ratio, and augments cardiac output.

IABP is used in adult patients with inadequate cardiac performance not responsive to optimized preload, afterload, and heart rate or to moderate doses (up to 10 µg · kg\(^{-1} \cdot \text{min}^{-1}\)) of dopamine or equivalent doses of dobutamine or epinephrine (see Appendix 5B). Whenever possible, the decision to insert an IABP is made in the OR rather than postoperatively. It is used in preference to catecholamines postoperatively for patients with severe LV dysfunction, with or without evidence of myocardial necrosis, and for patients with evidence of myocardial necrosis and inadequate cardiac output or severe ventricular arrhythmias. This technique has led to survival of some patients who would otherwise have died.\textsuperscript{D18,D19,P14} Survival is less than 50% if renal failure develops from low cardiac output postoperatively.\textsuperscript{D19} IABP has been effective in patients with ischemic heart disease and valvar and congenital heart disease.\textsuperscript{D19}

Preoperative prophylactic insertion of the IABP is sometimes advisable. In addition to its use in myocardial infarction with low cardiac output or shock, preoperative insertion is often helpful in unstable angina, left main disease with ongoing ischemia, and ischemia leading to ventricular arrhythmias. In the era of more complex arterial revascularization for ischemic heart disease (see Chapter 7), IABP support is helpful intraoperatively for pre-bypass support of patients with low ejection fraction. For patients with acute mitral regurgitation or ventricular septal rupture, insertion upon diagnosis is often lifesaving. Perhaps the most frequent indication for preoperative IABP insertion is poor perfusion from either low cardiac output or peripheral arterial disease. It follows that the best survival following IABP occurs when the device is in place preoperatively.\textsuperscript{D19}

Insertion by arterial puncture is generally used, despite its somewhat higher prevalence of vascular complications,\textsuperscript{G14} because of the technical ease of balloon insertion and removal. When the patient is still on CPB, or the femoral pulse cannot be palpated because of hypotension, an incision only in the skin is made over the femoral artery. Through this incision, the femoral artery can nearly always be palpated and the arterial puncture technique used.

Important aortoiliac occlusive disease and abdominal aortic aneurysm greatly increase the risk of vascular complications or failure of insertion when the femoral route is used.\textsuperscript{G15} In their presence, the balloon can be inserted into the ascending aorta through a purse-string suture. This is usually performed before discontinuing CPB. A pledged mattress suture of 2-0 or 3-0 polypropylene is placed in the midportion of the ascending aorta. A tie is placed on the shaft of the intraaortic balloon to indicate the point that should be level with the aortic wall when the balloon is in proper position within the descending aorta. An aortic stab wound is made and controlled digitally, and the balloon is introduced through the wound and passed into the descending aorta. Proper position is verified by appearance of the characteristic aortic pressure pulse when pumping is begun. The balloon shaft is usually brought out through the lower end of the sternotomy incision. When pumping is no longer needed, the patient is returned to the OR, the median sternotomy reopened, and another pledged mattress suture placed outside the original one. As the balloon is removed, the stab wound is controlled digitally, and the pledged mattress suture is made snug and tied. In severe atheromatous aortic wall disease, use of other assist devices is probably indicated (see “Temporary Ventricular Assistance” in text that follows).

IABP is begun in a 1:1 ratio with ventricular diastole, as judged by electrocardiographic (ECG) and arterial pressure pulse signals. Often the patient’s hemodynamic state improves promptly; consideration is then given to weaning the patient from IABP as early as 6 to 12 hours after insertion. If catecholamines have also been required, they are reduced as
is established by connecting the right atrium via the right superior pulmonary vein or via the roof of the left atrium through a purse-string stitch with a short tourniquet. The purse-string stitch may be felt-reinforced if tissues are thin or friable, because bleeding around the perfusion cannulae is frequently troublesome and may require reexploration. An arterial cannula (24F wire thin-wall) is placed in the pulmonary trunk.

**Left heart bypass** is established by connecting the left atrial cannula to the aortic cannula via a centrifugal pump. This ventricular bypass circuit provides continuous blood flow.

**Right heart bypass** is established by connecting the right atrial cannula to the pulmonary trunk cannula via a centrifugal pump. Pump flow is increased gradually to 4.0 to 5.0 L · min⁻¹ for adult patients as CPB flow is reduced and discontinued. The cannulae are brought through the fascia, muscle, and skin into the left and right upper quadrants of the abdomen at the time of insertion or connection to the extracorporeal circuit. Polytetrafluoroethylene (PTFE) felt strips are placed tightly around the cannulae in the subcutaneous tissues to seal the exit tract. In some cases, the cannulae are simply brought through the wound. The midline incision may be closed primarily in some cases. More often, cardiac compression results from wound closure. The skin only may then be closed, leaving the sternal edges apart; alternatively, a silicone membrane is sewn to the skin edges to seal the mediastinum. The edges of the membrane are sealed with iodine ointment to eliminate ingress of air and present a barrier to bacteria. Bulky dressings are applied and sealed to the skin with a large iodine-impregnated plastic adhesive.

Heparin-coated tubing and centrifugal pumps are desirable to reduce trauma to blood elements by providing a more blood-compatible extracorporeal circuit. Roller pumps can also be used but seldom are, because of the perception that more blood elements are injured. Short tubing reduces foreign blood contact surface and heat loss in the extracorporeal circuit.

An alternative, pulsatile extracorporeal blood pump system is also available (ABIOMED Inc., Danvers, Mass.). The pump consists of a compliant inflow chamber to which blood is drained by gravity, separated from a rigid pumping chamber by a polyurethane inflow valve. The pumping chamber is fitted with a polyurethane outflow valve. A sac within the pumping chamber is expanded pneumatically to propel the blood. Components of the system are arranged vertically and placed at the bedside. A console provides pneumatic power, senses filling of the pumping device, and synchronizes pumping so that little attention to the system is required. Anticoagulation with heparin is necessary, and the patient must remain immobile, as with other temporary systems. It may be used in left, right, or biventricular assist configuration. Although the system provides the possible advantages of pulsatile flow and less operator attention, it costs substantially more than centrifugal pump systems.

Bypass support of a single failing ventricle is used when possible. It is frequently possible to bypass a failing RV using an extracorporeal ventricular assist system combined with IABP to support the LV. Bypass support of the failing LV seems more complicated. In theory, the LV can be sustained by left atrial–to-aortic bypass while the unassisted RV continues to provide adequate pulmonary flow. Experience has shown, however, that RV function also declines. Biventricular support is frequently advisable even when there is apparent isolated LV failure.
**Management.** Each of these devices has specific methods and equipment for insertion and late management. In general, anticoagulation with heparin followed by warfarin is required for all devices with mechanical valves, and low-dose anticoagulation with heparin, warfarin, or aspirin is used for those with biological valves. However, management details vary among institutions and devices.

Bleeding from the primary operative site is controlled by reversal of heparin with protamine. Platelet infusion, transfusion of fresh frozen plasma (FFP) or other blood products, and pharmacologic agents to promote normalization of the blood clotting subsystem are administered as indicated. A heparin-bonded extracorporeal circuit is adequate to prevent clotting in the short term. When bleeding from the operative site has ceased or slowed, heparin therapy is restarted. Usually this occurs within 12 hours after completing the operation. Activated clotting time (ACT) is used to monitor heparin effect; desired ACT is approximately 160 to 200 seconds (assuming a control level of 100 to 120 seconds).

Postoperative care of patients on left, right, or biventricular bypass is labor intensive. Continuous bedside care, often by more than one nurse, is required, as is ready availability of a cardiopulmonary perfusionist or other personnel capable of managing the extracorporeal assist system. Bleeding is frequently a nuisance or even a major complication requiring frequent monitoring of blood clotting by ACT. Smooth operation of the system requires frequent infusion of blood products to maintain adequate atrial pressures. Body temperature is monitored continuously, and measures are taken to heat or cool the blood in the extracorporeal circuit or the patient’s body with a heating/cooling blanket. The VAD system may be fitted with ports for hemofiltration to remove excess extracellular fluid if there is marked edema. Occasionally, hemodialysis is necessary. Ventilatory assist is required.

Separating the patient from temporary ventricular assistance requires judgment and patience. There is a tendency to remove systems too early to avoid complications directly related to prolonged extracorporeal circulation. It is advisable to wait a day or so longer rather than rush the process of separation. Ability of the heart to support the circulation is tested by reducing flow into the extracorporeal circuit, thereby raising atrial pressures and allowing flow through the supported ventricle. There is a limit to which flow in an extracorporeal circuit can be reduced without introducing danger of clotting. Flow of less than about 1 L · min$^{-1}$ should be avoided. Heparin levels should be maintained, and duration of testing interval should be short. Cardiac function is monitored by TEE and continuous measurement of arterial and pulmonary artery pressures, atrial pressures, cardiac output, and $\text{SvO}_2$. If the heart cannot sustain adequate cardiac output under conditions of low-flow bypass, the separation process is abandoned, full flow is resumed, and plans are made for later attempts at separation or conversion to an implantable device. Simply removing the temporary device in anticipation that the heart will sustain adequate function is usually unsuccessful.

**Results.** Results are judged either by recovery and long-term survival after removal of the device or by success in maintaining the patient until cardiac transplantation is accomplished. Clearly, some patients not only survive but also have an excellent long-term functional result.$^{37,42,13,6,42}$ Of some importance in this regard is the finding that myocardial cellular atrophy is not a complication of prolonged ventricular assistance.$^{32}$ Despite excellent intensive care, patients with VADs are at risk of thromboembolism, hemorrhage, and infection.

The report of the combined registry for clinical use of mechanical VADs summarized experience with 965 patients.$^{23}$ For about half of them, successful weaning from the device was accomplished, and about half of those weaned were discharged from the hospital alive. Two-year survival among patients discharged from the hospital was 82%, with most being in NYHA functional class I or II. A higher proportion of patients receiving LV assist devices had satisfactory outcomes than was the case in those receiving biventricular assist devices. The probability of survival was similar in patients receiving nonpulsatile centrifugal pump devices and those receiving pulsatile pneumatic devices. Survival to discharge for the multi-institutional experience was about 30% for postcardiotomy support. Individual institutions have recorded discharge of up to 60%, and this seems to be related to greater experience with the devices and earlier establishment of support.$^{35,64,72}$

**Indications.** The complex scientific, surgical, ethical, moral, political, philosophical, and financial considerations necessarily involved in the decision for mechanical circulatory support do not permit a simple listing of indications for this therapy.

There is general agreement that a low cardiac output (cardiac index $\leq 1.5$ L · min$^{-1}$ · m$^{-2}$) and elevated ventricular diastolic pressure (reflected in high left or right atrial pressure) after continuing CPB an hour beyond the usual time of discontinuance, with IABP support and administration of catecholamines in moderate doses, indicate a low probability of survival.$^{19}$ Trial separation from CPB has failed (usually reflected in a progressive drop of systemic arterial blood pressure, elevation of atrial pressures, reduction of venous oxygen saturation, and metabolic acidosis). Under these conditions, in institutions prepared for it and, if necessary, cardiac transplantation (even if this means transportation to another institution), temporary ventricular assistance is usually indicated. Patients with continuing low cardiac output in the ICU despite IABP and catecholamine support also should be considered for temporary ventricular assistance. Use of temporary ventricular assistance is appropriate for patients of any age whose myocardial problem is expected to resolve within a few days, and for patients younger than 65 to 70 years of age whose myocardial problem is not expected to resolve but who are acceptable candidates for cardiac transplantation. In the latter group, the temporary device is used for support while it is determined whether there is good function of major organ systems and the patient is neurologically intact.

Further experience with VADs may lead to discarding current criteria in favor of more liberal use; in part, this is because LV assistance is more effective than IABP in preserving myocardial structure and function, at least in experimental studies.$^{52}$ In general, the younger the patient, the better the prognosis from the now-repaired cardiac disease, and the fewer the other subsystem diseases and failures, the stronger the indication for temporary ventricular assistance.

**Cardiopulmonary Support and Extracorporeal Membrane Oxygenation**

Right and left heart bypass (biventricular assist) works only if pulmonary function is adequate to support gas exchange. In situations of severe compromise of the respiratory system,
support of that system is also required. Portable CPB systems (cardiopulmonary support [CPS]) include both a centrifugal blood pump and a membrane oxygenator, with heparin-coated tubing. These systems are usually referred to as extra-corporeal membrane oxygenation (ECMO). Successful use has been reported, particularly in infants and children, and there is little doubt that in some patients, it is an effective means of biventricular support. (It may be used occasionally in venovenous configuration to support respiration in the face of severe postoperative arterial desaturation from impaired pulmonary function. This methodology has also been used in patients undergoing myocardial infarction or sustaining a catastrophic event in the cardiac catheterization laboratory, and as a support technique during angioplasty.

Only two cannulae have to be inserted, one in the right atrium and the other in a systemic artery. These cannulae are present during surgery and may simply be attached to the system. Oxygenation is achieved in a closed system without an air-to-blood interface. Alternatively, separate venous and arterial cannulae may be inserted through the femoral artery and femoral or jugular vein by percutaneous technique (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2). This places the cannulae in a position for ready control of hemorrhage. Centrally placed cannulae are removed so that the wound may be closed. Percutaneous placement of cannulae and use of the CPS system can be used for emergency support of the failing circulation at the bedside. The CPS system does not ordinarily provide decompression of the LV. LV unloading depends on total diversion of blood from the right atrium to the extracorporeal circuit and the ability of the LV to empty pulmonary venous return to the aorta. A beating heart and absence of aortic valve regurgitation are necessary.

**Management.** Heparin anticoagulation is required to prevent clotting or excess fibrin formation in the oxygenator membrane. ACT is maintained at approximately 160 to 220 seconds by continuous infusion of heparin.

**Results.** In the pediatric population, overall survival after ECMO support following a cardiac operation is 30% to 40%. It may be more effective in situations complicated by pulmonary hypertension or in the presence of a two-ventricle repair, for example, CAST patients for the most part had persisting ischemia; most postoperative patients (coronary disease or not) are probably well revascularized. In the postoperative period, however, many antiarrhythmic agents are proarrhythmic; therefore, treating ventricular arrhythmias other than ventricular tachycardia is probably not necessary.

In patients with an ejection fraction under 40% with postoperative ventricular tachycardia, early electrophysiologic study is indicated. Paradoxically, patients in whom such studies demonstrate acute suppression of PVCs or ventricular tachycardia with the administration of drugs have a good prognosis without drug treatment; such patients probably should be discharged from the hospital on no drug therapy. By contrast, patients whose ventricular arrhythmias cannot be suppressed with drugs have a relatively poor prognosis, and consideration should be given to implating an implantable cardioverter-defibrillator (ICD; see “Ventricular Tachycardia and Ventricular Fibrillation in Ischemic Heart Disease” in Section V of Chapter 16).

When during the first day or two of convalescence, ventricular electrical instability develops in the form of PVCs occurring more than six times per minute or ventricular tachycardia persisting more than 20 to 30 seconds, treatment is prudent even if cardiac performance is good (Appendix 5C). Often, PVCs or bursts of ventricular tachycardia can be suppressed by atrial or ventricular pacing using temporary electrodes, without need for drug therapy. When the hemodynamic state is impaired by ventricular tachycardia,
immediate direct current cardioversion (100 J initially in adults and, if ineffective, 200 J) is indicated. When these measures are ineffective, advice of an experienced electrophysologically oriented cardiologist is indicated.

**Atrial Arrhythmias**

**Prevalence and Risk Factors for Atrial Fibrillation.** Reported prevalence of atrial fibrillation after adult cardiac operations is 20% or higher.\(^3^4\) New-onset atrial fibrillation usually occurs within 5 days of cardiac surgery, with peak occurrence on the second day.\(^3^8\) This arrhythmia uncommonly results in major morbidity or death but can complicate convalescence considerably. It is most likely to develop in patients in whom chronic atrial fibrillation has been present before operation and who have left the OR in sinus rhythm.\(^3^7\)

The largest group of patients in whom atrial fibrillation occurs but who did not have it preoperatively are those undergoing CABG. In this group, discontinuance postoperatively of a β-adrenergic receptor blocking agent that has been taken regularly before operation increases the risk of developing atrial fibrillation during the postoperative period; this complication can be expected in about 40% of such situations.\(^3^1\) Older age at operation is also a risk factor for developing atrial fibrillation postoperatively. This arrhythmia develops in about 4% of patients younger than 40 years of age undergoing CABG, compared with 30% of those aged 70 or older.\(^1^9\) Chronic obstructive pulmonary disease, chronic renal disease, valvar heart disease, atrial enlargement, increased sympathetic tone, obesity, and prior pericarditis\(^3^0,3^1^6\) also appear to increase its prevalence.\(^1^8\) Other preoperative and intraoperative variables do not appear to be correlated with development of atrial fibrillation after cardiac operation.\(^1^9\)

New-onset atrial fibrillation after cardiac surgery increases morbidity, length of stay, and cost.\(^3^1\) Morbidity includes hemodynamic compromise and occasionally embolic events. New postoperative atrial fibrillation is statistically correlated with advanced age but is also seen across a wide spectrum of adult cardiac operations. The peak incidence is 2 to 3 days postoperatively, but it may occur earlier or following discharge. Postoperative atrial fibrillation is usually transient; with treatment, most patients return to sinus rhythm within 2 to 3 days. Patients with preoperative atrial fibrillation are unlikely to return to sinus rhythm, especially if atrial fibrillation has been present for more than 6 months.

**Prevention of Atrial Fibrillation.** Prevalence of new atrial fibrillation after cardiac surgery can be reduced by prophylaxis with a β-adrenergic receptor blocking agent.\(^3^1\),\(^3^5\) Three drugs are available. For this purpose, propranolol may be given in doses of 10 to 20 mg three or four times a day, beginning the morning after operation. Alternatively, atenolol may be given in doses of 25 mg three times per day, which is often better tolerated than propranolol. The benefit from β-blockers as prophylaxis against postoperative atrial fibrillation is greatest when the drug is initiated either prior to or immediately after surgery.\(^3^1\) Amiodarone (a class III antiarrhythmic agent) is also an effective drug for preventing atrial fibrillation, with approximately a 4% to 50% reduction in its prevalence after cardiac surgery. A meta-analysis suggested that amiodarone provided similar protection against postoperative atrial fibrillation as β-blockers and sotalol (another class III antiarrhythmic agent).\(^3^2\) Pretreatment with digoxin or verapamil does not reliably prevent atrial fibrillation.\(^3^0,3^3\)

**Treatment of Atrial Fibrillation.** When atrial fibrillation develops postoperatively, several protocols are appropriate, depending on need for rate control versus conversion to sinus rhythm. In postoperative patients with **chronic atrial fibrillation** with stable and effective hemodynamics who are not in the ICU, digoxin is usually effective for rate control, and is indicated for patients with heart failure and LV dysfunction. In the ICU, rate control of atrial fibrillation with preserved ventricular function is most effectively accomplished with intravenous administration of β-blockers (esmolol, metoprolol, or propranolol)\(^3^1\) or non-dihydropyridine calcium channel antagonists (verapamil, diltiazem), exercising caution in the presence of hypotension. Intravenous amiodarone is also useful for rate control (Table 5-3). It should be noted that intravenous digoxin or calcium channel antagonists should not be used in patients with a preexcitation syndrome; these agents may paradoxically accelerate the ventricular response.

When digoxin is used for rate control, a recommended protocol is found in Appendix 5D. When approximately two thirds of the estimated digitalizing dose has been given and has not accomplished control of the ventricular rate, oral administration of propranolol should be started unless the patient has poor ventricular function or pulmonary disease. If the situation is urgent, propranolol may be given intravenously in doses of 0.5 mg every 2 minutes, to a total intravenous dose of 4 mg in adults. Alternatively, treatment with verapamil may be initiated in doses of 40 mg orally two to three times daily. This drug may be infused intravenously in a dose of 0.075 mg · kg\(^{-1}\) to a maximum dose of 5 mg, but its action is very short when given in this manner, and oral administration should be started promptly.

In patients with new-onset or recurrent postoperative atrial fibrillation, successful conversion to sinus rhythm is usually possible and is advantageous for postoperative hemodynamics. Digoxin is not effective in converting postoperative atrial fibrillation. Amiodarone is currently the first-line drug for pharmacologic conversion of atrial fibrillation.\(^3^8\) A bolus dose of 5 mg · kg\(^{-1}\) in saline is given over a 30- to 40-minute period, followed by a continuous infusion of 0.25 to 0.5 mg · min\(^{-1}\) for 4 to 8 hours. Following conversion, oral amiodarone is generally recommended for 4 to 6 weeks.\(^3^9,3^6,3^8\)

Ibutilide (a class III antiarrhythmic agent)\(^3^3\) is also highly effective in converting postoperative atrial fibrillation and is at least as effective as amiodarone at converting new-onset atrial fibrillation (greater than 75% success).\(^3^1\) Adult patients are pretreated with intravenous magnesium (1-2 g) to reduce risk of torsades de pointes, and the serum potassium level is normalized. Higher doses of magnesium (up to 4 g divided into pre- and post-ibutilide infusion) have been recommended by some.\(^7^4\) Under continuous ECG monitoring, 1 mg of ibutilide is administered intravenously over 10 minutes. The dose can be repeated once. The major risk is a 1% to 4% occurrence of torsades.\(^3^6,3^7\) Ibutilide should be avoided in patients with very low ejection fraction, because of the high risk of ventricular arrhythmias.\(^3^6\) When ventricular response rate is rapid, pretreatment with esmolol may increase the efficacy of conversion with ibutilide.\(^3^1\)

Theoretical concerns have been raised about using ibutilide (which can be proarrhythmic with prolongation of QT interval) after amiodarone (which also prolongs QT interval but rarely causes torsades). When intravenous amiodarone is
Table 5-3  Intravenous Pharmacologic Agents for Heart Rate Control in Patients with Atrial Fibrillation

<table>
<thead>
<tr>
<th>Drug</th>
<th>Loading Dose</th>
<th>Onset</th>
<th>Maintenance Dose</th>
<th>Major Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute Setting</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esmolol</td>
<td>0.5 mg · kg⁻¹ IV over 1 min</td>
<td>5 min</td>
<td>60-200 µg · kg⁻¹ · min⁻¹ IV</td>
<td>↓ BP, HB ↓ HR, asthma, HF</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>2.5-5 mg IV bolus over 2 min; up to 3 doses</td>
<td>5 min</td>
<td>NA</td>
<td>↓ BP, HB ↓ HR, asthma, HF</td>
</tr>
<tr>
<td>Propranolol</td>
<td>0.15 mg · kg⁻¹ IV</td>
<td>5 min</td>
<td>NA</td>
<td>↓ BP, HB ↓ HR, asthma, HF</td>
</tr>
<tr>
<td>Diltiazem</td>
<td>0.25 mg · kg⁻¹ IV over 2 min</td>
<td>2-7 min</td>
<td>5-15 mg · h⁻¹ IV</td>
<td>↓ BP, HB, HF</td>
</tr>
<tr>
<td>Verapamil</td>
<td>0.075-0.15 mg · kg⁻¹ IV over 2 min</td>
<td>3-5 min</td>
<td>NA</td>
<td>↓ BP, HB, HF</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>150 mg over 10 min</td>
<td>Days</td>
<td>0.5-1 mg · min⁻¹ IV</td>
<td>↓ BP, HB, pulmonary toxicity, skin discoloration, hypothyroidism, hyperthyroidism, corneal deposits, optic neuropathy, warfarin interaction, sinus bradycardia</td>
</tr>
</tbody>
</table>

Adapted from Fuster 2006.¹¹⁸
Key: BP; Blood pressure; HB; heart block; HF; heart failure; HR; heart rate; IV; intravenous; NA, not applicable.

not effective in conversion to sinus rhythm, several studies indicate that ibutilide is frequently successful and reasonably safe.²⁰,²¹ In a study of ICU patients (noncardiac surgical) who were not successfully converted from atrial fibrillation to sinus rhythm with amiodarone, 80% were successfully converted with ibutilide.²⁰,²¹ Non-sustained torsades de pointes occurred in 11% of patients, all of whom had depressed LV function. Torsades de pointes has been reported in about 5.5% of women and 3% of men who receive ibutilide.²⁰ It usually occurs within 45 minutes of completion of ibutilide infusion and resolves without treatment in about 40% of patients. Treatment of more than transient torsades includes intravenous magnesium plus lidocaine or cardioversion if the patient is hemodynamically unstable.²⁰,²¹ Deaths from torsades have rarely been reported in this setting.²⁰,²¹ Similarly, amiodarone can be safely administered if initial treatment with ibutilide fails.²¹⁴

Alternatively, in patients in whom atrial fibrillation or flutter is importantly embarrassing circulation, electrical cardioversion is indicated.²⁰,²¹ Using bipolar temporary atrial wires placed at operation (one each on the right atrium and left atrium), low-energy cardioversion techniques have been developed that result in an 80% conversion early postoperatively; anesthesia is unnecessary.²⁰,²¹

When atrial fibrillation persists for more than 48 hours, anticoagulation with heparin or warfarin is indicated for stroke prevention.²⁰,²¹

**Atrial Flutter.** Atrial flutter can be a difficult arrhythmia to control when it occurs postoperatively. Although not always successful, the best treatment is rapid atrial pacing via the two atrial epicardial wires placed at operation (see Appendix 5E).

Ibutilide is also effective in converting atrial flutter (>80% success) and is probably more effective than amiodarone.²¹ Ibutilide is also effective in converting atrial flutter in pediatric patients.²¹ The recommended dose is 0.01 mg · kg⁻¹ intravenously over 10 minutes.

**Paroxysmal Atrial Tachycardia.** Important episodes of paroxysmal atrial tachycardia or paroxysmal atrial contractions occurring after cardiac operations may also be treated by rapid atrial pacing. If these arrhythmias persist, however, the diagnostic and therapeutic advice of an electrophysiologically expert cardiologist is needed. Specific treatment depends on the precise nature of the supraventricular tachycardia. In general, administration of catecholamines should be reduced as much as possible; if additional support is necessary, milrinone is considered (see “Noninvasive Methods” under Treatment of Low Cardiac Output earlier in this section). β-Adrenergic receptor blocking agents such as propranolol are useful (see earlier discussion). Multifocal atrial tachycardias are often best treated by verapamil given intravenously.

**Junctional ectopic tachycardia (JET)** may be a particularly difficult problem in children, with a prevalence of 5% to 8%.²⁰,²¹ It is associated with operations to close VSDs, perioperative transient AV block, repair of AV septal defect,²¹ and young age. In 70 of 71 patients with postoperative JET, Walsh and colleagues obtained control of the arrhythmia and hemodynamic stability using a combination of sedation, hypothermia to 34°C, and procainamide.²¹⁰ Amiodarone may also be effective.²¹

**PULMONARY SUBSYSTEM**

**Adequacy**

**During Intubation**

Adequacy of pulmonary function early postoperatively while the patient is still intubated and receiving controlled ventilation is judged by the response of PaO₂ and arterial carbon dioxide pressure (PaCO₂) to the minute volume of ventilation and ventilating gas mixture being used. The response of the arterial oxygen levels can be expressed as the alveolar-arterial oxygen difference, P(A − a)O₂, which in intact humans is normally only a few mmHg. Nearly all patients early after cardiac operations have abnormally large alveolar-arterial oxygen differences due to intrapulmonary right-to-left shunting of 3% to 15%.²³,²⁹,³¹¹ This assumes that no right-to-left intracardiac shunting is present. Response of
the carbon dioxide levels can be expressed as the minute volume of ventilation required to maintain $P_{aCO_2}$ at 30 to 45 mmHg. Usually this is about 15 to 20 mL · kg$^{-1}$ in both adults and children.

When anesthesia and heavy sedation are no longer present and the ventilator is in a mode of intermittent mandatory ventilation (IMV), the patient’s ventilatory rate is a useful guide to the ease with which the respiratory center’s needs are met, and thus to the adequacy of pulmonary function. In an adult, a patient-triggered respiratory rate of 8 to 12 breaths · min$^{-1}$, with the usual tidal volume, inspiratory gases, and end-expiratory pressure, indicates adequacy of lung function.

Positive end-expiratory pressure (PEEP) may be used as a routine or on indication, with a setting of 5 to 8 cm H$_2$O for adults and children older than 12, and 4 cm H$_2$O for younger patients. Unless the hemodynamic state is suboptimal, PEEP does not alter it, even in infants.$^{13}$ PEEP is used because of studies that suggest it is associated with larger lung volumes, fewer perfused but nonventilated alveoli during ventilation, and smaller $P_{a}/(A – a)O_2$ after extubation.$^{14,15}$ PEEP is generally not advisable in patients with chronic obstructive lung disease (to avoid air trapping and rupturing a bulla, with consequent pneumothorax) and in infants and children who have undergone a Fontan operation or cavopulmonary anastomosis (to avoid still further elevation of jugular venous pressure; see Chapter 41).

Continuous positive airway pressure (CPAP)$^{41,85,86}$ may be used in infants once their cardiovascular state is stable, obviating the need for intermittent positive-pressure breathing (IPPB) and IMV. Should IPPB be required initially, the

![Figure 5-9](image)

**Figure 5-9** A, Arterial oxygen tension ($P_{aO_2}$), venous admixture ($Q_{\text{va}}/Qt$), and arteriovenous oxygen content difference [$\{C(a – v)O_2\}$] measured preoperatively and at intervals early postoperatively in 10 adults undergoing operation with cardiopulmonary bypass. B, Pre- and postoperative values for minute ventilation ($V_e$), frequency ($f$), and tidal volume ($V_t$) in the same patients. Air- and $O_2$-breathing results have been combined, and mean values for the group at each time are shown. (Data from Rea and colleagues.$^{84}$)

Infant is transferred to IMV and sometimes to CPAP for several hours before extubation.

**Exubation**

Traditionally, continued intubation after cardiac operations has been recommended to maintain more precise control of cardiopulmonary physiology. However, early extubation may shorten ICU and hospital stay. Therefore, a protocol beginning with anesthesia induction may be designed to expedite awakening and spontaneous breathing.

Once the patient has been extubated, $P_{aCO_2}$ and $P_{aO_2}$ levels, as well as the visually estimated work of breathing, are useful indices of pulmonary function. $P_{aCO_2}$ of less than 45 mmHg in adults, less than 50 mmHg in young children, and less than 55 mmHg in small infants indicates an adequate minute volume of ventilation. Higher values indicate inadequate alveolar ventilation. $P_{aO_2}$ is often mildly depressed at this time and usually remains so for the first few days after cardiac surgery performed with CPB (Fig. 5-9). This results from the somewhat widened alveolar-arterial oxygen difference. These measurements are valuable, but when a patient is comfortable, breathing easily and slowly, and the chest radiograph is essentially normal, it is highly probable pulmonary function is adequate and convalescence will be satisfactory.

**Causes of Dysfunction**

After cardiac surgery with CPB, the lungs are more likely to have dysfunction, albeit mild and transient, than any organ other than the heart itself. This dysfunction has multiple
Figure 5-10 Relationship between age at operation and duration of cardiopulmonary bypass (represented by solid isobars and their dashed 70% confidence limits) to probability of pulmonary dysfunction after cardiac surgery. Nomogram depicts specific solutions of a multivariable equation; value entered for C3a was 882 ng·mL⁻¹ (see original publication for details). (From Kirklin and colleagues.)

Causes. In part it is caused by absence of pulmonary blood flow during total CPB and by its near absence during partial CPB. Among other things, this results in very low shear stresses in the pulmonary capillaries. This appears to accentuate neutrophil activation, because neutrophils appear to be exquisitely sensitive to shear stress. Leukocytes are also activated by the general damaging effects of CPB and incite an inflammatory response in the pulmonary vasculature. During total CPB and lung ischemia, plasma thromboxane B₂ increases, and this may contribute to a pulmonary vascular inflammatory response. Cytokines interleukin (IL)-6 and IL-8 increase with CPB and may also contribute to membrane damage and neutrophil activation in the lung. The alveolar-capillary barrier becomes more permeable than normal and after cardiac surgery using CPB, macromolecules enter the pulmonary interstitium and ultimately the alveoli, promoting development of pulmonary edema. During the early hours after CPB, radioactive albumin injected intravenously can be detected in considerable quantity in fluid aspirated from the tracheobronchial tree (Digerness SB, Kirklin JW: personal communication; 1972). Postoperative disturbances of lung function and increases of alveolar polymorphonuclear leukocytes have been linked to important reduction of pulmonary surfactant activity. In addition, multiple and not yet totally defined factors encourage development of large areas of atelectasis, either segmental or occasionally lobar; in particular, the left lower lobe has a strong tendency to atelectasis, even in patients who are otherwise convalescing normally.

In some patients, direct trauma to the lungs occurs and contributes to pulmonary dysfunction. Should secretions be retained during or early after the operation, these also contribute to dysfunction. Left (and occasionally, right) phrenic nerve injury may occur after carefully performed cardiac operations, increasing the tendency to pulmonary dysfunction early postoperatively. However, left lower lobe atelectasis is considerably more common than left phrenic nerve paralysis; Markand and colleagues found the left phrenic nerve to be paralyzed in only 11% of patients experiencing left lower lobe atelectasis early after open heart operations. In most patients, the left phrenic nerve recovers within 6 months from its paralysis. Mechanical obstruction of the lower trachea or the bronchi can produce pulmonary dysfunction that may go unrecognized unless care is taken to identify and treat it. Localized or more extensive pulmonary edema may develop in the presence of low or normal left atrial pressure, no doubt related to changes in pulmonary venular and capillary permeability, the causes of which are only partially understood. This phenomenon seems to be more marked in elderly patients. Less commonly, frank pulmonary hemorrhage developing as CPB is discontinued or early thereafter can cause serious bronchial obstruction and contribute in a major way to pulmonary dysfunction. This is probably a more severe result of the same factors that lead to pulmonary edema in patients with normal or low left atrial pressures.

Risk Factors for Acute Dysfunction

Patient-Specific

Patient-specific risk factors for pulmonary dysfunction after cardiac surgery have long been recognized, but formal identification and quantification are rare. In a formal observational study, young age at operation was identified as a risk factor, particularly when the patient was younger than about 2 years old (Fig. 5-10). Similar observations were made by Lell and colleagues. Increased risk with young age is associated with the increased tendency of the very young to develop whole body edema after CPB. In the experience of most institutions, and in a study by Gallagher and colleagues, older age, particularly older than 60 years, has also been associated with increased prevalence of pulmonary dysfunction after cardiac surgery. Chronic obstructive lung disease is an important risk factor for pulmonary dysfunction postoperatively and increases the overall risk of operation because it predisposes patients to increased work of breathing and air trapping. Preoperative pulmonary arterial hypertension, even when associated with low pulmonary arteriolar resistance, predisposes infants to pulmonary dysfunction and also to paroxysms of pulmonary
arteriolar constriction and pulmonary hypertension early postoperatively (see “Pulmonary Hypertensive Crises” later in this section). Congenital morphometric pulmonary abnormalities like the alveolar hypoplasia frequently present in patients with congenital heart disease and Down syndrome increase the prevalence of postoperative pulmonary dysfunction. \textsuperscript{71} Some drugs given during the period before operation increase the prevalence of pulmonary complications postoperatively; amiodarone, used to control cardiac arrhythmias, has been linked to severe pulmonary dysfunction after cardiac surgery. \textsuperscript{D22,K12,M9}

**Procedural**

The type of oxygenator used is probably related to the amount of pulmonary dysfunction generated by the operation, with oxygenators other than membrane-type being risk factors for pulmonary damage. \textsuperscript{K21} Proper filters in the arterial tubing may reduce pulmonary dysfunction postoperatively. \textsuperscript{K17} Longer duration of CPB is a risk factor. This is probably related in part to the direct correlation between duration of CPB and increase in the patient’s extracellular water. \textsuperscript{E1,E16,P1} (Fig. 5-11). The amount of C3a generated by complement activation during CPB is a risk factor for pulmonary dysfunction; this may relate to a greater amount of neutrophil activation with higher levels of C3a. \textsuperscript{K18} Use of external cardiac cooling, particularly by ice slush rather than cold saline, increases the prevalence of left phrenic nerve paralysis, hence the tendency to postoperative pulmonary dysfunction. \textsuperscript{K12}

**Postoperative**

Postoperative events can increase the probability of pulmonary dysfunction. Elevated left atrial pressure, with consequent elevation of pulmonary capillary and venular pressures, aggravates the tendency toward increased lung water and pulmonary dysfunction. The longer the patient is on a ventilator, the greater the chances of continuing pulmonary dysfunction. Paralysis of the phrenic nerve and the consequent elevation of the left hemidiaphragm predispose patients to continuing pulmonary dysfunction, particularly small patients. \textsuperscript{R20,S25}

**Course of Dysfunction after Cardiac Surgery**

Mild pulmonary dysfunction in normally convalescing patients slowly improves without specific therapy except for ambulation and breathing exercises; however, residues of dysfunction may still be present 10 days after operation. \textsuperscript{K24} Occasionally in the patient who appears to be convalescing normally and is out of the ICU for 3 to 6 days, orthopnea and paroxysmal nocturnal dyspnea may develop insidiously. This is particularly likely to occur in patients who have marked LV hypertrophy or poor LV function preoperatively, and it may occur even though their left atrial pressure was less than 15 mmHg when last monitored in the ICU. The chest radiograph may have been normal or may have shown evidence of a mild increase in interstitial fluid. Response to diuresis in such a patient is dramatic and, as a rule, terminates the problem. The hypothesis is that fluid that has accumulated in the interstitial spaces throughout the body during and early after CPB returns to the vascular space 24 to 72 hours after operation. Blood volume is thereby increased at a time when the renal response is subnormal, and diuresis and control of blood volume do not follow. \textsuperscript{C18,P1} In this setting, LV end-diastolic, left atrial, and pulmonary venous pressures rise and symptoms develop. Weight gain and other gross evidence of fluid retention may be absent.

Occasionally, patients who have convalesced without difficulty begin to cough up thick tracheobronchial secretions 48 to 72 hours after operation. Often, seemingly paradoxically, whatever dyspnea and tachypnea may have been present begins to lessen with these events. Presumably at this time, protein-rich fluid that has been in the alveoli and interstitium of the lung since CPB (or soon thereafter) begins to be moved by ciliary action out of the terminal bronchioles and into the larger airways, from which it can be cleared by coughing.

**Figure 5-11** Relationship between duration of cardiopulmonary bypass and increase in interstitial fluid (ECF-PV) 4 to 6 hours after operation. The x’s represent patients undergoing closure of left-to-right shunts; circles represent those undergoing operation for valvar heart disease. Patients with heart failure were not included. The regression equation is:

\[
\text{Ln (ECF−PV)} = -3.248 + 0.8248 \times \text{Ln (CPB time)}
\]

\[r = 0.86; \ P < 0.0001\]

Key: CPB, Cardiopulmonary bypass; ECF, extracellular fluid; \text{ln}, natural logarithm; PV, plasma volume. (Data from Cleland and colleagues. \textsuperscript{K16})
Lung volumes are usually reversibly decreased early after cardiac surgery, particularly vital capacity and total lung volume. This is probably the result of the summation of multiple small areas of atelectasis, occasionally left lower lobe collapse, occult pulmonary edema and pleural fluid, and reduced inspiratory efforts. These usually revert to normal within 3 to 6 months.

Management and Treatment

The goal of treatment of the pulmonary subsystem is the earliest possible return of the patient to extubated spontaneous breathing and ambulation. In an era characterized by the ability to intensively treat both large and small patients after cardiac surgery, the distinctly beneficial effects of early extubation are often forgotten. These include a decline in intrapleural pressure and an increase in LV end-diastolic diameter (or volume), improved ventricular systolic function (due to increased preload associated with shifting of some of the blood volume toward the chest), and improved cardiac output.

General Measures

Patients who are convalescing normally are extubated either in the OR or during the early hours after operation. In most ICUs, it is advisable to extubate patients in the daytime rather than at night; this consideration is a reasonable cause of delay of extubation for a few hours. Otherwise, when pulmonary function is good, extubation should be delayed only under special circumstances, including the presence of cardiac assist devices and the possibility of early reoperation. In general, criteria for extubation include stable and satisfactory cardiac performance, lack of important cardiac arrhythmia, and appropriate awakening with satisfactory neurologic status. There should be no anticipation of return to the OR (e.g., for bleeding) and satisfactory mechanics and ventilatory lung function, as assessed by arterial blood gas analysis and a clinical estimate of inspiratory force and volume. Increasing emphasis has been placed on the advisability of routine extubation of the normally convalescing patient within 6 hours of arrival in the ICU.

A major cause of postoperative pulmonary dysfunction is atelectasis and the associated loss of functional alveolar units. Standard prophylactic measures include chest physiotherapy and use of devices to encourage deep inspirations to recruit atelectatic areas. Zarbock and colleagues demonstrated a beneficial effect of prophylactic nasal positive airway pressure at 10 cm H₂O for at least 6 hours.

Treatment of patients with pulmonary dysfunction who are still intubated during the early hours after operation is in large part an intensification of the usual management, as effective specific therapy is not available. Fractional inspired oxygen (FIO₂) is appropriately adjusted upward if P(A – a)O₂ is large. Minute volume of respiration (not only measured, but judged visually by excursion of the chest wall) and respiratory rate are adjusted to maintain PaCO₂ at about 30 to 35 mmHg. The airway is kept clear by appropriate tracheal suctioning (see “Pulmonary Hypertensive Crises” later in this section for special precautions in neonates and infants). When hemoconcentration develops from leakage of plasma from the intravascular space into the interstitial space of the lungs, and at times into all other organs and the pleural and peritoneal spaces, administration of concentrated serum albumin is helpful in counteracting this trend. Diuretics are useful because they reduce extracellular fluid volume and, in turn, extravascular lung water. During all this, efforts continue to reduce ventilatory support and work toward extubation of the patient (see Appendix 5F). Spontaneous breathing trials and decreasing levels of pressure support appear equally effective in patients who are difficult to wean.

Prolonged Intubation

A prolonged period of endotracheal intubation is necessary when:

- Criteria for extubation are not met.
- Neurologic complications are present.
- Severe dysfunction of the cardiac subsystem is present.
- Persistent chest drainage or a residual cardiac defect make early return to the OR likely.

During periods of prolonged ventilation, active decisions are required regarding use of continuous vs. intermittent sedation and neuromuscular blockade, depending on hemodynamic stability, effectiveness of ventilation, and timing of ventilator weaning. Commonly used sedation and paralytic agents are described in Tables 5-4 and 5-5.

When patients are agitated after cardiac surgery, particularly during ventilator weaning, the first priority is evaluating cardiac and pulmonary subsystems to ensure that agitation is not an indicator of important cardiac or pulmonary dysfunction. If these subsystems have satisfactory function, the next level of intervention targets communication with the patient by nursing or physician staff, or both, to allay patient anxiety. When these interventions are insufficient, pharmacologic agents commonly used to alleviate agitation and anxiety in the ICU include benzodiazepines (e.g., diazepam, lorazepam, midazolam), opioid analgesics (e.g., fentanyl, hydromorphone, morphine, remifentanil), propofol, dexmedetomidine, and neuroleptics (e.g., haloperidol).

Prolonged intubation (≥48 hours) entails problems necessitating fastidious care of the patient. A pneumothorax occasionally develops from positive-pressure breathing, usually requiring urgent aspiration and underwater drainage. Bronchospasm may become a particular problem, probably as a reflex response to proteinaceous tracheobronchial fluid often present under these circumstances. Administration of nebulized isethionate every hour can be helpful. In extreme cases, aminophylline is given as a continuous intravenous infusion in 10% dextrose in a dose of 0.15 mg · kg⁻¹ · min⁻¹. An initial loading dose of about 4 mg · kg⁻¹ is given over 20 minutes. Neonates, infants, and young children who require intubation and ventilation for more than about 14 days often have phrenic nerve paralysis; in these patients, plication of the hemidiaphragm often permits prompt extubation.

In those unusual circumstances when intubation in older children and adults is necessary for more than about 10 days, consideration is given to tracheostomy. Both patient comfort and effectiveness of ventilation are thereby usually increased. This procedure has disadvantages but is sometimes helpful in weaning the patient from the ventilator. Tracheostomy is rarely performed in neonates, infants, and young children, because it is difficult to manage in this age group.
Table 5-4  Commonly Used Neuromuscular Blockers for Paralysis during Ventilator Support

<table>
<thead>
<tr>
<th>Drug</th>
<th>Action</th>
<th>Bolus Dose</th>
<th>Onset</th>
<th>Duration</th>
<th>Continuous Infusion</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cisatracurium</td>
<td>Non-depolarizing</td>
<td>0.15-2 mg · kg(^{-1})</td>
<td>1-2 min</td>
<td>25-90 min</td>
<td>3 µg · kg(^{-1}) · min(^{-1})</td>
<td>Generally given as continuous infusion. Preferred for renal or hepatic failure</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>Non-depolarizing</td>
<td>Initial: 0.05-0.1 mg · kg(^{-1}) Maintenance: 0.1-0.2 mg · kg(^{-1}) every hour</td>
<td>2-3 min</td>
<td>45-90 min</td>
<td>0.8-1.7 µg · kg(^{-1}) · min(^{-1})</td>
<td>Preferred agent for patients without hepatic or renal failure. Given as intermittent bolus or continuous infusion</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>Non-depolarizing</td>
<td>Initial: 0.1 mg · kg(^{-1}) Maintenance: 0.01 mg · kg(^{-1}) every hour</td>
<td>2-3 min</td>
<td>60-100 min</td>
<td>Not recommended</td>
<td>Higher risk of tachycardia. Rarely used because of long duration and potential for accumulation</td>
</tr>
</tbody>
</table>

Table 5-5  Control of Anxiety and Agitation during Ventilator Support

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
<th>Initial Bolus Dose</th>
<th>Maintenance Bolus</th>
<th>Continuous Infusion</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>Benzodiazepine</td>
<td>0.02-0.08 mg · kg(^{-1}) up to max of 5 mg</td>
<td>Same as initial</td>
<td>0.04-0.2 mg · kg(^{-1}) · h(^{-1}) titrate to sedation</td>
<td>Adverse effects: hypotension, nausea, vomiting. May accumulate; use with caution in patients with renal dysfunction</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>Opioid analgesic</td>
<td>0.35-1.5 µg · kg(^{-1})</td>
<td>Same as initial, every 30-60 min</td>
<td>0.7-10 µg · kg(^{-1}) · h</td>
<td>Adverse effects: bradycardia, nausea, vomiting, respiratory depression</td>
</tr>
<tr>
<td>Propofol</td>
<td>Short-acting lipophilic general anesthetic</td>
<td>1-3 mg · kg(^{-1}) over 20-30 s</td>
<td>50-200 µg · kg(^{-1}) · h</td>
<td></td>
<td>May cause hypotension and bradycardia</td>
</tr>
<tr>
<td>Dexmedetomidine</td>
<td>(\alpha_2)-Adrenergic agonist; sedative</td>
<td>Adults: 1 µg · kg(^{-1}) infused over 10 min Pediatric: none</td>
<td></td>
<td>0.2-0.7 µg · kg(^{-1}) · h</td>
<td>Not recommended for more than 4 days to avoid withdrawal symptoms. May cause bradycardia and hypotension</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>Antipsychotic agent</td>
<td>Adults: 2-5 mg intramuscularly or intravenously</td>
<td>Adults: same as initial dose every 4-8 hours as needed to stabilize psychiatric symptoms</td>
<td></td>
<td>May alter cardiac condition and prolong QT interval. May cause extrapyramidal symptoms</td>
</tr>
</tbody>
</table>

Reintubation

When the patient meets all criteria for extubation, reintubation is usually unnecessary. However, reintubation is indicated when:

- PaCO\(_2\) rises above 50 mmHg over 4 hours in the absence of appropriate respiratory compensation for metabolic alkalosis.
- Signs of decreasing cardiac output are noted.
- Signs of exhaustion from breathing spontaneously are observed.
- Excessive pulmonary secretions with ineffective coughing are evidenced.

When the situation is borderline, proper management requires careful observation by senior members of the team. Reintubation should be performed by a competent professional.

Pulmonary Hypertensive Crises

Description. **Pulmonary hypertensive crisis** is a phrase used to describe a serious syndrome of hyperacute rise in pulmonary arterial pressure usually accompanied by bronchospasm, often followed within seconds or accompanied by profound reduction in cardiac output and fall in SaO\(_2\); these sequelae may be irreversible. The syndrome occurs most commonly, but not exclusively, among neonates and infants who are intubated after an operation for repair of a congenital cardiac defect associated with pulmonary arterial hypertension. Pulmonary artery pressure is usually essentially normal or mildly elevated after repair, until an episode of pulmonary hypertensive crisis. The crisis may appear spontaneously but usually occurs during or shortly after endotracheal tube suctioning, particularly if the endotracheal tube is too far down the trachea and makes contact with the carina. Multiple crises may occur in a single patient. The prevalence of pulmonary hypertensive crises is greatest about 18 hours after operation, but they can occur before or after that time.\(^{1,2,8}\) During an acute hypertensive crisis, atypical cardiac tamponade can result from acute RV dilatation.\(^{13,8,11}\)

Incremental Risk Factors. Although recognized for many years, its precise cause at the time it occurs is unknown.\(^{1,17,22}\) Congenital cardiac defects accompanied by large pulmonary blood flow and relatively low pulmonary vascular resistance
are strong patient risk factors for their development. Chief among them are truncus arteriosus and AV septal defect. The histology of the pulmonary arteries and arterioles is normal or mildly abnormal, with all changes considered to be clearly reversible. The syndrome is not seen in patients with fixed pulmonary hypertension or severe pulmonary vascular disease. Procedural risk factors have not been clearly identified, although absence of pulmonary blood flow during CPB, accumulation of neutrophils in the lung, and damage to pulmonary endothelial cells are known to occur and provide a favorable setting for development of pulmonary hypertensive crises. Release of arachidonic metabolites from some cells in the lung (probably pulmonary endothelial cells), failure of pulmonary endothelial cells to inactivate bradykinin, and release by injured pulmonary endothelial cells of the vasoconstrictive platelet-activating factor are probably all encouraged by events during CPB, perhaps particularly if these cells were preconditioned before operation by a high pulmonary blood flow. Postoperative risk factors nearly certainly include acute hypoxia, which is known to produce acute hypoxic vasoconstriction, probably using some of the mechanisms just described. Catecholamine administration appears to predispose patients to these crises.

Prevention. Because pulmonary hypertensive crisis may be fatal despite intense therapy, its prevention is critical. An important preventive measure in neonates and infants is maintenance of paralysis and sedation (with pancuronium or fentanyl) for at least the first 20 to 24 postoperative hours, and for at least another 24 hours or longer if the patient remains intubated (see Section IV, “General Care of Neonates and Infants,” later in this chapter). Fentanyl has been shown to be a safe agent in neonates and adults, with little adverse effect on cardiac function or systemic and pulmonary circulations. A paralytic agent (see Table 5-4) is given along with fentanyl to prevent rigidity. Fentanyl (in a dose of 25 μg · kg⁻¹), along with pancuronium, should be given before suctioning the endotracheal tube in any neonate or infant who is not already well paralyzed and sedated, because it appears to minimize the possibility of a pulmonary hypertensive crisis. In addition to sedation, aggressive treatment of acidosis, including hyperventilation to PCO₂ = 30 to 34 mmHg, decreases prevalence and severity of pulmonary hypertensive crises. When the monitored pulmonary artery pressure becomes paroxysmally elevated early postoperatively, efforts are made to control and reduce it. A high FiO₂ is maintained because this is as useful an agent as exists for reducing pulmonary vascular resistance. Direct infusion of nitroprusside into the pulmonary artery has also been useful. Many agents have been advanced as being optimal on the grounds that they selectively reduce pulmonary vascular resistance, but few do so, and no clearly superior one has been identified. There are encouraging results from use of inhaled nitric oxide to reduce pulmonary artery pressure in cardiac transplant recipients, patients on LV assist devices, and generally in infants and children prone to pulmonary hypertensive crises. Journis and colleagues found that 15 of 17 children having critical pulmonary hypertension following operation for congenital heart disease responded to inhaled nitric oxide (20 ppm) after failure of conventional medical treatment (Table 5-6). Pulmonary arterial pressure decreased without a change in systemic arterial pressure but with concomitant increase of SaO₂ and SVo₂. Other investigators have also shown an increase in cardiac index and improvement of indices of RV function after nitric oxide treatment. Intra-pulmonary shunt fraction may decrease as well. The response in postoperative patients with valvar heart disease may be less satisfactory.

<table>
<thead>
<tr>
<th>Table 5-6</th>
<th>Effects of Inhaled Nitric Oxide on Hemodynamics after Operations for Congenital Heart Defects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T₀ (before NO)</td>
</tr>
<tr>
<td>HR (beats · min⁻¹)</td>
<td>153 ± 22</td>
</tr>
<tr>
<td>Systolic PPa (mmHg)</td>
<td>60 ± 14</td>
</tr>
<tr>
<td>Mean PPa (mmHg)</td>
<td>42 ± 14</td>
</tr>
<tr>
<td>Diastolic PPa (mmHg)</td>
<td>31 ± 14</td>
</tr>
<tr>
<td>Systolic PAo (mmHg)</td>
<td>68 ±12</td>
</tr>
<tr>
<td>Mean PAo (mmHg)</td>
<td>55 ± 11</td>
</tr>
<tr>
<td>Diastolic PAo (mmHg)</td>
<td>44 ± 10</td>
</tr>
<tr>
<td>PLA (mmHg)</td>
<td>7.2 ± 1.9</td>
</tr>
<tr>
<td>PCV (mmHg)</td>
<td>6.6 ± 2.5</td>
</tr>
<tr>
<td>SVo₂ (%)</td>
<td>50 ± 13</td>
</tr>
<tr>
<td>SaO₂ (%)</td>
<td>87 ± 8</td>
</tr>
</tbody>
</table>

Nitric oxide inhaled at 20 ppm reduces pulmonary artery pressure and improves SVo₂ within 10 min, while having no effect on systemic arterial pressure when given to a group of patients following operations for defects associated with pulmonary hypertension.

Key: HR, Heart rate; NO, nitric oxide; PPa, systemic arterial pressure; PAo, pulmonary arterial pressure; SaO₂, arterial oxygen saturation; SVo₂, mixed venous blood oxygen saturation.

RENAL SUBSYSTEM

Adequacy

As a guide to the continuing evaluation of the renal subsystem, a urinary catheter is inserted preoperatively in the OR and left for a minimum of 48 hours to monitor hourly urine flow. In some cases, consideration should be given to use of a trocar-introduced suprapubic catheter in adults, rather than a urethral catheter, because this type of catheter is more comfortable, easier to manage, and associated with less urinary tract infection. Serum potassium concentration is measured every 4 hours during the first 24 postoperative hours and, if the patient is still in the ICU, every 8 hours for at least the next 48 hours. Serum creatinine and blood urea nitrogen (BUN) levels are measured each morning for at least the first 48 hours.

Convalescence early after cardiac surgery can, arbitrarily, be considered adequate with regard to urine flow when urine volume is greater than 500 mL · 24 h⁻¹ · m⁻², or 167 mL · 8 h⁻¹ · m⁻², or 20 mL · 1 h⁻¹ · m⁻². Some prefer to use the criterion of 0.5 to 1 mL · h⁻¹ · kg⁻¹ in the case of infants and small children.

In most postoperative patients, CPB induces a diuresis early after operation. Factors responsible for this are hemodilution with a clear fluid prime (lactated Ringer solution, D₅W + ½ NaCl normal saline, or PlasmaLyte A), and often glucose and mannitol additions to increase tubular oncotic load. Low cardiac output therefore can exist early postoperatively even
in the presence of nominally adequate urine flow. Renal function is inadequate when solute excretion is insufficient to keep serum potassium below 5 mEq · L\(^{-1}\), BUN below 40 mg · dl\(^{-1}\), and creatinine below 1.0 mg · dl\(^{-1}\). Convalescence cannot be considered normal when urine is pink but without red blood cells early postoperatively, because this indicates a free plasma hemoglobin greater than 40 mg · dl\(^{-1}\) and an inordinate and potentially dangerous amount of hemolysis.

Acute renal failure requiring dialysis is rare in adults,\(^5\) but postoperative renal dysfunction (doubling or greater of serum creatinine) occurs in approximately 1% of adult patients if preoperative renal function is normal. If any degree of renal dysfunction is present preoperatively, it occurs in 16% to 20% of patients, about one fifth of whom will need dialysis. Acute renal failure occurred in less than 3% of children undergoing open intracardiac operation.\(^6\) Acute renal failure (in patients without preexisting renal disease) after cardiac surgery is nearly always associated with low cardiac output, but rarely may occur when the other criteria of cardiac subsystem performance are satisfactory.\(^3\)\(^,\)\(^4\)\(^,\)\(^1\)\(^9\)

Causes of Acute Dysfunction after Cardiac Surgery

There are no usual intraoperative events during well-conducted cardiac operations that are damaging to renal function and can be considered causes of acute renal failure.

Risk Factors for Acute Dysfunction

**Patient-Specific**

Poor preoperative renal function is intractable to therapy considerably increases the risk of acute renal failure early postoperatively.\(^1\)\(^)\(^9\)\(^,\)\(^1\)\(^2\)\(^0\) Therefore, preoperative evaluation includes assessment of renal function.

The predictive value of serum creatinine and glomerular filtration rate (GFR) on the risk of postoperative dialysis has been quantified by Mehta and colleagues\(^4\)\(^,\)\(^1\)\(^9\)\(^)\(^,\)\(^4\)\(^1\)\(^9\) for adult patients undergoing cardiac surgery (Fig. 5-12). Although traditionally GFR is the standard measure of renal function, its formal measurement is frequently not feasible in the clinical setting. A useful approximation of creatinine clearance can be made with the Cockcroft-Gault equation\(^1\)\(^7\)\(^,\)\(^9\)\(^2\)\(^1\),

\[
Cr \text{ Clearance} = \frac{(140 - \text{age} \times \text{lean body weight [kg]})}{Cr \text{ (mg · dl}^{-1}\text{) \times 72}}
\]

where \(Cr\) = creatinine. For women, multiply the result by 0.85 to account for smaller muscle mass.

Chronic heart failure (preoperative NYHA class IV) considerably increases risk of acute renal failure after operation, as does cyanotic heart disease after cardiac surgery in older patients.\(^3\)\(^1\) A renal lesion is known to exist preoperatively in many such patients. This does not appear to be the case in young patients; for example, renal failure is rare in infants and children undergoing repair of tetralogy of Fallot.\(^3\)\(^2\)\(^1\)

Young age is a risk factor for acute renal failure. When cardiac output is importantly reduced after cardiac surgery in neonates and infants, a prevalence of acute renal failure as high as 8% to 10% has been reported\(^4\)\(^1\)\(^4\)\(^,\)\(^8\) (Srinivasan and colleagues: personal communication; 1981). One reason for this apparently increased prevalence may be that immature kidneys have less ability to concentrate urine in the face of reduced renal blood flow. Compared with older patients, infants may develop more tissue hypoxia during and early after CPB, with a resulting increase in production of potassium, BUN, and other substances, some of which may be nephrotoxic. Uric acid levels, for example, were shown by Hencz and colleagues to rise to nephrotoxic levels (10 mg · dl\(^{-1}\)) in some patients within 24 hours of operation, and the levels were higher (\(P = .001\)) in patients younger than 3 years of age than in older children.\(^3\)\(^1\)\(^5\) At the other end of the spectrum, older age (>70 years) is a risk factor for developing acute renal failure.\(^3\)\(^1\)\(^2\)

Obesity has also been identified as a risk factor for postoperative acute renal failure.\(^3\)\(^4\)

**Procedural**

A long period of CPB increases the risk of acute renal failure.\(^8\)\(^8\) This has been demonstrated by a prospective study\(^8\)\(^1\)\(^8\) and is probably in part related to the damaging effects of CPB. There is an additional risk imposed by a longer duration of hypothermic circulatory arrest, particularly in infants and children.\(^3\)\(^1\)\(^6\) However, a CPB flow of 1.6 L · min\(^{-1}\) (at body temperatures of 28°C or higher) with a mean arterial blood pressure of at least 30 mmHg seems to minimize occurrence of acute renal failure when postoperative cardiac output is good.\(^3\)\(^2\)\(^0\)
Several studies suggest that using a CPB prime of whole blood (rather than hemodilution) increases the risk of acute renal failure, as does high plasma hemoglobin level (>40 mg · dL⁻¹) during and early after CPB.

**Postoperative**

Acute reduction in cardiac output early after operation is the most common and most important risk factor for developing acute renal failure. Yet the prevalence of acute renal failure varies among patients with low cardiac output, in part because of the role played by other risk factors. Picca and colleagues found a 79% mortality in children developing acute renal failure.

Management and Treatment

One important aspect of managing the renal subsystem is a reasonable program of fluid administration (see “Fluid, Electrolyte, and Caloric Intake” in Section II of this chapter) early after open cardiac operations. Its purpose in part is avoidance of fluid overload that can easily develop with even mild impairment of renal function. There is no evidence that larger amounts of fluids reduce the prevalence of acute renal failure in this setting. Maintaining good function in other subsystems, particularly cardiac, is a second important aspect of managing the renal subsystem after cardiac surgery.

When oliguria occurs early postoperatively, cardiac preload and afterload are optimized, and administration of dopamine at 2.5 μg · kg⁻¹ · min⁻¹ is begun (see Appendix 5G). The direct diuretic effect of low-dose dopamine and its subsequent prevention of oliguric renal failure are controversial. At best, dopamine may increase cardiac output, blood pressure, or both, resulting in greater urine volume, but its therapeutic effect on GFR, creatinine clearance, and serum creatinine is doubtful, particularly in high-risk patients. If these measures do not quickly suffice, furosemide (1 mg · kg⁻¹ or up to 40 mg in adults) is administered intravenously. If a good response is obtained, this dosage is repeated every 6 to 12 hours for 3 days. If a response is not obtained within 30 to 60 minutes, the dose is doubled and then quadrupled, and then 8 mg · kg⁻¹ is given. Because of the propensity for increasing osmolarity with mannitol, an alternative recommendation is a pure furosemide infusion at a dose of 1 to 15 mg · h⁻¹ in adults and 0.1 to 0.5 mg · kg⁻¹ · h⁻¹ in infants and children. This technique produces a more consistent urine output, often with a smaller total dose of furosemide than intermittent furosemide administration. This therapy is based on the reasonable hypothesis that maintenance of urine production, even though dilute, is advantageous to renal function. When serum potassium rises above 5.5 mEq · L⁻¹, a glucose and insulin solution is given intravenously, and sodium polystyrene sulfonate enemas are used (see Appendix 5H). These are temporary palliative measures to be used until dialysis can be initiated.

Alternatively, when urine flow does not respond to the first few doses of the furosemide schedule, infusion of a “renal cocktail” may be effective. This consists of a mixture of 400 mg of furosemide in 100 mL of 20% mannitol (both amounts are halved for small patients); it is administered continuously at a furosemide rate of 1 mg · kg⁻¹ · h⁻¹. During infusion of the renal cocktail, the serum osmolarity of the patient is measured every 2 to 4 hours; if it exceeds 310 mOsm · L⁻¹, the infusion is immediately discontinued. Otherwise, it is administered for 4 hours, discontinued for 4 hours, then administered for another 4 hours, and so forth. If a large urine flow develops, the “cocktail” is usually discontinued after 24 hours, or after 3000 mL of urine (in an adult) has been excreted. If a large urine flow does not develop within about 2 hours of beginning this infusion, it is stopped. Occasionally in the absence of a diuretic response to furosemide, intravenous ethacrynic acid (100 mg for an adult) may be effective.

Unless oliguria and hyperkalemia respond to treatment within a few hours, especially in neonates and infants, a considerable probability of death exists. Therefore, peritoneal dialysis or continuous arteriovenous hemodialysis is initiated on an emergency basis; the urgency is in part due to the frequent coexistence of an increased extracellular fluid volume (“fluid overload”) dating back to the time of CPB. More optimally, preventive measures are applied earlier, including (1) ultrafiltration during the closing phases of CPB (see “Components” under Pump-Oxygenator in Section III of Chapter 2); (2) limitation of fluid administration during the early hours after operation; and (3) routine placement, in neonates and infants, of a small silicone peritoneal dialysis catheter through the lower end of the incision used for the median sternotomy. The advantages of this last
technique have been developed and emphasized by Mee.\textsuperscript{M18} His protocol includes using the catheter simply as a drain initially, occasionally the tube drains large amounts of peritoneal fluid with a protein content similar to that of plasma. Should oliguria develop that is unresponsive to furosemide, or should serum potassium rise above 5 mEq $\cdot$ L$^{-1}$, rapid-cycle low-volume peritoneal dialysis is recommended. Dialysates, alternatively isotonic and hypertonic, are used in volumes of 10 mL $\cdot$ kg$^{-1}$. Potassium content depends on serum potassium concentration. Particularly in neonates, infants, and children, dialysis by this or other techniques usually improves cardiac performance and decreases ventilatory requirements.\textsuperscript{M18,Z2} Complications of such protocols are rare; the most frequent error in their use is delay in beginning intervention.\textsuperscript{B20,H4,N14,R8,Z21} At least one study has demonstrated beneficial effects of prophylactic peritoneal dialysis in neonates and infants after complex cardiac operations.\textsuperscript{S7}

In older children and in adults, who more commonly develop nonoliguric renal failure,\textsuperscript{S40} conventional hemodialysis may be appropriate when indicated. However, continuous pumped or unpumped arteriovenous or venovenous hemofiltration is the technique preferred in this setting, with the unpumped technique having advantages in patients who are hemodynamically unstable.\textsuperscript{B6,M28}

**NEUROPSYCHOLOGICAL SUBSYSTEM**

Neuropsychological symptoms and signs after cardiac surgery are difficult to categorize, arguable as to etiology, and often overlooked. Literature concerning them is voluminous, and inferences from the available information are controversial.\textsuperscript{B28}

The neuropsychological sequelae of hypothermic circulatory arrest are described separately in “Brain Function and Structure: Risk Factors for Damage” and “Effects of Brain Damage” under Damaging Effects of Circulatory Arrest during Hypothermia in Section I of Chapter 2. (For a discussion of the emergency treatment of seizures, one sequela of hypothermic circulatory arrest, see Appendix 5I.)

**Generalized (Diffuse) Neuropsychological Function**

Intelligence, problem-solving, concentration, learning, memory, error-free performance, and dexterity are components of the general neuropsychological subsystem, and all or some of these have been included in the term cognitive functions. It is believed that changes in these cognitive functions reflect genuine disturbances in the brain and are testable, usually by psychometric study.

**Adequacy**

Concentration, memory, learning, and speed of visuomotor responses have been reported to be adequate early postoperatively in less than half of patients who undergo cardiac surgery with CPB.\textsuperscript{N7,S14,S15} However, in many patients this inadequacy (or decrease in function) is only mild (and presumably transient); in about 20% of patients it is moderate in severity, and in 5% it is severe.\textsuperscript{S14} By contrast, after peripheral vascular surgery, mild inadequacy is present in 30% of patients, and moderate or severe disturbances in none.\textsuperscript{S14} These findings have been disputed, however, and the early prevalences remain uncertain.\textsuperscript{H3,M25,R12,S26} By 8 weeks after operation, at least 60% of patients have adequate (normal) cognitive functions. Six months to 5 years after operation, more than 80% of patients have adequate (normal) function of this subsystem,\textsuperscript{S31} although Newman and colleagues observed an increase in cognitive decline between 6 months and 5 years.\textsuperscript{S26}

These estimates from objective testing of patients after open cardiac operations have seemed incompatible with the general experience of many physicians and surgeons. The general experience is that patients are not commonly disabled by neuropsychological problems unless they have experienced an overt stroke.\textsuperscript{O1,T16} In no instance among a carefully studied group of 165 patients was neuropsychological dysfunction sufficient to prevent return to work.\textsuperscript{S15}

**Causes of Dysfunction**

Presumably, organic changes in the brain cause disturbances of the general neuropsychological subsystem. Embolization and hypoperfusion, with resultant ischemia, have most generally been considered etiologic to these organic changes. Additional studies have also implicated the inflammatory response to CPB and genetic susceptibility as additional contributors to neuropsychological dysfunction.\textsuperscript{S24} In adults randomized to either pH-stat or alpha-stat acid-base management during CPB, cerebral blood flow was greater using the pH-stat strategy. However, patients with higher cerebral blood flow suffered greater postoperative neurophysiological impairment, suggesting that hyperemia as well as hypoperfusion may be factors in postoperative cerebral dysfunction.\textsuperscript{P11} Speculatively, the causes of both general neuropsychological subsystem dysfunction and localized subsystem dysfunction (e.g., stroke) are the same except in degree, distribution, or both.

Emotions and moods of patients appear to be causally related to cognitive function. For example, patients who sense cognitive deterioration after CPB usually are not found to have it by objective testing; instead, they are found to have more depression postoperatively than preoperatively.\textsuperscript{N8} Also, preoperative depression and lower socioeconomic status appear to appreciably increase risk of deterioration of cognitive function postoperatively.\textsuperscript{P8} In a study of patients randomized to either coronary angioplasty or surgical revascularization, cognitive function was similar in each group after 5 years of follow-up, suggesting no lasting detrimental effect of CPB,\textsuperscript{H21} a finding contrary to that of Newman and colleagues.\textsuperscript{N6}

**Risk Factors for Acute Dysfunction**

Knowledge in this area remains incomplete, in part because of difficulty in defining and measuring the endpoints of acute dysfunction, as well as the variables that are possible risk factors for development of dysfunction. Older age at operation is a mild risk factor for diffuse neuropsychological dysfunction postoperatively.\textsuperscript{T7} Mild or moderate carotid artery stenosis is not a risk factor.\textsuperscript{T7} Longer duration of CPB has been found to be a risk factor for general neuropsychological disturbances after the cardiac operation.\textsuperscript{N7,N9,S6,S26} As has a greater amount of microembolization, both particulate and gaseous.\textsuperscript{B17,F20} Normothermic CPB (used in combination with warm myocardial management) was noted by one group to have a comparatively higher occurrence of central neurologic system events than standard hypothermic perfusion.\textsuperscript{C29} However, other studies have not corroborated these findings.\textsuperscript{B6} Engelman and colleagues\textsuperscript{E4} performed a randomized study to evaluate the effect of perfusion temperature on prevalence of postoperative neurologic dysfunction; 291 patients were divided among perfusion temperatures of 20°,
32°C, and 37°C. In the group as a whole, there was a 36% prevalence of neurologic dysfunction at 1 month postoperatively but no difference in cognitive function, elemental skills, or neurologic functional capacity among the groups. Aside from that for pH-stat regulation, no other correlation has been found between total cerebral blood flow during CPB and prevalence of general neuropsychological dysfunction after operation.\textsuperscript{V3} Oxygenators other than the membrane type and absence of 40-μm arterial blood filtration somewhat increase the risk of this type of dysfunction.\textsuperscript{B16}

Course of Dysfunction
As indicated earlier, the prevalence of general neuropsychological dysfunction declines considerably as time passes after the operation.

Management and Treatment
Management and treatment involve prevention and intelligent counseling and reassurance. The former consists of further improvements in CPB and techniques of cardiac operations. The latter is highly important in determining the final overall result of the operation, because perceived continuing dysfunction can limit quality of life. For example, Bhudia and colleagues performed a randomized clinical trial of 350 adults to evaluate magnesium as a neuroprotector during CPB (780 mg MgSO\textsubscript{4} in 100 mL normal saline intravenously over 15 minutes during anesthesia induction, followed by 3160 mg in 100 mL normal saline over 24 hours; the CPB circuit was primed with MgSO\textsubscript{4} to a concentration of 3.6 mg \textcdot dL\textsuperscript{-1}).\textsuperscript{B15} Magnesium was found to preserve short-term memory and cortical control over brainstem functions (primitiive reflexes).

Mood State

Adequacy
An adequate mood state after a cardiac operation is one without unusual anxiety, depression or euphoria, or delirium. Prevalence of an inadequate mood state has received little study, for reasons similar to those in the case of the general neuropsychological subsystem. In one study of 759 patients undergoing CABG, 7% showed transient confusion without delirium, and in no case did delirium develop thereafter.\textsuperscript{C1}

Causes and Risk Factors for Acute Dysfunction
Preoperative emotional characteristics of the patient play a major role in postoperative mood state. In a study performed during the early era of open cardiac operations, Burgess and colleagues found all patients to have acute preoperative anxiety in varying degrees; a few were frankly depressed. Absence of daily access to an empathetic individual who is not part of the surgical team, both before and after operation, was an important risk factor for increased anxiety and depression postoperatively. These mood states were particularly apparent in the ICU and during the first few days thereafter.

Course of Dysfunction
Most patients have some degree of anxiety during the first few postoperative days, and severe delirium occurs in 2% to 10%; 10% to 20% of patients have hallucinations and frightening dreams late postoperatively, and 10% to 20% of patients may continue to have episodic alterations in mood state after hospital discharge. In some patients, this seems to be related to difficulty in adjusting to the situational demands of life with improved cardiac function.

Management and Treatment
Daily access to an empathetic individual not identified with the surgical team, and attention to the patient as a sensitive and threatened human being by physicians, are the most important methods of prevention. When the mood state becomes severely abnormal, psychiatric assistance is required.

Localized Neuropsychological Function

Adequacy
Most patients recover from open cardiac operations without gross localized neuropsychological subsystem dysfunction (e.g., hemipareses, hemiplegias), and in them the subsystem performs adequately throughout convalescence. Subtle defects occur more frequently. Visual field defects are sometimes perceived by the patient and confirmed by testing, and then usually regress or disappear.\textsuperscript{S26} Difficulty focusing, such as is required for reading, is sometimes experienced in the early postoperative period, but it usually disappears within 2 weeks. Disturbances of memory are nearly always transient but may be noticeable to the patient. Because of the known phenomenon of accentuation and prolongation of the patient's perception of the abnormality by fixation on it, patients and their families are provided supportive care and reassurance. Special diagnostic procedures are rarely indicated, because there is essentially no effective specific therapy (see “Management” later in this section).

Gross neurologic defects, usually hemipareses or hemiplegias, are less common than neuropsychological and mood abnormalities, but they are generally more serious. Prevalence of these abnormalities after open cardiac operations is about 0.5% in relatively young patients, gradually rising with increasing age to around 5% in patients older than about 65, and 8% in those 75 or older.\textsuperscript{C25,G66} In a study of 2108 patients undergoing isolated CABG, adverse cerebral outcomes occurred in 129 (6.1%). Approximately half of these were major deficits; the remainder had deterioration of intellectual function or seizures.\textsuperscript{R9} In a related multicenter study of 271 patients undergoing CABG combined with an intra-cardiac procedure, adverse cerebral outcomes occurred in 43 (16%).\textsuperscript{W25}

Causes and Risk Factors for Acute Dysfunction
These defects probably represent more severe forms of the same kinds of damage (i.e., greater quantities, more sensitive locations) that cause neuropsychological and mood disturbances. Thus, they are probably the result of emboli (e.g., platelet aggregates, clusters of microbubbles, aggregates of fibrin accumulations from pump-oxygenators or tubing surfaces, boluses of air, arteriosclerotic debris or plaques dislodged from the ascending aorta) and other facets of the damaging effects of CPB. When investigated using computed tomography (CT) scans in patients with evidence of stroke after cardiac operations, the defects are typically multiple and posteriorly located in the brain. These findings are most consistent with particulate atheromatous embolization.

Older age is a risk factor for stroke after cardiac operations such as CABG, but this may be only because of the increased prevalence of arteriosclerosis.\textsuperscript{B18,W77} Severe arteriosclerosis of the ascending aorta clearly increases risk of perioperative stroke,
as does known preexisting cerebral vascular disease.66 Duration of CPB and low cardiac output after operation also appear to be risk factors.66,89 Cardiac microbubbles identified by intraoperative TEE have not been a risk factor for diffuse or localized neuropsychological dysfunction; furthermore, such microbubbles can rarely be eradicated by what might appear to be effective surgical maneuvers.79

Management
Precise recommendations for complete prevention of localized neurologic dysfunction remain elusive. However, certain precautions may reduce the frequency of major neurologic events, such as maintaining adequate perfusion pressure, minimizing duration of circulatory arrest, and using blood filters and appropriate de-airing procedures (see Chapter 2). In adults, Blauth and colleagues88 and Wareing and colleagues97 have stressed the importance of ascending aortic atheromatous disease as etiologic in postoperative stroke. Perioperative detection of severe atheromatous disease of the ascending aorta is facilitated by ultrasonographic interrogation by the surgeon.94 Management may consist of (1) modification of the techniques of aortic cannulation or aortic clamping, (2) aortic endarterectomy or resection, (3) grafting of the ascending aorta, and (4) use of an intraaortic filter at the time of aortic clamp removal.115,131,136

The only general therapeutic intervention that seems to be of value is use of hyperbaric oxygenation. This has been demonstrated only in patients with massive air embolization, but even in this setting, evaluation is difficult because spontaneous recovery may occur. The interval from the embolic event (which nearly always occurs in the OR and usually during or at the end of CPB) to hyperbaric therapy plays a major role in outcome; beyond 12 to 24 hours, this therapy probably is not useful.114,115,118 Because these patients, as well as many others without these localized neurologic disorders, are intubated and heavily sedated during this period, localized neuropsychological disturbances are rarely discovered within 24 hours of operation.138 Intense diagnostic efforts, such as lumbar puncture and CT scanning, are generally not indicated in the absence of any therapeutic implication. In addition, CT scanning may fail to be diagnostic.114

Moazami and colleagues have reported the safety and efficacy of intraarterial thrombolysis in a group of 13 patients suffering strokes after cardiac operations.146 A "stroke" team is organized to evaluate all patients with an acute neurologic deficit recognized within 6 hours of operation. Patients with a clinically important stroke (National Institutes of Health [NIH] stroke scale > 10) or isolated disabling symptoms are considered for study. They undergo emergent contrast cranial CT; evidence of hemorrhage or major early signs of infarction preclude thrombolytic therapy. Otherwise, four-vessel arterial angiography is performed using the transfemoral approach. Digital subtraction angiography permits the site of occlusions to be located and collateral circulation evaluated. Patients with middle cerebral, internal carotid, or basilar artery occlusions are considered for thrombolysis. A 2.3F microcatheter is steered to the occlusion by fluoroscopy and embedded within or through the center of the thrombosis. Thrombolysis is attempted at 5- to 10-minute intervals for up to 2 hours. Additional mechanical manipulation of the clot is also used. Among the 13 patients studied, NIH stroke scale improved importantly in 5 (38%; CL 23%-57%) and did not worsen appreciably in the 8 who did not improve.

The prognosis is variable, as is the case with strokes in general. In some patients, the signs and symptoms gradually disappear, whereas in others there is only partial or no recovery from the neurologic defect. At times, the defects are so massive as to be fatal.

GASTROINTESTINAL SUBSYSTEM

Adequacy
Abnormalities of function of the gastrointestinal tract, including the liver and pancreas, are not clinically detectable when convalescence after cardiac surgery is normal; oral intake is usually allowed on the morning after operation. Patients who remain intubated are exceptions. In these cases, fluid intake through a nasogastric tube is begun 12 to 24 hours after operation, gradually progressing to a nutritious one. Evidence of abdominal distention, absence of peristalsis, and hyperperistalsis is sought twice daily. If one of these develops, the gastrointestinal system is not adequate, and alimentation is discontinued, investigations are begun, and intravenously administered hyperalimentation is considered.

Patients with a history of peptic ulcer disease should be given 300 mg of cimetidine (or some other histamine H2-receptor antagonist) every 6 hours by mouth or intravenously during the postoperative hospitalization, beginning 6 to 12 hours after operation. Such a program is worthy of consideration as a routine.

Types of Acute Dysfunction
Acute dysfunction of the gastrointestinal subsystem is uncommon after open cardiac operations, occurring in only about 1% of patients.110,138 However, important dysfunction of the gastrointestinal subsystem is followed by death during the period of hospitalization in more than 50% of those patients. Emergency operations are required for some.

Gastrointestinal Bleeding
Gastrointestinal bleeding after open cardiac operations is usually from the upper part of the gastrointestinal tract.138 The pathology is usually hemorrhagic gastritis or duodenitis.132,136 Occasionally, a previously existing duodenal ulcer is the site of bleeding, and rarely, massive bleeding originates in the colon.139

Acute Cholecystitis
Acute cholecystitis, when it develops after open cardiac surgery, may be noncalculous, but it produces the same clinical syndrome of severe pain, leukocytosis, and right upper quadrant tenderness as when it develops in other patients.110,138 Perhaps because of delay in diagnosis that has been present, mortality among patients who have developed this complication is about 75%.110

Acute Pancreatitis
Some evidence of acute pancreatitis is present in about 25% of patients after open cardiac surgery and presents with hyperamylasemia,133 increased serum lipase, or both. In most cases, the increased level gradually declines, with few if any clinical sequelae. Occasionally (in <5% of patients with elevated amylase) severe pancreatitis develops, with pancreatic abscess or hemorrhagic pancreatitis.140 Indiscriminate
administration of large doses of calcium chloride contributes to development of pancreatic cellular injury after cardiac surgery.\textsuperscript{4}

\textbf{Jaundice}
Convalescence may be complicated by jaundice, with about 20\% of patients having a serum bilirubin concentration of at least 3 mg \cdot dL after cardiac surgery.\textsuperscript{155} Jaundice is moderate or severe (bilirubin concentration > 6 mg \cdot dL) in only about 5\% of patients. Severity of preoperative right atrial hypertension, hypoxia during operation, early postoperative hypotension, duration of CPB, and amount of blood transfused perioperatively all increase the probability of postoperative jaundice.\textsuperscript{155,411,413} Halothane, if used, and duration of CPB may be risk factors.\textsuperscript{415}

Provided postoperative cardiac output is good, hepatic dysfunction can be expected to improve gradually and disappear, but when cardiac output is low, prognosis is poor. Frank hepatic necrosis may develop when cardiac output is acutely and severely reduced. The only useful treatment is that directed at improving cardiac performance and supplying adequate nutritional support.

\textbf{Intestinal Necrosis}
Intestinal necrosis develops uncommonly but insidiously after cardiac operations. Inevitable perforation in the area of necrosis may be overlooked for a number of days because of the multiplicity of problems associated with the causative low cardiac output.

\textbf{Esophagitis}
Esophagitis, when it occurs after a cardiac operation, manifests with dysphagia, which is uncommon. Esophagitis may be related to an intrapericardial accumulation of blood or to pericarditis. When oral candidiasis is present, \textit{Candida esophagitis} is nearly certainly the cause of dysphagia \textsuperscript{421} and can be diagnosed by means of esophagoscopy or radiologic study of the barium-filled esophagus.\textsuperscript{427} When candidal esophagitis appears, antibiotic therapy is stopped unless it is essential. Every 2 to 6 hours, 500,000 to 1 million units of nystatin are given orally, preferably in methylcellulose to increase viscosity.\textsuperscript{422} Treatment is continued for 1 to 3 weeks.

\textbf{Watery Diarrhea}
As a complication of cardiac surgery, watery diarrhea may accompany or follow abdominal distention or appear de novo toward the end of the first week. Should it become frequent and explosive, with passage of mucus and blood, it has ominous implications. Any oral antibiotics should be discontinued when diarrhea develops. The diarrhea may be caused by ischemia of the bowel secondary to a long period of low cardiac output, and this ischemia may lead to small or large bowel infarction,\textsuperscript{435} or it may be a form of ulcerative colitis and proctitis. Diagnosis can be made by sigmoidoscopy and colonoscopy. If the bowel ischemia and ulceration progress, laparotomy and bowel resection are required, but even with such treatment, prognosis is poor.

An important and potentially serious cause of watery diarrhea after cardiac surgery is \textit{Clostridium difficile}, which colonizes the intestinal tract after the normal gut flora has been altered by broad-spectrum antibiotics. Prevalence of this complication is 0.7\% to 1\%.\textsuperscript{428} Risk factors for development of \textit{C. difficile}–associated diarrhea include advanced age, greater cumulative antibiotic days, longer ICU stay, and longer time on ventilator.\textsuperscript{428} \textit{C. difficile} is also the causative organism for antibiotic-associated pseudomembranous colitis. Both pediatric and adult patients who develop watery or persistent diarrhea after cardiac surgery should promptly have a stool specimen examined via a stool toxin assay. If the stool is positive for \textit{C. difficile} toxin, standard therapy is oral metronidazole (alternatively, oral vancomycin) for 14 days, which is usually curative.

\textbf{Abdominal Distention}
Occasionally, gas in the gastrointestinal tract produces abdominal distention within 24 to 48 hours of operation. Bowel sounds can be heard initially. Although not part of normal convalescence, this complication is usually benign and subsides after another day or so in response to fasting, use of glycerin suppositories, and application of heat to the abdomen. A rectal examination should be performed to exclude fecal impaction as a possible cause of distention. If distention does not promptly subside, other causes must be considered; it could be due to oral administration of procainamide or cephalosporins, and these drugs may have to be administered by another route. Mediastinitis and an infected median sternotomy incision may be causative and should be investigated. Abdominal distention may be the first sign of postoperative acute pancreatitis. When combined with marked weakness and fever, particularly in a patient on warfarin, postoperative adrenal insufficiency must be excluded by appropriate tests as a possible cause.

\textbf{Causes of Acute Dysfunction}
Nearly all acute intraabdominal dysfunctions (inadequacies of the gastrointestinal subsystem) result from localized or generalized severe hypoperfusion of either the gastrointestinal tract or the liver, or both.\textsuperscript{431,434,410,413,416,419} However, in neonates and infants, improper position of the inferior vena cava cannula during CPB and thrombosis or infection in umbilical arterial or venous catheters may cause intraabdominal problems early postoperatively.

\textbf{Risk Factors for Acute Dysfunction}
Preoperative \textit{peptic ulcer disease} predisposes patients to upper gastrointestinal bleeding after cardiac operations. Other chronic diseases of the intestinal tract also seem to increase the risk of gastrointestinal complications. \textit{Acute necrotizing enteritis} occurring in neonates who were severely acidic before operation is a risk factor for gastrointestinal dysfunction early postoperatively. \textit{Advanced age} increases the risk of acute dysfunction of the gastrointestinal subsystem after cardiac operations, as does valvar heart disease and congenital heart disease in adults.\textsuperscript{410}

\textit{Long duration of CPB} as a risk factor is arguable, but most believe it to be one. \textit{Low cardiac output} requiring prolonged catecholamine support and IABP increases the risk of serious intraabdominal complications.\textsuperscript{410} Increased prevalence of these complications is also associated with \textit{infection} during the postoperative period, preoperative chronic renal failure, and postoperative acute renal dysfunction.\textsuperscript{438}
Management and Treatment

Encouragement of normal convalescence is the best protection against gastrointestinal dysfunction. Routine administration of cimetidine or some other histamine H₂-receptor antagonist should be considered for any patient at increased risk of gastrointestinal complications.

Once complications appear, their precise nature is determined on an emergency basis, usually by fiberoptic endoscopic examination and with the collaboration of a gastrointestinal specialist. In the absence of massive hemorrhage or gastrointestinal perforation, or both, intense medical treatment rather than surgical intervention is advisable. In the presence of symptoms, however, the possibility of intestinal necrosis must always be entertained, even when symptoms and signs are mild.⁶⁸

ENDOCRINE SUBSYSTEM

Hyperglycemia (in both the OR and ICU) is associated with adverse outcomes after cardiac surgery. Both in diabetics and nondiabetics, serum glucose levels above 200 mg · dL⁻¹ are associated with increased risk for mortality and adverse events.⁵²¹ Insulin therapy is advisable in the ICU to avoid marked hyperglycemia. In patients with type 2 diabetes mellitus, continuous insulin infusion is advisable.⁷¹⁰

Few other abnormalities of the endocrine subsystem have been described as postoperative complications of cardiac surgery. An exception is acute adrenal insufficiency, found by Alford and colleagues in 5, or 0.1%, of 4364 patients.⁴⁶ Its cause is probably hemorrhagic infarction of the adrenal gland.⁴⁶ This can be precipitated by CPB, and the tendency toward it is aggravated by postoperative anticoagulant therapy. Symptoms generally appear between the fourth and tenth postoperative days and consist of abdominal pain and flank pain, abdominal distention, altered mental status, fever, and occasionally shock. When this diagnosis is suspected, a low serum cortisol level is virtually diagnostic. The diagnosis is also highly likely if the serum cortisol level remains low 60 minutes after administration of 25 units of intravenous or intramuscular adrenocorticotropic hormone (ACTH). Later, confirmatory evidence of acute adrenal insufficiency should be obtained.⁴⁶ Prompt treatment with intravenous cortisol and saline solutions results in rapid clearing of symptoms. Lifetime oral treatment is indicated subsequently.

Neither hypo- nor hyperthyroidism has been identified as a complication after cardiac surgery with the aid of CPB. However, an important reduction of plasma free triiodothyronine (T₃), although not of thyroxine (T₄), occurs early after cardiac operations. T₃ remains low for at least 24 hours, leading to the suggestion that its administration at that time is associated with an increase in myocardial function and energy stores.⁴¹⁸ Chronic excessive catecholamine stimulation may depress isometric force development in myocardial muscle. Timek and colleagues⁵⁹ found that exogenous T₃ may improve myocardial fiber shortening amplitude by accelerating Ca²⁺ transients in an in vivo preparation of catecholamine stimulation. There is some clinical evidence that exogenous T₃ (0.6 to 0.8 µg · kg⁻¹) may improve cardiac output immediately after CABG in patients with depressed ejection fraction⁴²² and also in brain-dead organ donors.⁵⁵ However, results have varied. When T₃ was given to patients expected to have an uneventful course, little change in outcome was noted.⁵²⁴ When it was given to adult patients undergoing CABG in a randomized study, improvement in cardiac output and a decreased prevalence of myocardial ischemia compared with controls were noted by Mullis-Jansen and colleagues.⁴⁵³ An increase in cardiac output was also apparent after CABG in patients with depressed LV function.⁴⁵²

HEMATOLOGIC SUBSYSTEM

Adequacy

Function of the hematologic subsystem is assessed in terms of volume of postoperative bleeding, adequacy of clotting, volume restoration, and resistance to infection (see Immune Subsystem later in this section).

Causes of Acute Dysfunction

Excessive blood loss after CPB may result from a variety of causes, either singly or in combination. A surgical (mechanical) cause must always be suspected. Reoperative procedures, complex procedures, and operations on the aorta are those most frequently associated with a mechanical etiology for bleeding. Often if there is excessive bleeding, it is obvious within the first hour after transfer from the OR. It is persistent but may vary in volume over successive hours, depending on hemodynamic status, coagulation status, and patient position and wakefulness. Surgical bleeding occasionally also presents as a delayed increase in chest drainage following an apparently normal early postoperative course, and this usually demands emergency reexploration. Likely causes include suture line leak, chamber rupture, or (in the case of CAGB) graft disruption or mechanical erosion. Occasionally in a patient with a low hourly blood loss persisting over 12 or more hours, a surgical cause is found at reexploration.

Prevalence of reexploration for bleeding varies between 0.5% and 5.0%,¹³ depending on institutional criteria and case mix. Moulton and colleagues⁴³⁰ identified increased patient age, preoperative renal insufficiency, operation other than CABG, and prolonged bypass time as independent risk factors for reexploration. In their series, the prevalence of reexploration was 4.2% (253/6015), and reexploration was strongly associated with increased operative mortality and morbidity, including sepsis, renal failure, respiratory failure, and atrial arrhythmias. Others report little or no increased mortality and morbidity associated with reoperation for bleeding.⁴²

Prevalence of bleeding attributable to nonmechanical (nonsurgical) causes is difficult to estimate, because in many instances reexploration results in cessation of bleeding even though no single site or only a minor site of bleeding can be identified.

Disturbances of coagulation may arise from a myriad of causes. It has long been recognized that the damaging effects of CPB and the magnitude of the resulting inflammatory response are related to postoperative blood loss, presumably via cytokine activation, platelet activation and aggregation, and kallikrein stimulation of neutrophils.¹³⁴,¹³⁸ Platelet abnormalities, both quantitative and qualitative, universally occur during and after CPB. Some consider platelet dysfunction the most common and most important deficit of hemostasis in the postoperative period.¹³¹,¹³⁶,¹³³ The qualitative abnormalities include degranulation and membrane fragmentation
attributable in part to changes in GPIb and GPIIb/IIIa receptor activity.

During CPB, coagulation factors are depleted by dilution, activation, and consumption. These effects center on activation of thrombin, plasmin, and fibrinogen. Antithrombin (AT) III normally inhibits thrombin and factors IV and V. Heparin leads to anticoagulation by enhancing the thrombin-inhibiting ability of AT III by a factor of 2000. Heparin also diminishes activation of factors IX and X and cofactors V and VIII. Residual heparin may lead to excessive bleeding by its effect on thrombin. This has also been characterized as rebound heparin effect.

The rationale for use of heparin-bonded circuits is based partially on the potential to reduce contact activation inherent in the CPB apparatus. Contact activation is due to vibration, blood/gas interfaces, and pericardial aspiration. Simple exposure of blood to tubing may lead to important fibrinolysis, diffuse intravascular coagulation, and various consumption coagulopathies.

Hypothermia that can impair thromboxane synthesis and suppress platelet aggregation may lead to coagulation defects. Thus, adequate rewarming on CPB is essential. Platelet transfusion, although controversial, may be beneficial. Further prevention of coagulation difficulties involves limitation or reversal of hemodilution, efforts to avoid contact activation of platelets and blood proteins, adequate rewarming, and use of pharmacologic agents, all discussed in Chapter 2.

Treatment of Bleeding

There are strong reasons to limit or avoid transfusion of blood products in stable patients. The public, patients, and physicians have become aware of the possibility, although small, of disease transmission from transfusion. The current estimated likelihood of contamination with the human immunodeficiency virus (HIV) is 1 in 440,000 to 640,000 screened units of blood. Hepatitis B is estimated to be present in 1 per 63,000 units, and hepatitis C in 1 per 103,000 units. With routine use of polymerase chain reaction (PCR) testing or nucleic acid testing (NAT), the risk of contamination by HIV and hepatitis B will be even less. The possibility of bacterial contamination is probably slightly greater than the figures just mentioned. Hemolytic reactions occur infrequently and are not generally due to human error, but rather to a delayed reaction from previously undetectable antibody that is activated following a series of transfusions. Finally, the estimated cost for the patient of 1 unit of packed red blood cells (RBCs) is U.S. $250 to $280, and efforts at cost control suggest prudence in transfusion will help lower overall hospital costs. Recent studies have shown a correlation between blood transfusions and greater risk of mortality, infection, and other adverse events.

Strategies to prevent excessive bleeding, or in some cases to treat it, begin with reversal of hypothermia. The importance of remaining on CPB to achieve a core temperature (measured at the tympanic membrane or in the nasopharynx) of 37°C has been stressed elsewhere (Chapter 2). In the ICU, use of warming blankets (or in infants, overhead heaters) supplements this process.

Control of arterial blood pressure using nitroglycerin, nitroprusside, or diazoxide may be helpful. Use of PEEP has been advocated, but its effect on the magnitude of blood loss is controversial. Residual heparin effect or heparin rebound can be diagnosed by a prolonged ACT. Additional protamine can be administered, usually 50 to 75 mg in adults and 5 to 10 mg in children. (There is a remote possibility of a protamine reaction in this setting, which may vary from mild hypotension to anaphylaxis; see “Whole Body Perfusion during Cardiopulmonary Bypass,” in Section II of Chapter 2.)

Use of antifibrinolytic agents in the ICU is controversial. Tranexamic acid, ε-aminocaproic acid (EACA), and aprotinin (now unavailable in the United States) are each more effective when given during CPB than after (see Chapter 2). Transfusion therapies include cryoprecipitate, FFP, platelets, and whole blood or packed RBCs.

Each institution may establish different thresholds for transfusion. As an example, whole blood or packed RBCs could be given for hemoglobin under 7.0 g · dL⁻¹, hematocrit under 20%, or Svo₂ under 65%. This threshold might be raised to hemoglobin under 10 g · dL⁻¹ in severely ill or elderly patients or in those with unstable hemodynamics, because they are unlikely to increase cardiac output in response to acute anemia.

Transfusion of platelets should be considered for patients with a platelet count under 70,000 and excessive bleeding. Similarly, FFP should be administered for an International Normalized Ratio (INR) greater than 1.5 to 1.7 in patients with excessive bleeding and a history of warfarin treatment. Specific treatment with cryoprecipitate, FFP, or other components is indicated in the presence of a consumption coagulopathy reflected by a fibrinogen level less than 200 mg · dL⁻¹, a positive D-dimer assay, or presence of fibrin degradation products.

In recent years, recombinant activated factor VIIa (rFVIIa) has been added to the surgical armamentarium. Originally conceived as therapy for bleeding in patients with hemophilia, rFVIIa promotes hemostasis by increasing generation of thrombin on platelets, producing a more stable fibrin plug that is resistant to fibrinolysis. In the setting of persistent elevation of INR, partial thromboplastin time and/or reduced platelet count/aggregation, rFVIIa has been shown to be effective in treating bleeding associated with postoperative coagulopathy. However, it is expensive (about $7000 per treatment), and concern remains about possible development of a hypercoagulable state that could induce bypass graft or mechanical valve thrombosis. Acute thrombotic complications have been observed in pediatric patients on ECMO support. Thus, it should not be used in the usual postoperative patient, but is an important adjunct in the setting of ongoing bleeding with severe coagulopathy.

Chest drainage tubes must be properly placed in the OR for them to function well early postoperatively and keep the pericardial and pleural spaces free of blood (see “Positioning Chest Tubes” under Completing Cardiopulmonary Bypass in Section III of Chapter 2). During transport to the ICU, chest tubes are connected to an underwater seal. Once the patient is in the unit, the tubes drain into an initially empty container in which a negative pressure of 40 cm H₂O is continuously maintained. Routine “stripping” of the chest tubes by nursing personnel is unnecessary and potentially dangerous, and the technique should be used only for clearing clots. Provisions are made for continuous precise measurement of drainage from the chest tubes; this can be incorporated into
Box 5-1 Indications for Prompt Reoperation for Bleeding

1. Excessive bleeding from the chest tubes, as defined in Table 5-7 for infants and children. Drainage in excess of these criteria means that bleeding will probably continue and reach clearly excessive total amounts (in adults ≥ 1500 mL) within 12 hours. Exceptions to prompt reentry when this criterion is met are rare and are generally limited to patients in whom prolonged efforts at hemostasis have been made already and a bleeding diathesis is present, suture lines are known to be secure, and tamponade is not present.

2. Marked widening of the cardiac silhouette in the portable chest film 8 to 24 hours after operation. Such widening nearly always indicates retention of some clots and blood in the pericardium. Even if the patient's condition is good, elective reoperation and evacuation of blood and clots are usually advisable.

3. Sudden increase (≥300 mL·h⁻¹ in adults) in chest drainage that has been small in the first few postoperative hours. Such an increase usually results from bleeding from an incision in the heart or great arteries.

4. Evidence of acute cardiac tamponade.

Table 5-7 Chest Drainage Criteria for Reoperation in Infants and Children

<table>
<thead>
<tr>
<th>Preoperative Weight (kg)</th>
<th>Hourly Amount (mL·h⁻¹)</th>
<th>Total Amount (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>70 60 50</td>
<td>120 130</td>
</tr>
<tr>
<td>6</td>
<td>70 60 50</td>
<td>130 155</td>
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<td>70 60 50</td>
<td>150 180</td>
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<td>380 300 230</td>
<td>760 900</td>
</tr>
<tr>
<td>40</td>
<td>430 350 260</td>
<td>800 1035</td>
</tr>
<tr>
<td>45</td>
<td>500 400 300</td>
<td>975 1150</td>
</tr>
<tr>
<td>50</td>
<td>500 400 300</td>
<td>1000 1200</td>
</tr>
</tbody>
</table>

*Reoperation is advisable if the patient has bled the amount indicated in any 1 hour (column 1), the lesser amount in column 2 during each of any 2 successive hours, or the still smaller amount (column 3) in each of any 3 successive hours.

*Reoperation is advisable if, by the end of the fourth or fifth postoperative hour, the patient has bled in total the amount indicated.

Heparin Resistance

Heparin resistance may be encountered at operation. It may result from a congenital defect in the coagulation cascade, but usually is the result of chronic heparin therapy. Diagnosis is made by an ACT less than 480 seconds after administration of a minimum of three times the calculated dose of heparin. It is treated by administration of FFP or, more appropriately, antithrombin III concentrate.

Thrombocytopenia

Moderate thrombocytopenia to levels of 100,000 platelets·mL⁻¹ is to be expected following CPB. A level of 70,000 platelets·mL⁻¹ may meet a threshold for transfusion if there is excessive bleeding. Under ordinary circumstances, platelet counts as just noted are decreased by dilution, destruction, and aggregation. Platelet function is diminished by changes in platelet membrane receptor activity, which includes down-regulation of GPIb and GPIIb/IIIa receptors.

Heparin-Induced Thrombocytopenia

Heparin-induced thrombocytopenia (HIT) is an immuno-mediated syndrome that can occur after prior exposure to...
Heparin products. Unfractionated heparin (and to a lesser degree, low-molecular-weight heparin) binds to circulating platelet factor 4 (PF4), which creates a heparin/PF4 complex that is recognized by immunoglobulin (Ig)G antibodies. The neoepitopes recognized by HIT antibodies are located on PF4 (found in platelet α granules) and are formed by the binding of PF4 to heparin. When IgG antiheparin/PF4 antibody titers are sufficiently elevated, binding of the heparin/PF4/IgG complexes to platelet receptors induces platelet activation and aggregation. Clinical diagnosis of HIT syndrome requires presence of antiheparin/PF4 antibodies and a 30% to 50% decrease in platelet count or absolute platelet count of less than about 80,000. HIT syndrome can also be identified by skin lesions or necrosis at the site of heparin injections in the presence of HIT antibodies. The full-blown syndrome (HIT with thrombosis [HITT]) includes additional presence of arterial or venous thrombotic events, most commonly deep vein thrombosis, but can include pulmonary embolism, disseminated intravascular coagulation, stroke, limb ischemia, renal failure, intestinal ischemia, or coronary thrombosis. Mortality of HITT following cardiac surgery exceeds 25%. Laboratory diagnosis, clinical implications, and management strategies remain without consensus, related to several important observations. Of primary importance is the absence of specificity of current serologic testing. The serologic enzyme-linked immunoabsorbent assay (ELISA) that is commercially available and used in most hospitals is not specific for IgG antibodies (which are responsible for HIT) and does not differentiate among IgG, IgM, and IgA antibodies. As a result, this ELISA is very sensitive (>95% of clinical HIT patients have a positive ELISA for antiheparin/PF4 antibodies) but not highly specific (75%-85%). Furthermore, the predictive value of the ELISA is directly related to the strength of the test result, which is measured in optical density (OD) values. Based on a threshold positive OD value of 0.40, Zwicker and colleagues noted a sixfold increase in the likelihood of a thrombotic event in patients with HIT who had an OD > 1.0 compared with those with an OD of 0.4 to 0.99. When considering all patients with a positive ELISA test (OD > 0.4), 5% or more of patients have evidence of antiheparin/PF4 antibodies before cardiac surgery, and more than 20% are reported to form HIT antibodies following cardiac surgery. The prevalence is somewhat higher with bovine lung heparin than with heparin derived from porcine gut mucosa. Given the low occurrence of clinical HIT after cardiac surgery with heparin (1%-2%), it is not surprising that some studies indicate that positive anti-HIT antibodies preoperatively predict an increased risk of postoperative thrombosis, whereas others show no such relationship.

Functional assays measure platelet activation and detect heparin-dependent IgG antibodies capable of binding to and activating the Fc receptors on platelets. Serotonin Release Assay, which measures serotonin release from activated platelets, has high specificity but is not widely available. Thus, immunoassays are the mainstay of current laboratory diagnosis.

HIT syndrome is most likely to occur 5 to 14 days after exposure to heparin during cardiac surgery and is more likely to occur with repeated or prolonged exposure, including heparin flushes in pressure transducers and prophylactic subcutaneous heparin for preventing deep vein thrombosis. Rarely, HIT presents days to several weeks after hospital discharge. The relationship of falling platelet counts to HIT after cardiac surgery is confounded by the usual decline in platelet count that occurs with hemodilution and platelet aggregation related to CPB. The decreasing platelet count usually reaches its nadir by about the second postoperative day. HIT is uncommon in the first 4 days after cardiac surgery, but is much more likely in the setting of new-onset decreasing platelet count after about postoperative day 4. In this setting, prompt laboratory testing for HIT antibodies is advisable.

Treatment of HIT initially involves prompt discontinuation of unfractionated or low-molecular-weight heparin. In patients who can tolerate systemic anticoagulation, continuous infusion of a direct thrombin inhibitor (argatroban, bivalirudin, or lepirudin) is advisable with appropriate anticoagulation monitoring. Limbs should be routinely screened for clinically silent deep vein thrombosis. Platelet transfusions should be avoided. This therapy should be continued until the platelet count has substantially recovered and there is resolution of any arterial or venous thrombosis events. Anticoagulation should then be gradually transitioned to oral warfarin therapy, with an overlap of at least 5 days and achieving target INR before discontinuing the direct thrombin inhibitor infusion.

In patients who are diagnosed with HIT before planned cardiac surgery, elective operations should be delayed until HIT antibody titers are no longer detectable. In most cases, HIT antibodies disappear within 3 to 4 months. If urgent operation is needed, standard heparinization is recommended during CPB, but a direct thrombin inhibitor is likely preferable for “off-pump” procedures. Although its benefit is unproven, plasmapheresis may be a valuable adjunct for patients with positive HIT antibody titers (OD > 1.0) who cannot safely defer operation. Whether a strategy of repeated plasmapheresis treatments until ELISA OD is less than 1.0 is more protective than a single pre- or intraoperative treatment is unknown. When the ELISA OD is weakly (0.4-0.99) positive, no special pre- or intraoperative therapy is probably necessary. The HIT ELISA should be followed serially after surgery, beginning at 24 to 48 hours. If the OD exceeds 1.0 or platelet count falls with a positive ELISA, early plasmapheresis should be considered until it is deemed safe to begin anticoagulation with a direct thrombin inhibitor.

IMMUNE SUBSYSTEM

Some have suggested that the immune subsystem is mildly depressed for several weeks after CPB. In general, however, specific immunologic responses (in contrast to general responses such as those expressed in the whole body inflammatory response) in nonsensitized patients are weak ones. Interleukin levels are increased after CPB, and some believe this to be responsible for the hyperthermia frequently present early after operation (see “Body Temperature” under Special Considerations after Cardiac Surgery in Section II of this chapter). In adult patients, the number of helper/inducer T-lymphocyte subsets (CD4+) is decreased after CPB, and suppressor/cytotoxic T cells (CD8+) are elevated. This possible overall depression of the immune response can be modulated by pretreatment with indomethacin and thymopentin. Ultrafiltration, glucocorticoids, or lymphocyte...
depletion may even further complicate the immune response by their salutary effects on the whole body inflammatory response.

Section II Special Considerations after Cardiac Surgery

FLUID, ELECTROLYTE, AND CALORIC INTAKE

**Children and Adults**

Because of the increase in extracellular fluid and total exchangeable sodium and the decrease in exchangeable potassium that develop during cardiopulmonary bypass (CPB), postoperative fluid administration early after cardiac operations should be precise. Based on pioneering work by Sturtz and colleagues, a standardized approach to fluid administration has been developed that meets the requirements. For approximately 48 hours after operation in children and adults, no sodium is administered, and minimal amounts of water (as 5% glucose in water) are given intravenously (see Appendix 5K). Larger amounts of water are disadvantageous because they result in higher urine volumes and an increased potassium loss if renal function is good, and fluid overload if renal function is impaired. A modest amount of potassium (10 mEq · m⁻² · 24 h⁻¹) is given on the day of operation, because large amounts generally are not needed in normally convalescing patients, despite the decrease in total exchangeable potassium; larger amounts simply escape in the urine. Exceptions to this are patients receiving digitalis preparations, in whom serum potassium is kept at 4.0 mEq · L⁻¹ or more. In the presence of ventricular ectopic beats, the level is increased to 4.5 to 5.0 mEq · L⁻¹.

Liquids are taken orally a few hours after extubation, and intravenous administration can then cease by the second postoperative day. Ability of the kidneys to excrete sodium may be impaired for some days after operation even in normally convalescing patients, so a diet low in sodium is needed until the patient’s weight (measured daily) falls below preoperative level.

When extubation is delayed beyond the second postoperative day, adequate caloric intake must be ensured. Once bowel sounds are present, caloric needs can be met through nasogastric tube feedings using an appropriate high-calorie formula. Rarely, intravenous hyperalimentation is required.

**Neonates and Infants**

In neonates and infants, more exacting management is required. Care is taken to avoid fluid overload from the solution used to keep the pressure-recording catheters patent. Because the infant’s energy requirements are relatively large, 10% glucose is more appropriate than 5%. Small amounts of sodium are administered from the beginning because of the requirements of infants; a special protocol that includes 250 mL · m⁻² · 24 h⁻¹ of a balanced salt solution is used (see Appendix 5K).

In infants, oral feeding is not begun until 8 hours after extubation. Small feedings of glucose water are then given every 4 hours; if well tolerated, an appropriate formula low in sodium is started after two or three feedings. Mothers who are breastfeeding may resume nursing their infant once he or she is strong enough. The infant must be picked up and held for the feedings and burped thereafter. If the infant is too weak to suck, gavage feedings of the mother’s milk are given through a nasogastric tube.

Placement of a transpyloric feeding tube and initiation of feeding by continuous infusion is started in infants who have been intubated longer than about 2 days. If enteral feeding is necessary for more than a few days, the baby’s caloric and other metabolic needs must be calculated and a determined effort made to meet them. If this does not become possible within 48 to 72 hours, or if abdominal distension or excessive diarrhea persists, intravenous hyperalimentation is begun.

During the first 48 postoperative hours, hypoglycemia may develop, particularly in neonates and infants less than 3 months old. Therefore, blood glucose is routinely measured twice daily in these patients, and as a precaution against hypoglycemia, 10% dextrose in water is used in maintenance fluids (see Appendix 5K). When hypoglycemia (blood glucose level < 80 mg · dL⁻¹) occurs, 50 mg · kg⁻¹ of glucose is given (1 mL · kg⁻¹ of 50% dextrose mixed with an equal amount of 5% glucose in water and administered intravenously over a 15-minute period). Blood glucose levels are measured 30 minutes later and at 4-hour intervals for 24 hours.

**Special Problems**

As indicated earlier, some metabolic acidosis (base deficit of 2 mEq · L⁻¹ or greater) may be present during the early hours after cardiac surgery even when the patient is convalescing normally. It is left untreated if arterial pH is 7.4 or greater and PaCO₂ is 30 mmHg or above. When PaCO₂ is less than 30 mmHg, the base deficit is treated before adjusting PaCO₂ appropriately upward. When pH is less than 7.4, the base deficit is treated (see Appendix 5L). However, if convalescence is otherwise normal, treatment is delayed for 4 to 8 hours in adults and for 2 to 4 hours in infants, by which time the base deficit may have cleared spontaneously. In infants particularly, it is best to avoid an additional sodium load whenever possible.

A mild metabolic alkalosis may be present 24 hours after operation in normally convalescing patients, probably related in part to the citrate load contained in the anticoagulant solution of banked blood. Metabolic alkalosis is self-correcting under these circumstances and is not treated. When large amounts of homologous blood containing sodium citrate have been transfused, important metabolic alkalosis can occur. Metabolism of the citrate leaves bicarbonate as the only anion available to balance sodium ions. This situation may be exacerbated after 2 to 4 days by migration of hydrogen ions from the cells, because hydrogen ions are replaced by potassium ions, and serum potassium falls, sometimes precipitously, in association with potassium loss in urine. Relatively large amounts of potassium chloride must be given under such circumstances (up to 200 mEq in 24 hours), but the dose should be titrated against 4-hourly serum potassium measurements. The alkalosis is associated with a fall in serum chloride and a compensatory rise in PaCO₂. Provided renal function is adequate, the situation will correct itself. If it
continues to worsen, the carbonic anhydrase inhibitor acetazolamide is administered, usually intravenously at a dose of 5 mg · kg⁻¹ up to 250 mg in adults once or twice a day as needed until the alkalosis is corrected.

**BODY TEMPERATURE**

The most frequently misunderstood phenomenon after cardiac surgery is abnormality in body temperature. Most normally convalescing patients are febrile for at least 4 to 5 days after operation, and in some the hyperthermia persists 2 weeks or longer️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️️езды Mountains.ма,
Clinical signs and symptoms may be subtle, but one or more of the following are usually present: progressive and unexplained weakness and lethargy; progressive dyspnea on exertion or orthopnea; unexplained hepaticomegaly, ascites, or peripheral edema; elevated jugular venous pressure; pulsus paradoxus; widening of the cardiac silhouette on chest radiography; and unexplained prerenal azotemia.\[K17\] A chest radiograph (which should be taken routinely the day before hospital discharge or the seventh postoperative day, whichever comes first) usually shows enlargement of the cardiac silhouette before symptoms appear. Cardiac tamponade may, however, not become apparent until as late as 4 months after operation.\[O4\]

Treatment consists of pericardial decompression by either pericardiotomies or surgical drainage. If performed surgically, the subxyphoid portion of the incision is reopened, and the pericardial space is entered at the diaphragm. When a week or more has elapsed from surgery, great care is required to gently dissect along the diaphragmatic surface until the fluid collection is entered. Undue haste can result in inadvertent entry into the right ventricle, which can be friable and soft. Mortality has occurred under such circumstances. After drainage of the fluid with a surgical sucker, a flexible drain is generally left in the pericardial space for 24 hours to drain any residual fluid.

## INFECTION

### Prevalence

Fortunately, important wound complications are uncommon after cardiac surgery. These complications are usually caused in the form of mediastinitis and sternal dehiscence. In a prospective study by Breyer and colleagues, prevalence was 0.8%,\[B26\] but it has been reported to be 1.5% by Culliford and colleagues and as high as 8% when bilateral internal thoracic artery–to–coronary artery bypass grafting is performed.\[C35\] Reported mortality after this complication varies widely, from 6% to 70%.\[C11\] With early effective treatment, it is 5% to 10%.\[J9\]

Although edema and some hematomas are common in a leg from which a saphenous vein has been removed, infection occurs infrequently (1%-2% of cases).\[W26\]

### Risk Factors

Imperfect aseptic technique in the OR is the cause of infected median sternotomy wounds. An undrained retrosternal hematoma is an incremental risk factor.\[C55\] This is one reason for leaving the pericardium open as a routine after cardiac operations; retrosternal bleeding falls into the pericardial space and is aspirated by the pericardial drainage tubes. Prolonged operative time is also a risk factor for development of mediastinal infections.\[F10\,W26\] Inaccurate and insecure sternal closure increases the occurrence of important sternal infections.\[H34\] Reoperation for bleeding is not a risk factor.

Obesity is clearly a risk factor for infection in the median sternotomy wound.\[W26\] The combination of diabetes, obesity, and harvesting of both internal thoracic arteries has been associated with increased prevalence of wound infections.\[K32\] Intraoperative hyperglycemia has been correlated with more postoperative infections in adults\[H17\] and children\[O2\] after cardiac surgery. Among pediatric patients, hyperglycemia (>130 mg · dL\(^{-1}\)) during the first 24 hours after operation has been identified as a risk factor for mediastinitis.\[G8\]

Chronic obstructive lung disease predisposes patients to sternal dehiscence and infection. Male gender is a risk factor, probably related to the common practice of shaving the patient the day before operation when hair is present.

Prolonged mechanical ventilation after operation also increases risk of infection in the median sternotomy,\[N25\] as does need for postoperative dialysis.\[C6\] Corticosteroids greatly increase the risk of sternal wound infection. These drugs must therefore be discontinued completely or reduced to the lowest possible dose for several weeks (ideally, 6 or more) before operation. Despite the clear association between steroids and depressed wound healing, cardiac transplantation (with nearly routine use of pre- and postoperative steroids) has been performed with a low occurrence of mediastinal infection in many centers (see Chapter 21).

### Prevention

A precise aseptic technique by the surgical, anesthetic, and perfusionist team is an essential part of prophylaxis against infection in open cardiac operations. The many people involved and the length and complexity of the operations make bacterial contamination more likely than in shorter and simpler procedures. It has been demonstrated that control of the surgical and ICU environment and awareness of the problem among personnel importantly reduce the prevalence of infection.\[S3\] Preoperative shaving should be done immediately before the operation, if at all.\[T1\]

Infection inside or around the heart, particularly when prostheses have been used, is a major threat to the patient’s life. Therefore, prophylactic antibiotic therapy is recommended for cardiac operations.\[F6\,M35\] Adequate blood levels of antibiotics should be present immediately before and during operation and while any intravascular or endotracheal device is in place.\[R29\] Administration is therefore commenced at induction of anesthesia, an additional dose is given before CPB, and a dose is given immediately after CPB. An appropriate intermittent dosage schedule is continued through the second postoperative day or 24 hours after removal of the last intravascular or endotracheal device.\[B29\] Drug and dosage vary according to prevalence of organisms and their susceptibility.

For many reasons, including to minimize the risk of infection, all intravascular and endotracheal devices should be removed as early postoperatively as possible. Infection is also minimized by simplifying postoperative care, early transfer out of the ICU, early ambulation and oral alimentation, and early hospital discharge.

### Treatment

Occasionally a small, localized, subcutaneous collection of serum or necrotic fat may suggest a wound infection when in fact none is present. These minor complications occur in about 2% of patients.\[B26\] Such collections should be left alone until it becomes clear that a wound infection is present. Even when a small amount of frank pus drains from the wound, mediastinitis should not be assumed to be present unless the sternum has become unstable, a retrosternal collection of fluid is demonstrated by CT, or drainage can be shown to be coming through the sternum from the retrosternal area. Even
sternal dehiscence is not unequivocally diagnostic of infection; occasionally the dehiscence is sterile.

Unusual fever and malaise, sternal tenderness, and persistent severe central chest pain not relieved by usual analgesics suggest the possibility of an important sternotomy infection despite absence of obvious inflammatory changes in the skin. Under these circumstances, the wound is examined twice daily for evidence of sternal instability or drainage coming through the sternum, and repeated blood and wound cultures are taken. Antibiotics are generally not begun until infection is confirmed, but should be initiated with suspected infection in the presence of prosthetic material in or around the heart. As soon as possible, the antibiotic regimen should be tailored to the cultures and microbial sensitivities in order to be specific for the organisms involved.

Diagnosis of an infected wound should be made before there is extensive breakdown of the wound skin edges. CT scans may be helpful and should be obtained when diagnosis is uncertain, but it must be remembered that at least edema and some hemorrhage in the anterior mediastinum are usually present in normally convalescing patients and are visible on CT. However, the diagnosis through CT scanning of retrosternal fluid with air pockets or sternal disruption is usually indicative of mediastinitis.\(^{110}\)

As soon as the diagnosis of an infected median sternotomy incision is made, the patient is returned to the OR and anesthetized, and a formal operation is undertaken.\(^{110}\) The entire median sternotomy incision is reopened, and all the sternal wires, other suture material, and necrotic tissue are removed. Usually the infection is most marked immediately in front of and behind the sternum, and minimal around the heart itself. In this situation, although a few small fragments of sternum may be removed, extensive débridement of the sternum is not performed. The wound is thoroughly irrigated first with warm saline solution and then with dilute povidone-iodine solution. Two small (16F) chest tubes are left anteriorly for the postoperative continuous infusion of dilute povidone-iodine or antibiotic solution, and two larger tubes (20F or 24Fr) are left posteriorly for aspiration of fluid. Generally, the sternum is closed by rewiring, and the tissues anterior to it, including the skin, are closed en bloc by vertical mattress sutures.

The wound is irrigated continuously with 1 to 2 mL · kg\(^{-1}\) · h\(^{-1}\) of dilute (0.5%) povidone-iodine or antibiotic solution through the anterior tubes, and suction is continuously applied to the dependent tubes.\(^{116}\) Full-strength povidone-iodine must be avoided because it injures tissue.\(^{115}\) When an antibiotic solution is used for irrigation, the level of the agent in the solution should be the same as the level in blood during maximal parenteral treatment. An input/output chart must be maintained. If the balance becomes positive, infusion is stopped until the fluid is recovered. Irrigations are not effective after 3 to 4 days, because by then the tubes have become sequestered from the retrosternal space. They are therefore removed at that time.

If the infection is extensive, more rapid recovery occurs when the wound is closed with musculocutaneous flaps\(^{14,110,55,537}\) or, when needed, omental transfer\(^{101,512}\) after débridement. In most cases, the most rapid recovery is accomplished with initial débridement and irrigation, followed by early planned pectoralis flaps and partial or complete sternectomy within several days. Generally, it is prudent to perform this with the plastic surgeon. Rarely, the infection is so extensive the wound is left open 3 to 5 days, with a bulky dressing and drainage tubes, and then the closure accomplished.\(^{76}\) These techniques are useful in infants and children as well as adults. With these protocols, most patients survive this potentially lethal complication and experience good long-term functional results.\(^{327,29}\)

### CHYLOTHORAX

Effused chyle may be present in the thoracic cavity after repair of coarctation of the aorta, after placement of Blalock-Taussig or (less frequently) PTFE interposition shunts, or (rarely) after repair of patent ductus arteriosus.\(^{37,518}\) In such instances, chylothorax probably results from cutting large tributaries of the thoracic duct or, less frequently, from injury to the thoracic duct itself. More complex and difficult to manage are the chylothoraces (and on occasion, pericardial accumulations of chyle with tamponade) that follow operations through a median sternotomy, such as atrial switch procedures for transposition of the great arteries, superior vena cava–right pulmonary artery anastomoses, and the Fontan procedure. Chylothorax probably results from the combination of inevitable transection of small lymph channels (probably in the thymus gland) and elevation of superior vena caval pressure that follows these procedures.

In these patients, the lipid content in chylothorax consists of triglycerides that enter the pleural space as chyle, originating from large lymphatics that have been divided or from generalized lymphatic leakage, presumably from elevated right atrial pressure. Chyle contains a high content of triglycerides in the form of chylomicrons, which produces a milky appearance of the lymphatic fluid. The potential for relative immunodeficiency developing during prolonged chylothoraces relates to the high content of lymphocytes (primarily T lymphocytes) in chyle. In addition, chyle is rich in immunoglobulins and fat-soluble vitamins absorbed from the intestines. Chyle flow increases with dietary intake of fat, particularly long-chain triglycerides, which are absorbed into the lymphatic system from the intestines.

Chylothorax may develop immediately after operation, in which case it may not be recognized initially because the fluid may appear to be serous. In most such cases, chylosus drainage subsides spontaneously, and continuation of effective tube drainage is all that is necessary. However, chylothorax may not develop for a week or more. In that case, needle aspirations repeated every 3 to 4 days usually constitute adequate treatment. Late-appearing chylothoraces after closed operations are particularly likely to subside without operation, and the aspirations can be continued on an outpatient basis.

In early-appearing and persistently large chylothorax, such as may occur after open cardiac operations, the outlook with conservative treatment is less favorable. Malnutrition resistant to therapy rapidly develops. When the chylothorax is a complication of the Fontan operation, its management is part of the overall management of the patient (see Chapter 41). The general strategy includes strong suction (40 cm H\(_2\)O) on the pleural chest tubes while maintaining nutrition with a low-fat diet and supplemental medium chain triglycerides. Octreotide may be a useful adjunct. If the drainage is persistent over about 7 days, surgical pleurodesis, thoracic duct ligation, and/or doxycycline installation into the chest tube is advisable. The tube is then returned to suction. Doxycycline is very irritating to the pleura, so pain control is important.
When chylothorax has developed as a complication of an operation performed through a lateral thoracotomy, surgical intervention is indicated if such drainage persists for more than about 7 days. The hemithorax in which the chyle is accumulating is entered through a posterolateral thoracotomy incision. Chylous leakage is sometimes easily seen and is oversewn. Unfortunately, the source is often not found, and watertight oversewing is not always possible. Under such circumstances, the thoracic duct can be sought behind the esophagus; if identified, it is doubly ligated, and this usually solves the problem. Even if these procedures are apparently successful, and certainly if they cannot be accomplished, the pleural space is scarified, and three properly placed intrapleural tubes are left for at least 96 hours to ensure the lung remains expanded and becomes adherent to the chest wall. Fibrin glue placed on the parietal pleura may enhance adherence. A good result is usually obtained from a combination of these maneuvers.

Rarely, after cardiac operations other than the Fontan operation, chyle accumulates in the pericardial space, with or without chylothorax. This problem was first reported after operations with CPB by Thomas and McGoon and has subsequently been reported by others. It has been reported after the Waterston anastomosis, in which, of course, the pericardium is opened. It has also been reported after a Blalock-Taussig shunt in which the pericardium was not opened. This is a difficult problem, and initial management consists of wide and prompt operative drainage of the pericardium into the pleural spaces by making large pericardial windows and then draining both pleural spaces with chest tubes. Following this, the measures just described are used.

Careful attention to nutrition is important during the period of chylous drainage. Fortunately, chylothoraces have never been reported to become infected.

Although the benefit is unproven, it is generally prudent to restrict oral intake of fats and initiate a low-fat diet with oral supplementation of medium chain triglycerides, which are not taken up by lymphatics. Octreotide is the synthetic polypeptide that mimics natural somatostatin by inhibiting the release of multiple intestinal enzymes. The end result is a decrease in lymph flow by reducing splanchic, hepatic, and portal blood flow, decreasing gastrointestinal motility, and inhibition of intestinal secretion of water and electrolytes. Octreotide is initiated at 1 to 2 µg · kg⁻¹ · h⁻¹, with a maximum dose of 10 µg · kg⁻¹ · h⁻¹ once a persistent chylothorax is identified. Efficacy has been reported in the pediatric cardiac surgical population with this intervention.

In situations in which an infant or child with persistent chylothorax is either too unstable to tolerate a thoracotomy with open pleurodesis or persistent drainage occurs following pleurodesis, chemical pleurodesis is carried out with doxycycline installation through the chest tubes. A standard dose of 20 mg · kg⁻¹ (up to a maximum dose of 1 g) diluted in saline at a concentration of 1 to 8 mg · mL⁻¹ is injected through a chest tube. A standard dose is 20 mL · kg⁻¹, and the chest tubes are clamped for 4 to 6 hours following installation of doxycycline. The patient is turned from side to side to promote even distribution of this irritating agent, and the chest tubes are then reopened and placed to high suction. Installation of doxycycline is irritating to the pleura and is accompanied by considerable pain, so adequate analgesia is of major importance during installation. The dose can be repeated every 1 to 2 days. Reported success exceeds 90% by 4 days.

For refractory cases, some success has been reported with lymphangiography followed by percutaneous coiling of large lymphatics.

### POSTPERFUSION AND POSTCARDIOTOMY SYNDROMES

Postperfusion syndromes are complex and not yet fully understood. Whether they are totally attributable to the body’s response to the damaging effects of CPB (see Chapter 2, Section II) or have multiple etiologies is uncertain.

A cytomegalic postperfusion syndrome has been described that consists of an infection with cytomegalovirus transmitted in homologous blood. The larger the volume of blood used, the greater the chance of infection. It produces moderate pyrexia beginning around the end of the first week, associated with a “flulike illness”; the patient complains of weakness, malaise, muscle pains, and sweating. Differential white blood cell count shows lymphocytosis and atypical mononuclear cells. The disease can be confirmed by demonstrating a rise in complement-fixing special antibody, and the virus can be isolated from the urine, although this is technically difficult. The Paul-Bunnell test is negative, excluding infectious mononucleosis (which can present an identical clinical picture) as a possible diagnosis. Although fever and symptoms usually persist for about 2 weeks, the disease is self-limiting, and no treatment is required. Depression is a common sequela.

Postcommissurotomy syndrome was described by Soloff and colleagues in 1953 when it was noted to follow closed mitral valve surgery. Although they interpreted the syndrome as reactivation of rheumatic fever, it subsequently became clear it was not related to rheumatic fever and could occur after any operation that involved opening the pericardium—hence the name postpericardiotomy syndrome, also called postcardiotomy syndrome. When Ito and colleagues coined the term postpericardiotomy syndrome, they suggested the syndrome was due to an immunologic reaction to damaged autologous tissue in the pericardial cavity. Subsequent work at the same institution confirmed an autoimmune theory of etiology. Apparently, heart-reactive antibodies appear in significant titers in most patients undergoing cardiac surgery, but the titer is much higher in patients who develop this syndrome.

Whether there are single or multiple etiologies, it is a fact that in many patients, symptoms appear a few weeks to a few months after cardiac operations. Nishimura and colleagues found the median postoperative time of onset to be 4 weeks. The most striking symptom is chest pain, both a central ache from pericarditis and severe pain from pleuritis. There may be no associated fever, but pericardial and pleural friction rubs are usually present, and often pericardial and pleural effusions. These are usually minor but may be major, and delayed pericardial tamponade can occur. There are no specific changes in the formed blood elements. Although the disease is self-limiting, its duration is highly variable, with a median of 22 days and a range of 2 to 100 days in the study by Nishimura and colleagues. Recurrences are common, appearing in 21% of patients in the Mayo Clinic series. In some of these patients, recurrence was as long as 30 months.
after a previous episode. The syndrome usually recurs should reoperation be required.

Pain and effusions are often relieved by bed rest and aspirin or nonsteroidal antiinflammatory drugs. Although these symptoms are quickly resolved by prednisone, steroids should be avoided whenever possible because of their side effects. However, when symptoms persist, and once the diagnosis is secure and infection has been excluded, prednisone may be given initially in high doses (40 mg · day⁻¹), gradually reduced, and completely discontinued within 4 to 8 weeks. Subsequent courses may be necessary.

An Italian multi-institutional randomized, double-blind placebo-controlled trial of colchicine for preventing postpericardiotomy syndrome (COPPS trial) enrolled 360 patients with a primary endpoint of reducing occurrence of the syndrome within 12 months of surgery. In the treatment arm, 1 mg of colchicine was given twice on the day of operation and followed by 1.5 mg twice daily for 30 days. The syndrome occurred less frequently (8.9% vs. 21%, P = .002) among treated patients. Most events occurred within 30 days.

Section III General Care of Children and Adults

General management of older children and adults after cardiac surgery, in the absence of specific complications, is relatively simple. This section describes general aspects of care, leaving many of the details and documentation to preceding discussions of subsystems.

Patients leave the OR with an arterial catheter in place and, optimally, pressure-monitoring catheters to reflect central venous pressure and, if desirable, left atrial or capillary wedge pressure. When elevated pulmonary artery pressures are anticipated, direct measurement of pulmonary artery pressure is also advisable. One or more routes of access to large central veins are in place. Risks associated with these devices are extremely low, but care is necessary in placing them, caring for them, and removing them. Proper placement of devices (see “Completing Operation” and “Left Atrial Pressure Monitoring” in Section III of Chapter 2) is key to preventing bleeding intraoperatively or at the time of their removal. Infection is a potential risk, but only 1.5% of such catheters have positive cultures when removed postoperatively. Use of antibiotic or antiseptic gels around the site of emergence of these catheters is nonetheless a prudent precaution. Sterile technique in their management is essential.

Patients often come to the ICU intubated, still anesthetized, and with a nasogastric tube in place. They are attached to a ventilator (usually a volume-controlled one), as described in “Management and Treatment” under Pulmonary Subsystem in Section I. Fluids to be administered until 7 AM of postoperative day 1 (the day after operation) are calculated (“calculated fluids”), and these are begun as described in “Fluid, Electrolyte, and Caloric Intake” in Section II. The urinary catheter placed in the OR (usually a typical Foley catheter, although at times a suprapubic catheter) is connected to a drainage system that permits hourly urine flow to be measured conveniently. Chest tubes are attached to a container in which there is a negative pressure of about 30 to 40 cm H₂O. Arrangements are made for measuring chest drainage at 30- to 60-minute intervals.

Many adult patients who are convalescing normally have systemic hypertension, at least in the early period after operation. Even when cardiac performance is good, prudence dictates controlling this hypertensive tendency. This is usually managed with sedation or a continuous infusion of nitroglycerin or nitroprusside (see Appendix 5A). If the hypertensive state continues, an oral hypertensive agent is usually started at the time of transfer out of the ICU. The dosage should be decreased, at least temporarily, at the time of hospital discharge; symptomatic arterial hypotension may otherwise develop. Finally, patients with impaired ventricular function and reasonable renal function may benefit from addition of afterload-reducing agents such as ACE inhibitors, Ca²⁺ channel blocking agents, or both. Ultimately, this can positively affect ventricular remodeling and benefit cardiac performance.

Chest tube drainage may be reinfused into the patient by an automated system. The system may be “instructed” as to the level of left (or right) atrial pressure above which automatic reinfusion of shed blood is not to be performed. When this limit is not violated, the system automatically reinfuses chest tube drainage at a prescribed rate. At the direction of the surgeon or intensivist, automatic chest tube drainage reinfusion is stopped 6 to 12 hours after the patient comes to the ICU. At times, infusion of shed blood appears to perpetuate a bleeding tendency; in this circumstance, reinfusion is promptly discontinued.

When chest tube drainage is sufficiently small that reoperation will clearly not be indicated, and when all subsystems give evidence of functioning well, consideration is given to extubating the patient. When patients are convalescing normally with appropriate cardiac and pulmonary reserves, the vast majority can be extubated either on the day of operation or the following morning. In concert with the anesthesiologist, many CPB operations in adults and children can be conducted using short-acting drugs that allow extubation within 1 to 4 hours following transfer to the ICU. It is thought this shortens ICU stay and decreases overall costs.

The nasogastric tube is removed just before extubation, and as before extubation, the head of the bed is elevated to about 30 degrees. Deep breathing exercises and spontaneous coughing are encouraged, and chest vibropercussion is carried out on a regular basis. Sips of water are allowed as well as other clear liquids, but no effort is made to attain a prescribed fluid intake by mouth, the intravenous route being relied upon for another 24 hours. In children, the urinary catheter may be removed, but in many of them and in adults it can remain in place another day.

Chest tubes are usually removed early on the morning of the first postoperative day, because appreciable chest drainage has usually ceased by then. When chest tubes are in the pleural space, the lower posterior tubes are removed first, and those in the upper and anterior parts of the thorax a few minutes to a few hours thereafter. This sequence allows for evacuation of air that may have been introduced with removal of the posterior tubes. Often it is most appropriate to remove the chest tubes before extubating the patient, but this is not necessary. Intracardiac monitoring devices generally may be removed on the morning after operation in older children and adults. It is advantageous but not necessary that they be removed before removing chest tubes. In neonates and young
infants, monitoring devices should be removed before the chest tubes, and this is usually not on the first day postoperatively. Some surgeons recommend leaving a soft, malleable drainage catheter in the mediastinum of children and adults for several days (attached to a negative pressure bulb) to drain any residual pericardial fluid while the patient is ambulatory.

After extubating the patient and removing intracardiac catheters and chest tubes, a final portable chest radiograph is obtained. If this is satisfactory, the arterial catheter is removed and the patient transferred to either the pediatric or adult cardiac surgical unit for continuation of convalescence. Because mild vasomotor instability is common after cardiac operations, adult patients frequently experience light-headedness on initial standing the day after surgery. Some surgeons recommend routine assessment of orthostatic blood pressure changes (lying, sitting, standing) prior to transfer out of the patient so that any orthostasis can be corrected before the patient begins ambulating in the hospital room. If the urinary catheter is still in place on the morning of postoperative day 2, it is removed; when a suprapubic catheter is used, the patient’s ability to void can be tested before removing the catheter. When normal convalescence to this point is confirmed, all intravenous catheters are removed. Patients are urged to ambulate and begin self-care to the extent possible.

When progress continues to be satisfactory, the patient is generally discharged from the hospital on the fourth or fifth postoperative day. Some institutions discharge on the third postoperative day, finding this management protocol highly satisfactory for some adult patients. Early hospital discharge implies daily follow-up in an outpatient facility or by a responsible physician for at least 2 to 3 more days. A final chest radiograph and ECG are obtained in the outpatient facility. Appropriateness of all medications and postoperative advice is ascertained at that time, and the patient is carefully instructed as to these matters. All information is conveyed to the patient’s general physician, cardiologist, or pediatric cardiologist, who then assumes responsibility for the patient.

At discharge, children may still be somewhat withdrawn and ill at ease, even with parents. Every effort is made to help parents understand the normality of this situation, and they are advised of ways the child’s return to an entirely normal relation with them can be expedited.

A program of daily exercise should be started as soon as the patient leaves the hospital and should emphasize regular walking for progressively longer periods. Patients who were active and gainfully employed before operation are urged to return to full activity (and employment in the case of adults) as soon as possible and, except under unusual circumstances, no later than 2 to 3 months after the procedure.

Section IV General Care of Neonates and Infants

Neonates, infants, and some small young children present postoperative care problems that differ in some ways from those of adults. Principles of subsystem and overall care remain the same, but the internal milieu of even normal neonates and infants is different in certain respects from adults. The cardiac operation has generally been more urgently indicated, and therefore these young patients often have more preoperative derangements and require more extensive operations. Cardiac reserve of neonates and infants is often less than that of adults after cardiac surgery because of the nature and seriousness of their preoperative cardiac condition. Their small airways are more apt to be suddenly obstructed by secretions, and they are subject to special problems such as episodes of pulmonary arterial hypertensive crises. Serum potassium level rises much more rapidly during oliguria in small patients than it does in older children and adults. These considerations do not necessarily indicate that young age per se is a risk factor for death after cardiac surgery; they do indicate that special attention must be given to them. As in Section III, we provide the general aspects of postoperative care of neonates and infants here, with details presented in the discussions of the various subsystems.

If the endotracheal tube has not been inserted through the nose initially, a nasotracheal tube may be substituted for the orotracheal tube before the patient leaves the OR. A urinary catheter, intracardiac recording devices, epicardial myocardial wires, and intravenous access to large central veins are in place when the patient leaves the OR, just as in adults. In the ICU, the patient is placed on a ventilator specifically designed for small patients. Often, 2.5 to 5 µg · kg⁻¹ · min⁻¹ of dopamine is infused, even in patients convalescing normally, and this is generally continued until the morning of postoperative day 1.

Because measuring devices and infusion of medications require some fluid, and because it is desirable to limit the total fluid intake in neonates and infants just as it is in adults, all continuously infused medications are mixed in sufficient concentration that the infusion rate does not exceed 2 to 3 mL · h⁻¹, the minimal rate at which reasonably accurate infusions can be given. No “calculated fluids” are planned for the day of operation, and this can be reconsidered early on the morning of postoperative day 1. Calculations are made as to the amount of fluid administered not only by the intravenous route but also in flushing pressure-measuring devices, and at 7 AM of postoperative day 1, consideration is given to beginning administration of “calculated fluids” or continuing without them (see Appendix 5K).

Once the patient is settled on the ventilator, the status of anesthetic and sedating medication is assessed. The goal in general is to keep the patient paralyzed and sedated at least until the morning of postoperative day 1. For paralysis, appropriate doses of pancuronium (or a comparable agent) are administered intravenously. This is insufficient to overcome many possibly deleterious reflexes. Therefore, fentanyl is also given as a continuous infusion of about 10 µg · kg⁻¹ · h⁻¹, and at times at the increased dose of 15 to 25 µg · kg⁻¹ · h⁻¹, not only for sedation but also for control of sympathetic activity. Particularly when the nasotracheal tube is suctioned, the patient must be under the influence of fentanyl. Ventilation is arranged to keep arterial PaCO₂ at about 30 mmHg, arterial PaO₂ above 120 mmHg, and if possible, pH at 7.45 or higher. This minimizes the tendency for pulmonary vascular resistance to rise paroxysmally (see
“Pulmonary Hypertensive Crises” under Pulmonary Subsystem in Section I).

We recommend irrigating the endotracheal tube with saline and suctioning every 2 hours, although some who do not use fentanyl favor no suctioning of the endotracheal tube. Whatever the policy, it must be recognized that this is a potentially hazardous procedure, and it should be undertaken only by skilled nurses with adequate backup should an emergency develop during or within a few minutes after suctioning.

Early on the morning of postoperative day 1, consideration is given to extubating the patient. If all subsystems appear to be functioning satisfactorily, the protocol leading to extubation is begun. A dose of dexamethasone (0.3 mg · kg⁻¹) is administered about 1 hour before extubation, for its presumed effect in minimizing laryngeal edema, and then 0.1 mg · kg⁻¹ is given 2 hours later and another dose 2 hours thereafter. Then, if the patient is awake and active, extubation is accomplished. After extubation, the baby is maintained in a humidified oxygen-enriched environment for at least another 24 hours in the ICU, although care is taken to avoid excessively high PaO₂.

If all subsystems are not functioning well on the morning after operation, there should be no hesitancy to continue control of ventilation as well as paralysis and sedation for another 24 hours. However, about 70% of normally convalescing neonates and small infants can be extubated the morning after operation and the remainder usually on the morning of postoperative day 2.

Following extubation and the passage of a few hours, oral feedings can be started. For the feedings, the patient is held at least in a semi-upright position, observing the usual precautions necessary in feeding small babies (see Appendix 5N). Neonates and young infants have little nutritional reserve. When oral intake is not possible on postoperative day 1 or 2, nasogastric tube feeding is begun. If this is not promptly effective, intravenous hyperalimentation is begun (see “Fluid, Electrolyte, and Caloric Intake” in Section II).

To avoid bleeding after their removal, intracardiac catheters should not be removed before postoperative day 2. It is prudent but not mandatory to leave all chest tubes in place until after intracardiac devices have been removed.

When convalescence is not normal for any reason, management is altered appropriately, generally as described in the earlier parts of this chapter.

A special situation is presented early postoperatively by neonates and young infants when the operation leaves pulmonary blood flow coming solely from a surgically created systemic–pulmonary artery shunt (see Special Features of Postoperative Care in Chapter 49). In these intubated patients, magnitude of pulmonary blood flow is largely determined by the relation of systemic to pulmonary vascular resistance. When pulmonary resistance is low, pulmonary blood flow tends to be excessive and systemic blood flow small. Should pulmonary vascular resistance gradually or suddenly rise, pulmonary blood flow declines, sometimes rapidly, and hypoxia develops. In this setting, pulmonary vascular resistance is largely determined by arterial PaCO₂ and arterial pH. Manipulation of PaCO₂ is the best method for regulating pulmonary vascular resistance. When pulmonary blood flow appears to be too high and systemic blood flow too low, arterial PaCO₂ is deliberately elevated modestly (to 40 to 45 mmHg) to increase pulmonary vascular resistance, decrease pulmonary blood flow, and increase systemic blood flow. When pulmonary blood flow seems too low and hypoxia too prominent, pulmonary arteriolar resistance is lowered by lowering the arterial PaCO₂ appropriately, usually to 25 to 35 mmHg.

Alterations in arterial PaCO₂ are conveniently accomplished by altering tidal volume and respiratory rate. The adjustments required are usually sufficiently small that they produce no change in other important variables. Alternatively, ventilatory variables are set so that arterial PaCO₂ is 25 to 30 mmHg; if subsequent pulmonary blood flow seems excessive or systemic blood flow too low, or both, PaCO₂ is increased by simply increasing the fractional concentration of carbon dioxide in the inspired air.

Because most treatment decisions in the ICU are based on use of numeric data and an orderly set of rules and logic, automation can be used for making, displaying, and storing observations and for intervening in some situations via a closed-loop computer system. These concepts were described in 1968, but bedside hardware and computers have been continuously modified since. Computers can be cost-effective, prevent rules-based errors (see “Human Error” in Chapter 6), serve as “cognitive prostheses” to simplify presentation of complex multidimensional data, and provide strategic decision support to the surgical faculty, house staff, and nurses. Although there are studies and opinions to the contrary, these reflect a difference in orientation and goals and thus a different method of using automated care. The ICU computer may do the following:

1. Using the patient’s age, height, weight, and hemoglobin level, the computer calculates and prints out surgeon-specific preoperative orders, directions for assembly and priming the pump-oxygenator, and postoperative orders.
2. At designated intervals (e.g., every 2 minutes), the computer can automatically measure, numerically display, and record systemic and pulmonary artery systolic, diastolic, and mean blood pressures; right and left atrial pressures; heart rate; chest tube drainage; urine flow; and temperature. Plots of these data can be displayed on command.
3. The computer, continually sensing drainage from the chest, automatically reinfuses all the shed blood and uses the desired atrial pressure limit to interrupt infusions when the limit is exceeded.
4. Using computer logic and the rules described under “Bleeding” in Section II, messages can be displayed suggesting reoperation.
5. Arterial blood gas and hemoglobin levels are stored and displayed. The base excess or deficit is calculated. When metabolic acidosis is present, the recommended dose of bicarbonate is calculated using the rules and logic in Appendix 5L.
6. The appropriate concentration and drip rate of infusion of any inotropic agent can be calculated and displayed using the rules and logic in Appendix 5B.

7. The computer regulates infusion of nitroprusside by a closed-loop system, having been programmed with the desired mean arterial blood pressure and other relevant information, using the rules and logic in Appendix 5A.\(^{516,517}\) Studies indicate that this method of continuously maintaining a desired blood pressure is more effective than manual methods in avoiding sudden under- or overdosage.

8. The type and amount of fluid to be given intravenously after surgery is calculated according to the rules and logic in Appendix 5H and can be printed out.

9. The computer can generate surgeon-specific antibiotic orders, including dosages, accounting for the presence of drug allergies.

10. On request, the computer displays all recent data in a tabular or plotted form for review, with the time interval between measurements (e.g., 5 minutes, 15 minutes, 30 minutes, 1 hour) being selected by the reviewer.

### Section VI  Body Surface Area

Because cardiac output has traditionally been normalized according to body surface area ([BSA] as cardiac index), other variables related to cardiac surgical patients are optimally normalized in the same way. The computation of BSA by the classic Boyd formula (a more general statement of the original DuBois formula) requires knowledge of height and weight, and height is not always available in clinical studies. A nomogram (Fig. 5-15, A) can be used to estimate BSA from weight, but in some situations, not even weight is available. In these circumstances, a nomogram (Fig. 5-15, B) can be used to estimate BSA based on age alone.
**5A Protocol for Reducing Arterial Blood Pressure and Afterload**

*Sodium nitroprusside* is administered intravenously (IV) continuously or intermittently as required. It acts directly on arterial (and to a lesser extent, venous) smooth muscle and thus decreases systemic and pulmonary vascular resistance and systemic venous tone. Its onset and end of action are immediate. The dose is 1 to 10 µg · kg⁻¹ · min⁻¹ (doses larger than this are not used), regulated in most cases to maintain a mean arterial blood pressure 10% above the normal value for the patient’s age. In patients with thick left ventricular walls or coronary artery disease, concern about coronary perfusion pressure makes a mean arterial blood pressure 20% above normal desirable (or 150 mmHg in adults). Fifty or 100 µg of sodium nitroprusside are dissolved in 150 mL of 5% glucose in water. The drug may be administered with a servo-pump using a closed-loop system or with a slow-infusion pump. When nitroprusside is being administered, methods should be available for measuring blood thiocyanate levels, because values of >10 g · dL⁻¹ are potentially toxic. Toxity is manifested by signs of intracellular suppression of oxygen consumption (elevation of mixed venous oxygen levels, narrowing of arterial/venous oxygen difference, and metabolic acidosis) and by anorexia, muscular spasms, disorientation, and convulsions. Toxicity is due largely to the formation of cyanide, the major metabolic product of sodium nitroprusside. Toxicity is treated by IV infusion over 15 minutes of 150 µg · kg⁻¹ of a 25% solution of sodium thiosulfate (10 µg · kg⁻¹ · min⁻¹).

*Nitroglycerin* decreases venous tone but also decreases coronary resistance. It is therefore particularly useful when myocardial ischemia is present. Infusion rates of 0.5 to 3 µg · kg⁻¹ · min⁻¹ are recommended. Nitroglycerin is absorbed into polyvinyl tubing used for IV infusion, and the concentration reaching the patient is less than planned until the tubing becomes saturated. Nitroglycerin is not as effective as nitroprusside in lowering arterial pressure.

A single-dose longer-acting drug, *diazoxide*, is available although seldom used. The dose is 3 to 5 µg · kg⁻¹. *Phentolamine* (Regitine) is another vasodilator used on occasion. It has an α-adrenergic receptor blocking effect, produces direct smooth muscle relaxation, and reduces pulmonary vascular resistance. Its recommended infusion rates are 1.5 to 2 µg · kg⁻¹ · min⁻¹.

*Phenoxybenzamine* is a noncompetitive blocker of α-receptors with a prolonged (12- to 24-hour) effect and a delayed (30- to 60-minute) onset. It acts on both arterial and venous vessels and has no important side effects. It is administered IV in a dose of 1 mg · kg⁻¹, with the solution diluted in 20 to 50 mL of normal saline solution and infused slowly over about 15 minutes. The disadvantage of phenoxybenzamine is that its α-blocking effect is complete for at least 12 hours; thus, the drug is not used until the need for prolonged afterload reduction has been established by the patient’s response to a sodium nitroprusside infusion over about 12 hours. Rather than continue infusing sodium nitroprusside at a high rate, phenoxybenzamine may be substituted and the dose repeated in 12 to 15 hours when it is clear its effect is wearing off. The *phosphodiesterase inhibitors* milrinone and amrinone may also produce a salutary vasodilatory effect.

**5B Standard Infusion Rates of Inotropic Agents**

<table>
<thead>
<tr>
<th>Inotropic Agent</th>
<th>Standard Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dopamine</td>
<td>10 µg · kg⁻¹ · min⁻¹</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>10 µg · kg⁻¹ · min⁻¹</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>0.05 µg · kg⁻¹ · min⁻¹</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>0.1 µg · kg⁻¹ · min⁻¹</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>0.1 µg · kg⁻¹ · min⁻¹</td>
</tr>
</tbody>
</table>
5C Protocol for Managing Some Aspects of Ventricular Electrical Instability

Early Interventions for Ventricular Electrical Instability

1. Give lidocaine as an intravenous (IV) bolus injection (the dose is 1 mg · kg\(^{-1}\) for adults and children, although in adults the usual dose is 50 mg) if the arrhythmia is premature ventricular contraction (PVC) or ventricular tachycardia (VT) with a good hemodynamic state. If there is VT and reduction of cardiac output, use immediate DC cardioversion (100 and then 200 J).

2. Draw a blood sample for determination of serum K\(^+\); when the result is available, treat hypokalemia (K\(^+\) concentration < 4.0 mEq · L\(^{-1}\)) if present:
   a. Administer 5 mEq K\(^+\) as an IV bolus.
   b. Administer 20 mEq K\(^+\) in 50 mL of 5% glucose over 1 hour; then obtain repeat serum K\(^+\) level measurement and repeat treatment until serum level is satisfactory (at least 3.5 mEq · L\(^{-1}\) and preferably 4.0 mEq · L\(^{-1}\)).
   c. Double the IV maintenance K\(^+\) dose.
   d. Recheck serum K\(^+\) level. If it is <4.0 mEq · L\(^{-1}\), order oral K\(^+\) supplement as 20% KCl, 10 mL twice a day in orange juice (60 mEq approximate daily dose).

3. If the ventricular rate is <80 to 90 beats/min, initiate pacing. If basic rhythm is sinus or atrioventricular (AV) junctional, use atrial pacing. When cardiac rhythm is other than sinus or AV junctional, or atrial pacing fails to result in 1:1 AV conduction, use ventricular pacing (with the ventricular wire electrode attached to negative pole of pacer). In the presence of second- or third-degree AV block, consider AV sequential pacing.

Interventions after Control of the Urgent Situation

If the arrhythmia recurs promptly or is not controlled by these simple measures, begin continuous IV lidocaine infusion in a dose of 20 to 50 µg · kg\(^{-1}\) · min\(^{-1}\), or 0.02 to 0.05 mg · kg\(^{-1}\) · min\(^{-1}\).

5D Protocols for Acute Management of Postoperative Atrial Fibrillation

- In hemodynamically stable adult patients, intravenous verapamil, diltiazem, esmolol, propranolol, or amiodarone are effective alternative therapies:
  - **Ibutilide**: after pretreatment with intravenous magnesium (1g), 1 mg infused over 10 minutes; repeat once if no conversion
  - **Verapamil**: 5-10 mg IV as bolus; may repeat after 10-15 minutes
    Adverse effect: infrequently hypotension, later increase of heart rate
  - **Diltiazem**: 20 mg IV over 2 minutes, may repeat × 1
    Adverse effect: infrequently hypotension
  - **Esmolol**: 0.5 mg · kg\(^{-1}\) · min\(^{-1}\) IV infusion
    Adverse effect: hypotension, bronchospasm
  - **Propranolol**: 0.05 mg · kg\(^{-1}\) or 5-mg bolus IV
    Adverse effect: hypotension

- **Amiodarone**: 150 mg IV over 10 minutes
  Adverse effect: rarely hypotension

- **Unstable hemodynamics**
  Digoxin has classically been recommended, but it may be slow to act (3-8 hours) and relatively ineffective at decreasing heart rate in postoperative patients with increased sympathetic activity. In the elderly or in the presence of compromised renal function, the therapeutic window is narrow and toxicity may occur. An estimated digitalizing dose of digoxin provides a convenient guideline for the cardiac surgeon. The estimated dose of digoxin, when no digitalis has been given in the past 10 days, may be considered to be 0.9 mg · m\(^{-2}\) intravenously and 1.6 mg · m\(^{-2}\) orally. The digitalizing dose in infants may be considered 50 µg · kg\(^{-1}\) intravenously, and the maintenance dose 10 to 15 µg · kg\(^{-1}\) · day\(^{-1}\).
DC cardioversion

Amiodarone

■ Recurrent atrial fibrillation
  Procainamide: 500-1000 mg orally, every 6-8 hours
  Sotalol: initially 80 mg twice daily

■ Anticoagulation
  The prevalence of stroke attributable to postoperative atrial fibrillation is unknown. It seems justifiable to initiate anticoagulation if atrial fibrillation persists longer than 48 hours or is recurrent. In these instances, warfarin is recommended. If elective cardioversion is planned, IV heparin is recommended and is prescribed in therapeutic doses.

---

5E Protocol for Rapid Atrial Pacing via Atrial Wires

Rapid Atrial Pacing

The technique of rapid atrial pacing is applied to atrial flutter, defined as a general atrial rate of 250 to 350 beats · min\(^{-1}\) with a constant beat-to-beat cycle length that can be interrupted by rapid atrial pacing. This is rarely possible in atrial flutter-fibrillation, a more rapid type of atrial flutter with a rate > 350 beats · min\(^{-1}\), and is not possible in atrial fibrillation.

ECG limb leads are placed on the patient for monitoring, and the two atrial wires are connected to the rapid atrial pacer. Because the atrial pacing threshold is usually high during atrial flutter, output is set at 10 to 20 mA. Bipolar atrial pacing is used because the stimulus artifact then rarely distorts the ECG tracing, and the atrial complex in the ECG is clearly seen so that atrial capture can be verified.

A relatively slow pacing rate is used first, because occasionally, immediate one-to-one conduction occurs with rapid ventricular tachycardia, which is to be avoided. After this, there are several possible maneuvers for control of atrial flutter and its rapid ventricular response, as described by Waldo and MacLean.\(^{91}\)

Ramp Technique

Atrial pacing is begun at a rate 10 beats · min\(^{-1}\) faster than the atrial flutter rate. The rate of atrial pacing is then gradually increased. When the typical negative atrial complex in lead II changes to a positive atrial complex, indicating capture by pacing, atrial pacing is either abruptly stopped or gradually slowed until the ventricular rate is considered satisfactory.

Constant Rate Technique

Pacing is initiated at a rate 10 beats · min\(^{-1}\) faster than the spontaneous atrial flutter rate. After pacing at this rate for about 30 seconds, pacing is either abruptly stopped or the pacing rate quickly slowed until the ventricular rate is considered satisfactory. If these maneuvers are unsuccessful in interrupting the atrial flutter, they are repeated, with the initial atrial pacing rate increased in increments of 10 beats · min\(^{-1}\).

Continuous Rapid Atrial Pacing

When atrial flutter is interrupted by the procedures just described but recurs with unacceptable frequency, continuous atrial pacing at 400 to 600 beats · min\(^{-1}\) is used. This results in continuing atrial fibrillation with variable atrioventricular block. The ventricular rate can then be controlled by digoxin.

When premature atrial beats are continuous or recurrent despite pharmacologic treatment, continuous atrial pacing at about 200 to 230 beats · min\(^{-1}\) usually results in their suppression and a 2:1 atrioventricular conduction ratio with an acceptable ventricular rate.
Protocol for an Intubated Patient

1. The ventilator is used with its air heating and humidifying devices and the valves for intermittent mandatory ventilation and positive end-expiratory pressure (PEEP) functioning.

2. The patient has a well-positioned and well-secured orotracheal tube in place or, in infants and young children (for greater security and comfort) and adults in whom postoperative ventilation for more than 24 hours is likely, a well-positioned and well-secured nasotracheal tube in place (see Chapter 4).

3. Initially the fractional concentration of oxygen ($FIO_2$) is set at 0.6, tidal volume ($VT$) at 12 to 20 mL · kg$^{-1}$, and intermittent mandatory ventilation (IMV) at 12 to 14 breaths · min$^{-1}$ in adults, 20 to 25 breaths · min$^{-1}$ in older children, 30 breaths · min$^{-1}$ in young children, and 30 to 40 breaths · min$^{-1}$ in infants. End-inspiratory pressure should normally be $<40$ cm H$2$O. In all situations, visual, palpatory, and auscultatory observation of the patient’s chest must be used to confirm that $VT$ is adequate for good air movement in and out of the lungs. These observations must be made whenever the patient becomes restless or agitated or there is any other reason to suspect inadequate gas exchange. Except in patients with chronic obstructive lung disease and those in whom the Glenn or Fontan operation has been performed, PEEP of 5 to 10 cm H$2$O (4 cm H$2$O in patients < 4 years old) may be used.

4. When the patient is admitted to the ICU, baseline blood gas analysis is obtained and ventilatory parameters are adjusted accordingly. Continuous monitoring of oxygen saturation by use of a digital infrared sensor is advisable in most patients. In adults, additional arterial blood gas analyses are not done routinely thereafter unless there is a change in clinical status. In neonates and children, more frequent arterial blood gas analyses are usually necessary.

5. A supine portable chest radiograph is obtained upon arrival in the ICU and reviewed by a physician for placement of the tip of the endotracheal tube; the presence of pneumothorax, atelectasis, vascular congestion, or gastric distention; and size of the mediastinal silhouette. The chest radiograph is routinely repeated the first postoperative morning.

6. Turning of the patient and sterile suctioning of the airway are performed each hour to clear retained secretions and minimize atelectasis. Suctioning is performed after hand bagging with 100% oxygen, hyperventilation for several breaths, and instillation of 1 to 5 mL of sterile saline solution down the endotracheal tube (see Section IV, “General Care of Neonates and Infants,” for discussion of endotracheal tube suctioning in these patients). Suctioning is followed again by hand bagging with 100% oxygen. The length of the endotracheal tube must be known so that the suctioning catheter can be passed with certainty beyond the tube into the trachea.

7. In patients without severe preoperative pulmonary dysfunction, criteria for extubation include:
   a. Patient awake and alert, indicating recovery from anesthesia and ability to protect his or her airway
   b. Satisfactory hemodynamic state
   c. Absence of important drainage from chest tubes
   d. Arterial $P_O_2$ $\geq$ 70 mmHg or $S_{A_O_2}$ $>90\%$ to $92\%$ (in the absence of intracardiac right-to-left shunting) on IMV of 6 breaths · min$^{-1}$ and $FIO_2$ of 0.40
   e. Spontaneous respiratory rate $<25$ breaths · min$^{-1}$ in adults, $<40$ breaths · min$^{-1}$ in young children, and $<50$ breaths · min$^{-1}$ in infants
   f. Absence of increased work of breathing (use of accessory respiratory muscles)
   g. Normal Pa$CO_2$ and pH (Pa$CO_2$ may be somewhat elevated with a normal pH, if metabolic alkalosis is present)
Protocol for Oliguria

**Indication**

Urine output in the early postoperative period of <0.5 to 1.0 mL · kg\(^{-1}\) · h\(^{-1}\) in infants and children and <0.5 mL · kg\(^{-1}\) · h\(^{-1}\) (30-35 mL · h\(^{-1}\)) in adults.

**Rationale**

To reverse the nearly universal occurrence of fluid retention following cardiopulmonary bypass.

**Treatment**

1. Exclude low cardiac output as the cause of the oliguria.
2. Insert a urinary catheter if not already in place.
3. Administer a diuretic:
   a. *Furosemide*: 1 mg · kg\(^{-1}\) for infants and children and 20 to 40 mg for adults administered intravenously (IV) as a bolus. Usually, no greater diuretic response is elicited with higher doses. However, doses of up to 180 to 240 mg may be necessary in patients with chronic heart failure, cirrhosis, and the nephrotic syndrome.
   i. The expected result is at least a doubling of the urine output over 2 to 3 hours.
   ii. If the diuresis is inadequate, other diuretics may be used in adults.
   b. *Ethacrynic acid*: 50 to 100 mg IV in 50 mL of solute over 30 minutes; ototoxicity occurs in 2% to 3% of patients.
   c. *Bumetanide*: 0.5 to 2 mg IV over 1 to 2 minutes
   d. *Torsemide*: 10 to 20 mg IV as a bolus
e. A continuous infusion of the diuretics just mentioned may be safer and more effective in some patients. This is usually given after a bolus if the diuretic effect is not sustained. Furosemide is given at an initial infusion rate of 5 mg · h\(^{-1}\), increasing to 20 mg · h\(^{-1}\) if necessary. The equivalent dose of bumetanide is 0.5 mg · h\(^{-1}\), increasing to 1 mg · h\(^{-1}\); and for torsemide, 5 mg · h\(^{-1}\), increasing to 10 mg · h\(^{-1}\).

Protocol (Interim Measures) for a Serum K\(^+\) Level > 5.5 mEq · L\(^{-1}\) from Acute Renal Failure

1. Give glucose and insulin solution intravenously (IV). For adults, mix 20 units of regular insulin in 50 mL of 50% dextrose and give IV over 10 minutes. For children and infants, mix 0.5 mL of regular insulin per kilogram of body weight in 2 mL of 25% dextrose per kilogram and give IV over 10 minutes.
2. Administer a sodium polystyrene sulfonate enema. For adults, mix 50 g in 200 mL of sorbitol or 20% dextrose, and give as a retention enema; hold for 30 minutes, then remove; repeat hourly as necessary. For children and infants, give 1 g · kg\(^{-1}\) and 10 to 50 mL of sorbitol as a retention enema (total volume of sorbitol may be increased up to about 150 mL for children up to about 10 years of age).
3. Give 1 mEq · kg\(^{-1}\) sodium bicarbonate IV for infants and children. For adults, give 1 ampule (44 mEq) IV.
4. If potassium levels exceed 6.5 mEq · L\(^{-1}\) and the patient is not receiving digoxin, give 10 mg · kg\(^{-1}\) of IV calcium chloride for infants and small children, and about 200 mg · kg\(^{-1}\) for adults, to decrease the cardiovascular effects of hyperkalemia.
5. If these measures do not result in a potassium level < 5.5 mEq · L\(^{-1}\), nephrology consultation should be obtained.
Protocol for Seizures in Infants and Children

General Comments

Generalized or focal seizures are an infrequent but potentially serious occurrence following cardiac surgery in infants and children. In such cases a number of etiologies are possible (e.g., metabolic; infectious; cerebral edema, embolism, or hemorrhage; decreased cerebral perfusion), but in most patients no specific causative factor is identified. The following protocols outline initial evaluation to identify possible correctable causes and describe an initial treatment regimen. In most cases, a consultation is obtained with a neurologist knowledgeable about cardiac surgical patients. A few generalizations are useful:

1. In infants and small children, whether the seizure is generalized or focal is not helpful diagnostically.
2. Respiratory arrest, discoordinate respiratory activity, or sudden inability to adequately mechanically ventilate can be an indication of seizure activity in infants. Additional evidence of seizures is usually present on detailed evaluation.
3. After initial control of seizures, anticonvulsant therapy should be continued through the recovery period. Decisions regarding long-term therapy are made by the neurologist or pediatric cardiologist before hospital discharge.
4. Most children having a seizure in the early postoperative period will not have a chronic seizure disorder.
5. Choreiform movements are more serious symptoms than are seizures and are more apt to persist.
6. Because of its potential to cause cardiorespiratory depression and its short duration of action, diazepam is best avoided as an anticonvulsant unless the patient is being artificially ventilated.

Initial Evaluation and Treatment

1. At the onset of a seizure, arterial blood gases and pH; serum glucose, calcium, and electrolytes; cardiac index; and body temperature are determined.
2. Interventions are made in an attempt to correct:
   a. pH < 7.25 or > 7.50; PaCO₂ < 25 mmHg; PaO₂ < 80 mmHg; and base deficit > 10 to 15 mEq · L⁻¹. (In some patients, prompt control of seizures will correct low values.)
   b. Serum glucose level < 40 mg · dL⁻¹ in infants and < 60 mg · dL⁻¹ in older children (see “Fluid, Electrolyte, and Caloric Intake” in Section II)
   c. Serum calcium level < 7 mg · dL⁻¹ in infants and < 8 mg · dL⁻¹ in older children
   d. Serum sodium level < 125 mEq · L⁻¹. Usual management in this situation is restriction of salt and water intake.
   e. Cardiac index < 2.0 L · min⁻¹ · m⁻²
   f. Body temperature > 38.6°C (>101.5°F)

Initial Anticonvulsant Therapy

When seizures are first noted, steps are taken to terminate them or, if they are no longer present, prevent their recurrence while the chemical and other variables are being determined.

1. Give:
   a. 0.1 to 0.2 mg · kg⁻¹ of diazepam intravenously (IV) and
   b. 15 mg · kg⁻¹ of phenobarbital IV over 5 to 10 minutes as a loading dose.
2. If seizures are not controlled by these measures, additional doses of diazepam (if the patient is being ventilated) may be used. (The full effect of the loading dose of phenobarbital may not be apparent for several hours, but if problems continue at this stage, consider giving a further 5 mg · kg⁻¹.)
3. If there has been spontaneous termination of seizure activity and prevention of recurrence is desired, omit step la and proceed to step 1b.
4. Continuing major seizures will rarely be a problem. If they are, a loading dose of phenytoin (20 mg · kg⁻¹ orally) is given, followed by maintenance with 3 to 4 mg · kg⁻¹ · day⁻¹ given orally.
5. An alternative, especially when seizures interfere with effective ventilatory support, is paralysis with pancuronium.

Maintenance Anticonvulsive Therapy

Administration of phenobarbital (2.5 mg · kg⁻¹ · 12 h⁻¹) can be instituted 12 to 24 hours after giving the initial loading dose.
Protocol for Autotransfusion

1. Several commercial chest drainage systems that accommodate autotransfusion are available. The two general types are (1) those that transfuse shed blood directly from the drainage system and (2) those that contain a drainage receptacle (a collapsible bag) that is manually transferred as an independent infusion setup.
2. A filter is optional.
3. Often there is a threshold for autoinfusion (i.e., drainage > 100 mL in adults).
4. A time limit for duration of autotransfusion is set for 4 to 6 hours.
5. Reinfusion of shed blood is governed by:
   a. Amount of drainage
   b. Atrial pressure limits

6. With either system, the total volume of chest drainage must be noted. This is a simple arithmetic sum of volume currently occupying the chest drainage reservoir plus the amount of chest drainage autotransfused. This total is noted hourly.
7. Contraindications to autotransfusion include:
   a. Infectious endocarditis or other infection
   b. Exogenous chemicals in the mediastinum
      i. Disinfectants
      ii. Topical antibiotics
      iii. Hemostatic agents
      iv. Biological glue
   c. Hematologic abnormalities (e.g., sickling, diffuse intravascular coagulation, hemolysis)

Protocol for Intravenous Fluids

In adults and children (>2 years of age or >13 kg in weight):

1. Day of operation:
   a. 500 mL of 5% glucose in water · m⁻² · 24 h⁻¹
   b. 10 mEq of K⁺ · m⁻² · 24 h⁻¹
2. First and second postoperative days:
   a. 750 mL of 5% glucose in water · m⁻² · 24 h⁻¹
   b. 20 mEq of K⁺ · m⁻² · 24 h⁻¹
3. Third postoperative day:
   a. 750 mL of 5% glucose in water · m⁻² · 24 h⁻¹ or 1100 mL of 5% glucose in one-quarter-strength saline solution · m⁻² · 24 h⁻¹
   b. 350 mL of 5% glucose in saline solution · m⁻² · 24 h⁻¹
   c. 10 mEq of K⁺ · m⁻² · 24 h⁻¹
4. If oral intake has not been established on the third postoperative day, consider gavage feeding or intravenous (IV) hyperalimentation.

In infants and small children (<2 years old or <13 kg in weight):

1. Day of operation:
   a. Calculate patient’s saline requirement.
      i. 250 mL · m⁻² · 24 h⁻¹ are required.
   ii. If this is 75 mL or less for the individual patient, use only balanced salt solution for flushing the arterial catheter; if it is 75 to 150 mL, use balanced salt solution for flushing the arterial and left atrial catheters; if it is >150 mL, flush the arterial, left atrial, and right atrial (and, if present, pulmonary artery) catheters with balanced salt solution.
      iii. Give no additional sodium-containing fluids if step ii supplies the patient’s needs. Otherwise, subtract the amount in step ii from the requirement and give the difference.
   b. Calculate the patient’s water requirement.
      i. 500 mL · m⁻² · 24 h⁻¹ of 10% glucose in water are required.
      ii. Subtract 72 mL · the number of intracardiac recording catheters being flushed with 10% glucose solution

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4 An automatic, very slow (3 mL · h⁻¹ or 72 mL · 24 h⁻¹), continuous infusion system for all devices attached to pressure transducers is used. The solution flushing the arterial needle must be a heparinized balanced salt solution to prevent arterial spasm and pain. When salt restriction is important, as in infants, a glucose solution can be used for flushing the other pressure lines.
2. Days thereafter:
   a. Calculate patient’s saline requirement.
      i. $250 \text{ mL} \cdot \text{m}^{-2} \cdot 24 \text{ h}^{-1}$ are required.
   b. Calculate patient’s water requirement.
      i. $750 \text{ mL} \cdot \text{m}^{-2} \cdot 24 \text{ h}^{-1}$ of 10% glucose are required.
      ii. Subtract 72 mL · the number of intracardiac catheters being flushed with 10% glucose in

   Note that when medications such as lidocaine, catecholamines, and sodium nitroprusside are administered, the amount of fluid thereby infused must be determined and subtracted from the daily fluid requirement.

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### Protocol for Metabolic Acidosis

**Indication**
Metabolic acidosis exists if the base deficit is $>2 \text{ mEq} \cdot \text{L}^{-1}$ and pH is $<7.35$ or $\text{PaCO}_2$ is $<30 \text{ mmHg}$.

**Rationale**
Treatment is directed only at the extracellular fluid, and a conservative dose of $\text{NaHCO}_3$ is given because more can easily be administered if needed.

\[
\text{Extracellular fluid volume} = 30\% \text{ body weight (kg)}
\]

\[
\text{Base deficit (mEq} \cdot \text{L}^{-1}) \cdot 0.3 \cdot \text{body weight (kg)}
= \text{total extracellular base deficit}
\]

**Treatment**
1. Administer $\text{NaHCO}_3$ so that the amount of $\text{Na}^+$ (mEq) equals half the total extracellular base deficit.
2. Remeasure base deficit in 30 to 60 minutes and repeat treatment if indicated.

Note that in acute reduction of cardiac output or cardiac arrest, much larger doses of $\text{NaHCO}_3$ are indicated (44 mEq for adults, 1 mEq · kg$^{-1}$ for infants and children).

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### Protocol for Hyperthermia

**Indication**
Hyperthermia exists if rectal temperature is $\geq 38.3^\circ\text{C}$ ($\geq 101^\circ\text{F}$).

**Rationale**
Hyperthermia increases metabolic demands and thus myocardial oxygen consumption. Severe hyperthermia (central temperatures $\geq 41.1^\circ\text{C}$ [$\geq 106^\circ\text{F}$]) may permanently and severely damage the brain.

**Treatment**
1. If rectal temperature is $\geq 38.3^\circ\text{C}$ ($\geq 101^\circ\text{F}$), give acetaminophen as a rectal suppository every 4 hours. The dose in infants and children is 10 mg · kg$^{-1}$ (rounded to the nearest 30 mg), and in adults, 650 to 1300 mg.
2. Consider using a cooling blanket or cold syringing and a fan or ice bags applied to the body.
3. If rectal temperature is $\geq 39.4^\circ\text{C}$ ($\geq 103^\circ\text{F}$):
   a. Insert esophageal temperature probe for continuous monitoring of central temperature and intensify efforts...
to improve cardiac output. Check for possible transfusion reaction.

b. If esophageal temperature is ≥39.4°C (≥103°F):
   i. Make preparations for peritoneal dialysis with room temperature or cooled dialysate, to be initiated if simpler measures do not promptly control hyperthermia.
   ii. Give acetaminophen as in step 1.
   iii. Give dexamethasone, 0.25 mg · kg⁻¹ IV, then 0.1 mg · kg⁻¹ IV every 6 hours.

4. Give sodium nitroprusside, 1 µg · kg⁻¹ · min⁻¹, to increase peripheral heat loss if arterial pressure remains acceptable with this drug; if inotropic agents are necessary, give preference to amrinone and isoproterenol.

5. Abolish muscular heat production, particularly when an infant is restless, by paralyzing with pancuronium (0.1 mg · kg⁻¹).

6. Continue efforts to improve cardiac output.

5N

Protocol for Infant Feeding

Infants can rapidly develop a profoundly catabolic state after major surgery. Caloric intake should be raised to adequate levels as soon as possible after operation.

When respiratory assistance via an endotracheal tube continues into the third postoperative day, gavage feeding is begun unless specific contraindications exist. In extubated infants, weakness and underdevelopment may prevent proper feeding and result in aspiration, making intermittent gavage feeding necessary. The steps are as follows:

1. As a precaution, prepare the endotracheal suction catheter for immediate use.
2. Check to be certain that the nasogastric tube is in the stomach; if intermittent gavage is to be used, a feeding catheter is inserted for each feeding and then removed.
   a. Aspirate the tube. If stomach contents are not obtained or if large quantities of air with a little mucus are obtained, the tube is probably in the trachea.
   b. While listening over the stomach with a stethoscope, inject a little air and listen for the typical noise.
   c. Persistent coughing suggests that the tube is in the trachea.
   d. Absence of a normal cry suggests the tube is in the trachea (steps a, b, and d apply to patients without an endotracheal tube).
3. If these checks indicate the tube is in the stomach, and if aspiration does not reveal >10 to 15 mL of fluid in the stomach, initial feedings can be begun. Feedings are injected slowly over 2 to 3 minutes or allowed to enter by gravity, preferably with the infant sitting upright. Otherwise, the infant is placed on his or her right side, with the head inclined to at least a 15-degree angle.
4. Gavage feeding is given every 3 hours on the following schedule:
   a. Give sterile water, 10 to 15 mL × 1.
   b. If well tolerated, give 10% dextrose in water, 30 mL × 1.
   c. If well tolerated and residual is <5 mL, give SMA-20 or equivalent formula, 30 mL × 8; if well tolerated, give SMA-20 in increasing amounts.
5. If needed:
   a. Consider giving SMA-27 (27 calories per ounce) if diarrhea is not present.
   b. Consider continuous drip infusion to avoid a bolus effect (residual fluid in the stomach is aspirated and measured every 2 hours).

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What It Is About

Cardiac surgical procedures, particularly coronary artery bypass grafting (CABG), are the most quantitatively studied therapies in the history of medicine. These studies reveal a complex, multifactorial, and multidimensional interplay among patient characteristics, variability of the heart disease, effect of the disease on the patient, conduct of the procedure, and response of the patient to treatment. Because cardiac surgeons were “data collectors” from the beginning of the subspecialty, it is understandable that efforts to improve the quality of medical care while containing costs found cardiac surgical results (outcomes) an easy target. The dawn of medical report cards made it evident that multiple factors influencing outcome must be taken into account to make fair comparisons of outcomes (see “Risk Stratification” and “Risk Adjustment” in Section VI). This scrutiny of results, often by the media, reveals that variability in performing technical details of operations, coupled with environmental factors often not under direct control of cardiac surgeons, contribute to differences in results.

Propensity toward data collection in cardiac surgery was reinforced in the 1970s and early 1980s by challenges from cardiologists to demonstrate not simply symptomatic improvement from operative procedures, but improved survival and long-term quality of life (appropriateness). This resulted in one of the first large-scale, government-funded registries and an in-depth research database (Box 6-1) of patients with ischemic heart disease, as well as a rather small, narrowly focused randomized trial (Coronary Artery Surgery Study). It stimulated subsequent establishment by the Society of Thoracic Surgeons (STS) of what is now the largest non-governmental registry of cardiac surgical data.

Thus, it is important for all in the subspecialty of cardiac surgery, not just those engaged in bench, translational, or clinical research, to (1) understand how information generated from observations made during patient care is transformed into data suitable for analysis, (2) appreciate at a high level what constitutes appropriate analyses of those data, (3) effectively evaluate inferences drawn from those analyses, and (4) apply new knowledge to better care for individual patients.

It is our desire that the reader realize these goals and not conclude prematurely that this chapter is simply a treatise on biostatistics, outcomes research, epidemiology, biomathematics, or bioinformatics.

Who Should Read It

This chapter should be read in whole or in part by (1) all cardiac surgeons, to improve their comprehension of the medical literature and hone their skills in its critical appraisal; (2) young surgeons interested in becoming clinical investigators, who need instruction on how to pursue successful research (see Technique for Successful Clinical Research later in this section); (3) mature surgeon-investigators and other similar medical professionals and their collaborating statisticians, mathematicians, and computer scientists who will benefit from some of the philosophical ideas included in this section, and particularly from the discussion of emerging analytic methods for generating new knowledge; and (4) data managers of larger clinical research groups who need to fully

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"In its narrowest definition, bioinformatics is a collection of methods devised to process genomic data, representing the reality that advances in genomics require sophisticated and often new computer algorithms. Some would say bioinformatics is the next frontier for statistics, others for machine learning. This is the narrow view. The National Institutes of Health (NIH) in the United States has provided a broader view. The NIH Biomedical Information Science and Technology Initiative Consortium agreed on the following definition of bioinformatics, ‘recognizing that no definition could completely eliminate overlap with other activities or preclude variations in interpretation by different individuals and organizations’: Bioinformatics is research, development, or application of computational tools and approaches for expanding the use of biological, medical, behavioral or health data, including those to acquire, store, organize, archive, analyze, or visualize such data (http://grants1.nih.gov/grants/bioc/CompuBioDef.pdf). They go on to define computational biology in a broader context than genomics as ‘the development and application of data-analytical and theoretical methods, mathematical modeling and computational simulation techniques to the study of biological, behavioral, and social systems.’ Thus, to lead from information to new knowledge, they envision bringing together quantitative needs in structural biology, biochemistry, molecular biology, and genomics at the microscopic level, and medical, health services, health economics, and even social systems disciplines at the macroscopic level, with analytic tools from computer science, mathematics, statistics, physics, and other quantitative disciplines. This vision transcends current restrictiveness of traditional biostatistics in analysis of clinical information. This is why we emphasize in this chapter that the material is not simply for surgeons, their clinical research team, and consulting and collaborating biostatisticians, but also for a wider audience of professionals in a variety of quantitative disciplines."
appreciate their pivotal role in successful research (Appendix 6A), particularly as described in Sections I, II, and III of this chapter.

The potential obstacle for all will be language. For the surgeon, the language of statistics, mathematics, and computer science may pose a daunting obstacle of symbols, numbers, and algorithms. For collaborating statisticians, mathematicians, and computer scientists, the Greek and Latin language of medicine is equally daunting. This chapter attempts to surmount the language barrier by translating ideas, philosophy, and unfamiliar concepts into words while introducing only sufficient statistics, mathematics, and algorithms to be useful for the collaborating scientist.

Because this chapter is intended for a mixed audience, it focuses on the most common points of intersection between cardiac surgery and quantitative science, with the goal of establishing sufficient common ground for effective and efficient collaboration. As such, it is not a substitute for statistical texts or academic courses, nor a substitute for the surgeon-investigator to establish a collaborative relationship with biostatisticians, nor is it intended to equip surgeons with sufficient statistical expertise to conduct highly sophisticated data analyses themselves.

How It Has Evolved
At least three factors have contributed to evolution of Chapter 6 from edition to edition of this book: increasing importance of computers in analyzing clinical data, introduction of new and increasingly appropriate and applicable methods for analyzing those data, and growing importance of nontraditional machine learning methods for mining medical data.

Thus, the title of this chapter in Edition 1 was “Surgical Concepts, Research Methods, and Data Analysis and Use.” Its sections highlighted (1) surgical success and failure, (2) incremental risk factors, (3) research methods, (4) methods of data presentation and analysis and comparison, (5) decision making for individual patients, and (6) improving results of cardiac surgery. All remain important, but progress in each of these areas warrants a fresh approach. In the first edition, formulae were provided for surgeons to implement on a new generation of programmable calculators. These programs provided confidence limits and simple statistical tests that continue to be valuable, particularly in reading and evaluating the literature; however, with the passage of time, increasing sophistication and complexity of programmable calculators have taken implementation of the programs out of the reach of most surgeons. Therefore, we have eliminated those appendices.

In Edition 2, an organizing schema for clinical research was developed, and the name of the chapter was changed to reflect it: “The Generation of Knowledge from Information, Data, and Analyses.” But this schema did not lead to a matching organizational format for the chapter; it paved the way for one. At the time of its writing, there was explosive progress in techniques for analyzing time-related events, so an important portion of the chapter was devoted to this topic. Effective analysis of time-related events was no longer possible with programmable calculators; they demanded powerful computer resources.

In Edition 3, the progression from information to data to analyses to knowledge became the explicit organizing schema for the chapter. Sophisticated methods for longitudinal data analyses and comparative effectiveness assessment were...
introduced. Whereas the statistician was once the surgeon’s primary collaborator in data analysis, that edition introduced computer scientists and mathematicians as partners in collaborative research.

In this edition we introduce other collaborators in the fields of artificial intelligence, ontology, and machine learning. In doing so, we expand themes hinted at in the third edition and hint at new techniques on the horizon. This edition is also strongly influenced by the Institute of Medicine’s (IOM) Learning Healthcare System initiative and comparative effectiveness emphases of the IOM and NIH. Undoubtedly, evolution of this chapter will continue in subsequent editions, because new methods are constantly being developed to better answer clinical questions.

How It Is Organized

The organizational basis for this chapter is the Newtonian inductive method of discovery. It begins with information about a microcosm of medicine, proceeds to translation of information into data and analysis of those data, and ends with new knowledge about a small aspect of nature. This organizational basis emphasizes the phrase, “Let the data speak for themselves.” It is that philosophy that dictates, for example, placing “Indications for Operation” after, not before, presentation of surgical results throughout this book.

Information

In health care, information is a collection of material, workflow documentation, and recorded observations (see Section II). Information may be recorded in paper-based medical records or in electronic (computer) format.

Data

Data consist of organized values for variables, usually expressed symbolically (e.g., numerically) by means of a controlled vocabulary (see Section III). Characterization of data includes descriptive statistics that summarize parts or all of the data and express their variability.

Analysis

Analysis is a process, often prolonged and repeated (iterative), that uses a large repertoire of methods by which data are explored, important findings are revealed and unimportant ones suppressed, and relations are clarified and quantified (see Sections IV and VI).

Knowledge

Knowledge is the synthesis of information, data, and analyses arrived at by inductive reasoning (see Section V). However, generation of new knowledge does not occur in a vacuum; an important step is assimilating new knowledge within the body of existing knowledge.

New knowledge may take the form of clinical inferences, which are simple summarizing statements that synthesize information, data, and analyses, drawn with varying degrees of confidence that they are true. It may also include speculations, which are statements suggested by the data or by reasoning, often about mechanisms, without direct supportive data. Ideally, it also includes new hypotheses, which are testable statements suggested by reasoning or inferences from the information, data, and analyses.

New knowledge can be applied to a number of processes in health care, including (1) generating new concepts, (2) making individual patient care decisions, (3) obtaining informed consent from patients, (4) improving surgical outcomes, (5) assessing the quality and appropriateness of care, and (6) making regulatory decisions (see Section V).

How to Read This Chapter

Unlike most chapters in this book, whose various parts can be read somewhat randomly and in isolation, Section I of this chapter should be read in its entirety before embarking on other sections. It identifies the mindset of the authors; defends the rationale for emphasizing surgical success and failure; contrasts philosophies, concepts, and ideas that shape both how we think about the results of research and how we do research; lays out a technique for successful clinical research that parallels the surgical technique portions of other chapters; and for collaborating statisticians, mathematicians, and computer scientists engaged in analyzing clinical data, lays the foundation for our recommendations concerning data analysis.

Much of the material in this introductory section is amplified in later portions of the chapter, and we provide cross-references to these to avoid redundancy.

THE DRIVING FORCES OF NEW KNOWLEDGE

Many forces drive the generation of new knowledge in cardiac surgery, including the economics of health care, need for innovation, clinical research, surgical success and failure, and awareness of medical error.

Economics

The economics of health care are driving changes in practice toward what is hoped to be less expensive, more efficient, yet higher quality care. Interesting methods for testing the validity of these claims have become available in the form of cluster randomized trials. In such trials (e.g., a trial introducing a change in physician behavior), patients are not randomized, physicians are (patients form the cluster being cared for by each physician)! This leads to inefficient studies that nevertheless can be effective with proper design and a large enough pool of physicians. It is a study design in which the unit of randomization (physician) is not the unit of analysis (individual patient outcome). Such trials appear to require rethinking of traditional medical ethics.

Innovation

Just when it seems that cardiac surgery has matured, innovation intervenes and drives new knowledge, both from proponents and opponents. Innovation occurs at several levels. It includes new devices; new procedures; existing procedures performed on new groups of patients, such as the elderly and the fetus; simplifying and codifying seemingly disparate anatomy, physiology, or operative techniques; standardizing procedures to make them teachable and reproducible; and introducing new concepts of patient care (the intensive care unit, automated infusion devices, automated care by computer-based protocols). Many of these innovations have had applications beyond the boundary of cardiac surgery.
Yet, innovation is often at odds with cost reduction and is perceived as being at odds with traditional research. In all areas of science, however, injection of innovation is the enthral that prevents entropy, stimulating yet more research and development and more innovation. Without it, cardiac surgery would be unable to adapt to changes in managing ischemic heart disease, potential reversal of the atherosclerotic process, percutaneous approaches to valvar and congenital heart disease, and other changes directed toward less invasive therapy.

What is controversial is (1) when and if it is appropriate to subject innovation to formal clinical trial and (2) the ethics of innovation in surgery, for which standardization is difficult.

Reducing the Unknown

New knowledge in cardiac surgery has been driven from its inception by a genuine quest to fill voids of the unknown, whether by clinical research or laboratory research (which we do not emphasize in this chapter, although the principles and recipe for success are the same as for clinical research). This has included research to clarify both normal and abnormal physiology, but also to characterize the abnormal state of the body supported on cardiopulmonary bypass.

Clinical research has historically followed one of two broad designs: randomized clinical trials and nonrandomized studies of cohorts of patients (“clinical practice”), as detailed later in this section under “Clinical Trials with Randomly Assigned Treatment” and “Clinical Studies with Nonrandomly Assigned Treatment,” respectively. Increasing emphasis, however, is being placed on translational research—that is, bringing basic research findings to the bedside. John Kirklin called this the “excitement at the interface of disciplines.” Part and parcel of the incremental risk factor concept (see “Incremental Risk Factor Concept” in Section IV) is that it is an essential link in a feedback loop that starts with surgical failure, proceeds to identifying risk factors, draws inferences about specific gaps in knowledge that need to be addressed by basic science, generates fundamental knowledge by the basic scientists, and ends by bringing these full circle to the clinical arena, testing and assessing the value of the new knowledge generated for improving medical care.

Surgical Success and Failure

Results of operative intervention in heart disease, particularly surgical failure, drive much of the new knowledge generated by clinical research. In the late 1970s and early 1980s, a useful concept arose about surgical failures. That is, in the absence of natural disaster or sabotage, there are two principal causes of failure of cardiac operations (or other treatments) to provide a desired outcome for an individual patient: (1) lack of scientific progress and (2) human error.

The utility of this concept is that it leads to the programmatic strategies of research on the one hand and development on the other. Thus, lack of scientific progress is gradually reduced by generating new knowledge (research), and human error is reduced in frequency and consequences by implementing available knowledge (development), a process as vital in cardiac surgery as it is in the transportation and manufacturing sectors.

Error

Increased awareness of medical error is driving the generation of new knowledge, just as it is driving increasing regulatory pressure and medicolegal litigation. The UAB group was one of the first to publish information about human error in cardiac surgery and place it into the context of cognitive sciences, human factors, and safety research. This interface of disciplines is essential for facilitating substantial reduction in injury from medical errors.

Surgical Failure

Surgical failure has been a strong stimulant of clinical research aimed at making scientific progress. With increasing requirements for reporting both outcomes and process measures in the United States (with “pay for performance”), there is now also an economic stimulus to reduce human error. The term “human error” carries negative connotations that make it difficult to discuss in a positive, objective way in order to do a root-cause analysis of surgical failures. It is too often equated with negligence or malpractice, and almost inevitably leads to blame of persons on the “sharp end” (caregivers), with little consideration of the decision making, organizational structures, infrastructures, or other factors that are remote in time and distance (“blunt end”).

Human Error

As early as 1912, Richardson recognized the need to eliminate “preventable disaster from surgery.” Human errors as a cause of surgical failure are not difficult to find, particularly if one is careful to include errors of diagnosis, delay in therapy, inappropriate operations, omissions of therapy, and breaches of protocol.

When we initially delved into what was known about human error in the era before Canary Island (1977), Three Mile Island (1979), Bhopal (1984), Challenger (1986), and Chernobyl (1986), events that contributed enormously to knowledge of the nature of human error, we learned two lessons from the investigation of occupational and mining injuries. First, successful investigation of the role of the human element in injury depends on establishing an environment of non-culpable error. The natural human reaction to investigation of error is to become defensive and provide no information that might prove incriminating. An atmosphere of blame impedes investigating, understanding, and preventing error. How foreign this is from the culture of medicine! We take responsibility for whatever happens to our patients as a philosophical commitment. Yet cardiac operations are performed in a complex and imperfect environment in which every individual performs imperfectly at times. It is too easy when things go wrong to look for someone to blame. Blame by 20/20 hindsight allows many root causes to be overlooked.

Second, we learned that errors of omission exceed errors of commission. This is exactly what we found in ventricular septal defect (VSD) repair (Table 6-1), suggesting that the cardiac surgical environment is not so different from that of a gold mine, and we can learn from that literature.

These two lessons reinforced some surgical practices and stimulated introduction of others that were valuable in the early stages of growth of the UAB cardiac surgery program:
using hand signals for passing instruments, minimizing distractions, replying simply to every command, reading aloud the protocol for the operation as it proceeds, standardizing apparently disparate operations or portions thereof, and focusing morbidity conferences candidly on human error and lack of knowledge to prevent the same failure in the future. To amplify, these practices might be enunciated as a “culture of clarity”—in today’s terms, a culture of transparency—the end result of which is a reproducible and successful surgical endeavor. In the operating room, each individual on the surgical team is relaxed but alert:

- Hand signals serve to inform assistants and the scrub nurse of anticipated needs for a relatively small number of frequently used instruments or maneuvers.
- Spoken communication is reserved for those out of the field of sight (i.e., the anesthesiologist and perfusionist). When verbalized, “commands” are acknowledged with a simple reply: “thank you,” “roger,” “yes.” Even those individuals out of the field learn to anticipate these events or commands.
- Anticipated deviations from the usual are presented a few minutes to a day or two before the event. (In teaching settings, residents are encouraged to write an operative plan in the preoperative note.) Unexpected deviations are acknowledged to all concerned as soon as possible.
- Successful routines are codified. These include chronology for anticoagulation and its reversal, myocardial management routines (induction of cardioplegia, intervals of cardioplegia reinfusion, controlled myocardial reperfusion before aortic clamp removal), and protocols controlled by the surgeon for commencing and weaning the patient from cardiopulmonary bypass.
- Technical intuitive concepts are articulated. For example, some think the VSD in tetralogy of Fallot is a circular hole. Thus, closing such a hole would simply involve running a suture circumferentially to secure a patch. Kirklin and Karp were able to describe the suture line as having four different areas of transition in three dimensions and precisely articulated names for those transitions. Each had a defined anatomic relationship to neighboring structures, so the hole became infinitely more interesting!
- Discussion of surgical failure is planned for a time (e.g., Saturday morning) when distractions are minimal. The stated goal is improvement, measurable in terms of reproducibility and surgical success. The philosophy is that events do not simply occur but have antecedent associations, so-called root-cause analysis. An attempt is made to determine if errors can be avoided and if scientific knowledge exists or does not exist to prevent future failure.

A major portion of the remainder of this chapter addresses acquisition and description of this new knowledge.

**Categories of Human Error**

**Slips** are failures in execution of actions and are commonly associated with attention failures (Box 6-2). Some external stimulus interrupts a sequence of actions or in some other way intrudes into them such that attention is redirected. In that instance, the intended action is not taken. **Lapses** are failures of memory. A step in the plan is omitted, one’s place in a sequence of actions is lost, or the reason for what one is doing is forgotten. **Mistakes** relate to plans and so take two familiar forms: (1) misapplication to the immediate situation of a good plan (rule) appropriate for a different and more usual situation and (2) application of the wrong plan (rule).

Slips and lapses constitute active errors. They occur at the physician-patient interface. Mistakes, in addition, constitute many latent errors. These are indirect errors that relate to performance by leaders, decision makers, managers, certifying boards, environmental services, and a host of activities that share a common trait: planning, decisions, ideas, and philosophy removed in time and space from the immediate healthcare environment in which the error occurred. (blunt...
end). These are a category of error over which the surgeon caring for a patient (sharp end) has little or no control or chance of modifying because latent errors are embedded in the system. It is claimed by students of human error in other contexts that the greatest chance of preventing adverse outcomes from human error is in discovering and neutralizing latent error.8,7

Inevitability of Human Error
If one considers all the possibilities for error in daily life, what is remarkable is that so few are made. We are surrounded with unimaginable complexity, yet we cope nearly perfectly because our minds simplify complex information. Think of how remarkably accident-free are our early-morning commutes to the hospital while driving complex machines in complex traffic patterns.1,14

When this cognitive strategy fails, it does so in only a few stereotypical ways.3 Because of this, models have been developed, based largely on observation of human error, that mimic human behavior by incorporating a fallible information-handling device (our minds) that operates correctly nearly always, but is occasionally wrong.20 Central to the theory on which these models are based is that our minds can remarkably simplify complex information. Exceedingly rare imperfect performance is theorized to be the price we pay for being able to cope, probably nearly limitless, with complexity. The mechanisms of human error are purported to stem from three aspects of “fallible machines”: downregulation, upregulation, and primitive mechanisms of information retrieval. In the text that follows, we borrow heavily from the human factors work of James Reason.8,7

Downregulation We call this habit formation, skill development, and “good hands.” Most activities of life, and certainly those of a skillful surgeon, need to become automatic. If we had to think about every motion involved in driving a car or performing an operation, the task would become nearly impossible to accomplish accurately. It would not be executed smoothly and would be error prone. It is hard to quantify surgical skill. It starts with a baseline of necessary sensory-motor eye-hand coordination that is likely innate. It becomes optimized by aggregation of correct “moves” and steps as well as by observation. It is refined by repetition of correct actions, implying identification of satisfactory and unsatisfactory immediate results (feedback). Then comes individual reflection and codification of moves and steps by hard analysis. Finally, motor skills are mastered by a synthesis of cognition and motor memory. The resulting automaticity and reproducibility of a skillful surgeon make a complex operation appear effortless, graceful, and flawless.1,14 However, automaticity renders errors inevitable.

Skill-based errors occur in the setting of routine activity.3
They occur when attention is diverted (distraction or preoccupation) or when a situation changes and is not detected in a timely fashion.3 They also occur as a result of overattention. Skill-based errors are ones that only skilled experts can make—beautiful execution of the wrong thing (slip) or failure to follow a complex sequence of actions (lapse). Skill-based errors tend to be easily detected and corrected.

Rule-based errors occur during routine problem-solving activities.3 Goals of training programs are to produce not only skillful surgeons but also expert problem solvers. Indeed, an expert may be defined as an individual with a wide repertoire of stored problem-solving plans or rules. Inevitable errors that occur take the form of either inappropriate application of a good rule or application of a bad rule.

Upregulation Our mind focuses conscious attention on the problem or activity with which we are confronted and filters out distracting information. The price we pay for this powerful ability is susceptibility to both data loss and information overload. This aspect of the mind is also what permits distractions or preoccupations to capture the attention of the surgeon, who would otherwise be focused on the routine tasks at hand.3 In problem solving, there may be inappropriate matching of the patient’s actual condition to routine rules for a somewhat different set of circumstances. Some of the mismatch undoubtedly results from the display of vast quantities of undigested monitored information about the patient’s condition. Errors of information overload need to be addressed by more intelligent computer-based assimilation and display of data.

Primitive Mechanisms of Information Storage and Retrieval The mind seems to possess an unlimited capacity for information storage and a blinding speed of information retrieval unparalleled by computers. In computer systems, there is often a trade-off between storage capacity and speed of retrieval; not so for the mind. The brain achieves this, apparently, not by storing facts but by storing models and theories—abstractions—about these facts (i.e., it stores meaning rather than data behind the meaning). Furthermore, the information is stored in finite packets along with other, often unrelated, information. (Many people use the latter phenomenon to recall names, for example, by associating them with more familiar objects such as animals.) The implications for error are that our mental image may diverge importantly from reality.

The mind’s search strategy for information achieves remarkable speed by having apparently just two tools for fetching information. First, it matches patterns. Opportunity for error arises because our interpretation of the present and anticipation of the future are shaped by patterns or regularities of the past. Second, if pattern matching produces multiple items, it prioritizes these by choosing the one that has been retrieved most often. This mechanism gives rise to rule-based errors, for example, in a less frequently occurring setting.

Conscious Mind When automatic skills and stored rules are of no help, we must consciously think. Unlike the automaticity we have just described, the conscious mind is of limited capacity but possesses powerful computational and reasoning tools, all those attributes we ascribe to the thought process. However, it is a serial, slow, and laborious process that gives rise to knowledge-based errors.3 Unlike stereotypical skill- and rule-based errors, knowledge-based errors are less predictable. Furthermore, there are far fewer opportunities in life for “thinking” than for automatic processes, and therefore the ratio of errors to opportunity is higher. Errors take the form of confirmation bias, causality vs. association, inappropriate selectivity, overconfidence, and difficulties in assimilating temporal processes.

The unusual ordering of material presented in the clinical chapters of this book was chosen by its original authors to provide a framework for thinking with the conscious mind about heart disease and its surgical therapy that would assist in preventing knowledge-based errors. For example, an algorithm (protocol, recipe) for successfully managing mitral valve regurgitation is based on knowledge of morphology,
etiology, and detailed mechanisms of the regurgitation; preoperative clinical, physiologic, and imaging findings; natural history of the disease if left untreated; technical details of operation; postoperative management; both early and long-term results of operation; and from all these considerations, the indications for operation and type of operation. Lack of adequate knowledge results in inappropriate use of mitral valve repair, too many mitral valve replacements, or suboptimal timing of operation.

Reducing Errors

We have presented this cognitive model in part because it suggests constructive steps for reducing human error and, thus, surgical failure. It affirms the necessity for intense apprentice-type training that leads to automatization of surgical skill and problem-solving rules. It equally suggests the value of simulators for acquiring such skills. It supports creation of an environment that minimizes or masks potential distractions. It supports a system that discovers errors and allows recovery from them before injury occurs. This requires a well-trained team in which each individual is familiar with the operative protocol and is alert to any departures from it. In this regard, deLeval and colleagues’ findings are sobering. Major errors were often realized and corrected by the surgical team, but minor ones were not, and the number of minor errors was strongly associated with adverse outcomes. It was also sobering that self-reporting of intraoperative errors was of no value. Must there be a human factors professional at the elbow of every surgeon and physician?

James Reason suggested that other “cognitive prostheses” may be of value, some of which are being advocated in medicine. For example, there is much computers can do to reduce medication errors. A prime target is knowledge-based errors. Reducing these errors may not be achievable through computer artificial intelligence, but rather through more appropriate modes of information assembly, processing, and display for processing by the human mind. Finally, if latent errors are the root cause of many active errors, analysis and correction at the system level will be required. A cardiac surgery program may fail, for example, from latent errors traceable to management of the blood bank, postoperative care practices, ventilation systems, and even complex administrative decisions at the level of hospitals, universities with which they may be associated, and national health system policies and regulations within which they operate.

Lack of Scientific Progress

A practical consequence of categorizing surgical failures into two causes is that they fit the programmatic paradigm of “research and development”: discovery on the one hand and application of knowledge to prevent failures on the other. The quest to reduce injury from medical errors that has just been described is what we might term “development.” The remainder of this chapter focuses mainly on the portion of the paradigm that is research, but also more narrowly on clinical research.

PHILOSOPHY

Clinical research in cardiac surgery as emphasized in this chapter consists largely of patient-oriented investigations motivated by a serious quest for new knowledge to improve surgical results—that is, to increase survival early and long term; to reduce complications; to enhance quality of life; to extend appropriate operations to more patients, such as high-risk subsets; and to devise and evaluate new beneficial procedures that have been generalized into a strategy of managing not so much individual malformations as a physiologic situation (e.g., the Fontan operation and its variants [see Chapter 41] and the Norwood operation [see Chapter 49]).

This inferential activity, aimed at improving clinical results, is in contrast to pure description of experiences. Its motivation also contrasts with those aspects of “outcomes assessment” motivated by regulation or punishment, institutional promotion or protection, quality assessment by outlier identification, and negative aspects of cost justification or containment. These coexisting motivations have stimulated us to identify, articulate, and contrast philosophies that underlie serious clinical research. It is these philosophies that inform our approach to analysis of clinical experiences.

Deduction versus Induction

“Let the data speak for themselves.”

Arguably, Sir Isaac Newton’s greatest contribution to science was a novel intellectual tool: a method for investigating the nature of natural phenomena. His contemporaries considered his method not only a powerful scientific investigatory tool, but also a new way of philosophizing applicable to all areas of human knowledge. His method had two strictly ordered aspects that for the first time were truly systematically expressed: a first, and extensive, phase of data analysis whereby observations of some small portion of a natural phenomenon are examined and dissected, followed by a second, less emphasized, phase of synthesis whereby possible causes are inferred and a small portion of nature revealed by the observations and analyses. This was the beginning of the inductive method in science: valuing first and foremost the observations made about a phenomenon, then “letting the data speak for themselves” in suggesting possible natural mechanisms.

This represented the antithesis of the deductive method of investigation that had been so successful in the development of mathematics and logic (the basis for ontology-based computer reasoning today). The deductive method begins with what is believed to be the nature of the universe (referred to by Newton as “hypothesis”), from which logical predictions are deduced and tested against observations. If the observations deviate from logic, the data are suspect, not the principles behind the deductions. The data do not speak for themselves.

Newton realized that it was impossible at any time or place to have complete knowledge of the universe. Therefore, a new methodology was necessary to examine just portions of nature, with less emphasis on synthesizing the whole. The idea was heralded as liberating in nearly all fields of science.

As the 18th century unfolded, the new method rapidly divided such diverse fields as religion into those based on deduction (fundamentalism) and those based on induction (liberalism), roughly Calvinism vs. Wesleyan-Arminianism. This philosophical dichotomy continues to shape not just the scientific but the social, economic, and political climate of the 21st century.
Collectivism versus Individualism

To better convey how new knowledge is acquired from observing clinical experiences, we look back to the 17th century to encounter the proverbial dichotomy between collectivism and individualism, so-called lumpers and splitters or forests and trees.846

In 1603 during one of its worst plague epidemics, the City of London began prospective collection of weekly records of christenings and burials. In modern language, this was an administrative database or registry (see Box 6-1). Those “who constantly took in the weekly bills of mortality made little use of them, than to look at the foot, how the burials increased or decreased; and among the casualties, what has happened rare, and extraordinary, in the week current,” complained John Graunt.311 Unlike those who stopped at counting and relating anecdotal information, Graunt believed the data could be analyzed in a way that would yield useful inferences about the nature and possible control of the plague.

His ultimate success might be attributed in part to his being an investigator at the interface of disciplines. By profession he was a haberdasher, so Graunt translated merchandise inventory dynamics into terms of human population dynamics. He described the rate of goods received (birth rate) and the rate of goods sold (death rate); he then calculated the inventory (those currently alive).

Graunt then made a giant intellectual leap. In modern terms, he assumed that any item on the shelf was interchangeable with any other (collectivism). By assuming, no matter how politically and sociologically incorrect, that people are interchangeable, he achieved an understanding of the general nature of the birth-life-death process in the absence of dealing with specific named individuals (individualism). He attempted to discover, as it were, the general nature of the forest at the expense of the individual trees.

Graunt then identified general factors associated with variability of these rates (risk factors, in modern terminology; see Multivariable Analysis in Section IV). From the City of London Bills of Mortality, he found that the death rate was higher when ships from foreign ports docked in the more densely populated areas of the city, and in households harboring domestic animals. Based on these observations, he made inferences about the nature of the plague—what it was and what it was not—and formulated recommendations for stopping its spread. They were crude, nonspecific, and empirical: avoid night air brought in from foreign ships (which we now know is not night air but rats), flee to the country, separate people from animal vectors, and quarantine infected individuals.823 Nevertheless, they were effective in stopping the plague for 200 years until its cause and mechanism of spread were identified.

Lessons based on this therapeutic triumph of clinical investigation conducted more than 300 years ago include the following: (1) empirical identification of patterns of disease can suggest fruitful directions for future research and eliminate some hypothesized causal mechanisms, (2) recommendations based on empirical observations may be effective until causal mechanisms and treatments are discovered, and (3) new knowledge is often generated by overview (synthesis), as well as by study of individual patients.836

When generating new knowledge about the nature of heart disease and its treatment, it is important both to examine groups of patients (the forest) and to investigate individual therapeutic failures (the trees). This is similar to Heisenberg’s uncertainty principle in chemistry, thermodynamics, and mechanics, in which physical matter and energy can be thought of as discrete particles on the microhierarchical plane (individualism, splitting, trees), and as waves (field theory) on the macrohierarchical plane (collectivism, lumping, forests). Both views give valuable insights into nature, but they cannot be viewed simultaneously. Statistical methods emphasizing optimum discrimination for identifying individual patients at risk tend to apply to the former, whereas those emphasizing probabilities and general inferences tend to apply to the latter.83,847

Continuity versus Discontinuity in Nature

When we turn our focus from named individuals experiencing surgical failure to groups of patients, data analysis becomes mandatory to discover relationships between outcome and items that differ in value from patient to patient (called variables). A challenge immediately arises: Many of the variables related to outcome are measured either on an ordered clinical scale (ordinal variables), such as New York Heart Association (NYHA) functional class, or on a more or less unlimited scale (continuous variables), such as age. Three hundred years after Graunt, the Framingham Heart Disease Epidemiology Study investigators were faced with this frustrating problem.820,821 Many of the variables associated with development of heart disease were continuously distributed ones, such as age, blood pressure, and cholesterol level. To examine the relationship of such variables to development of heart disease, it was then accepted practice to categorize continuous variables coarsely and arbitrarily for cross-tabulation tables. Valuable information was lost this way. Investigators recognized that a 59-year-old’s risk of developing heart disease was more closely related to
that of a 60-year-old’s than to that of the group of patients in the sixth vs. seventh decade of life. They therefore insisted on examining the entire spectrum of continuous variables rather than subclassifying the information.

What they embraced is a key concept in the history of ideas—namely, *continuity in nature*. The idea has emerged in mathematics, science, philosophy, history, and theology.

In our view, the common practice of stratifying age and other more or less continuous variables into a few discrete categories is lamentable because it loses the power of continuity (some statisticians call this “borrowing power”). Focus on small, presumed homogeneous groups of patients also loses the power inherent in a wide spectrum of heterogeneous but related cases. After all, any trend observed over an ever-narrower framework looks more and more like no trend at all! Like the Framingham investigators, we therefore embrace continuity in nature unless it can be demonstrated that doing so is not valid, useful, or beneficial. (Modern methods of machine learning that use classification methods may seem to stumble at this point, but repetition of analyses over thousands of sampled data sets combined with averaging achieves a close approximation to continuity in nature; see Classification Methods in Section VI.)

**Single versus Multiple Dimensionality**

The second problem the Framingham investigators addressed was the need to consider multiple variables simultaneously. Univariable (one variable at a time) statistics are attractive because they are simple to understand. However, most clinical problems are multifactorial. At the same time, clinical data contain enormous redundancies that somehow need to be taken into account (e.g., height, weight, body surface area, and body mass index are highly correlated and relate to the conceptual variable “body size”).

Cornfield came to the rescue of the Framingham investigators with a new methodology called *multivariable logistic regression*¹²⁰ (see “Logistic Regression Analysis” in Section IV). It permitted multiple factors to be examined simultaneously, took into account redundancy of information among variables (covariance), and identified a parsimonious set of variables for which the investigators coined the term “factors of risk” or *risk factors*²² (see “Parsimony versus Complexity” later in this section and Multivariable Analysis in Section IV).

Various forms of multivariable analysis, in addition to logistic regression analysis, have become available to clinical investigators. Their common theme is to identify patterns of relationships between outcome and a number of variables considered simultaneously. These are not cause–effect relations, but associations with underlying causal mechanisms (see discussion of surrogates under Multivariable Analyses in Section IV). The relationships that are found may well be spurious, fortuitous, hard to interpret, and even confusing because of the degree of correlation among variables. For example, women may be at a higher risk of mortality after certain cardiac procedures, but female gender may not be a “risk factor,” because other factors, such as body mass index, may be the more general variable related to risk, whether in women or men. Even so, it is simultaneously true that (1) being female is not per se a risk factor, but (2) women are at higher risk by virtue of the fact that on average they are smaller than men.

This means that a close collaboration must exist between statistical experts and surgeons, particularly in organizing variables for analysis.

**Linearity versus Nonlinearity**

Risk factor methodology introduced another complexity besides increased dimensionality. The logistic equation is a symmetric S-shaped curve that expresses the relationship between a scale of risk, called *logit units*, and a corresponding scale of absolute probability of experiencing an event¹¹⁶,k⁹ (Fig. 6-1). Because the relationship is not linear, it is not possible to simply add up scores for individual variables and come up with a probability of an event, a technique that has been attempted in other settings¹¹¹,p² (see Risk Stratification in Section VI).

The nonlinear relationship between risk factors and probability of outcome makes medical sense. Imagine a risk factor with a logit unit coefficient of 1.0 (representing an odds ratio of 2.7; Box 6-3 and see Fig. 6-1). If all other things position a patient far to the left on the logit scale, a 1-logit-unit increase in risk results in a trivial increase in the probability of experiencing an event. But as other factors move a patient closer to the center of the scale (0 logit units, corresponding to a 50% probability of an event), a 1-logit-unit increase in risk makes a huge difference. This is consistent with the medical perception that some patients experiencing the same disease, trauma, or complication respond quite differently. Some are medically robust because they are far to the left (low-risk region) on the logit curve before the event occurred. Others are medically fragile because their age or comorbid conditions place them close to the center of the logit curve. For the latter, a 1-logit-unit increase in risk can be “the straw that breaks the camel’s back.” It is this kind of relation that makes it hard to demonstrate, for example, the benefit of bilateral internal thoracic artery grafting in relatively young adults followed for even a couple of decades, but easy in patients who have other risk factors.¹³² The same has been demonstrated for risk of operation in patients with aortic regurgitation and low ejection fraction.²²⁴

This type of sensible, nonlinear medical relation makes us want to deal with absolute risk rather than relative risk or risk ratios²²² (see Box 6-3). Relative risk is simply a translation of the scale of risk, without regard to location on that scale. Absolute risk integrates this with the totality of other risk factors.

**Raw Data versus Models of Data**

Importantly, the Framingham investigators did not stop at risk factor identification. Because logistic regression generates an equation based on raw data, it can be solved for a given set of values for risk factors. The investigators devised a cardboard slide rule for use by lay persons to determine their predicted risk of developing heart disease within the next 5 years.

Whenever possible and appropriate, results of clinical data analyses should be expressed in the form of mathematical models that become equations. These can be solved after “plugging in” values for an individual patient’s risk factors to estimate absolute risk and its confidence limits. Equations are compact and portable, so that with the ubiquitous computer,
they can be used to advise individual patients\textsuperscript{44,13,20,30} (see “Decision Making for Individual Patients” in Section V).

Nihilism versus Predictability

One of the important advantages of generating equations is that they can be used to predict future results for either groups of patients or individual patients. We recognize that when speaking of individual patients, we are referring to a prediction concerning the probability of events for that patient; we generally cannot predict exactly who will experience an event or when an event will occur. Indeed, whenever we apply what we have learned from clinical experience or the laboratory to a new patient, we are predicting. This motivated us to develop statistical tools that yield patient-specific estimates of absolute risk as an integral byproduct.\textsuperscript{844} These were intended to be used for formal or informal comparison of predicted risks and benefits among alternative therapeutic strategies.

Of course, the nihilist will say, “You can’t predict.” However, in a prospective study of 3720 patients in Leuven, Belgium, we generated evidence that predictions from
Box 6-3 Expressions of Relative Risk

Proportion
Consider two groups of patients, A and B. Mortality in group A is 10 of 40 patients (25%); in B, it is 5 of 50 patients (10%). For the sake of illustrating the various ways these proportions (see Box 6-13), 0.25 and 0.10, can be expressed relative to one another, designate a as the number of deaths (10) in A and b as the number of deaths (30) in A and b as the number alive (30). The total in A is a+b (40) patients, nA. Designate c as the number of deaths (5) in B and d as the number alive (45). The total in B is c+d (50) patients, nB. Designate P as the proportion of deaths in A, a/(a+b) or a/nA, and P as the proportion in B, c/(c+d) or c/nB.

Relative Risk (Risk Ratio)
Relative risk is the ratio of two probabilities. In the example above, relative risk of A compared with B is P/P = [a/(a+b)]/[c/(c+d)] = 0.25/0.10 or 2.5. Equivalently, one could reverse the proportions, P/P = 0.10/0.25 = 0.4. If P were to exactly equal P, relative risk would be unity (1.0). Another way to express relative risk when comparing two treatments is by relative risk reduction, which for relative risks greater than 1 is 1 minus relative risk. This is mathematically identical to dividing the absolute difference in probabilities by the higher of the two: (P − P)/P.

Odds and Gambler’s Odds
The odds of an event is the number of events divided by non-events. In the example above, the odds of death in A is a/b = 10/30 = 0.33; in B, it is c/d = 5/45 = 0.11. The mathematical interrelation of probability (P) of an event and odds (O) are these: O = P/(1 − P) and P = O/(1 + O). A probability of 0.1 is an odds of 0.11, but a probability of 0.5 is an odds of 1, of 0.8 an odds of 4, of 0.9 an odds of 9, and of 1.0 an odds of infinity. Often, it is interesting to examine the odds of the complement (1 − P) of a proportion, (1 − P)/P, which is gambler’s odds. Thus, a P value of .05 is equivalent to an odds of .053 and a gambler’s odds of 19:1. A P value of .1 has a gambler’s odds of 99:1, and a P value of 2 has a gambler’s odds of 4:1.

Odds Ratio and Log Odds
The odds ratio is the ratio of odds. In the above example, the odds ratio of A compared with B is (a/b)/(c/d) = ad/bc, which is either (10/30)/(5/45) = 3 or (10 · 45)/(30 · 5) = 3. Note that the logistic equation is Ln[P/(1 − P)]. For A, P/(1 − P) is a/b, the odds of A. Thus, Ln[P/(1 − P)] is log odds. Logistic regression can then be thought of as an analysis of log odds. Exponentiation is useful for dichotomous (yes/no) risk factor from such an analysis re-expresses it in terms of the odds ratio for those with versus those without the risk factor (see Box 6-5).

When the probability of an event is low, say less than 10%, relative risk (RR) and the odds ratio (OR) are numerically nearly the same. The mathematical relation is RR = [1−P]/[1−P] · OR. In the above example, the relative risk was 2.5, but the odds ratio was 3, and the disparity increases as the probability of event increases to 50%.

Relative risk is easier for most physicians to grasp because it is simply the ratio of proportions. It is unusual to encounter a physician without an epidemiology background who understands the odds ratio.

Expressing Relative Risk and Odds Ratios
Both relative risk and odds ratios are expressed on a scale of 0 to infinity. However, all odds ratios less than 1 are squeezed into the range 0 to 1, in contrast to those greater than 1, which are spread out from 1 to infinity. It is thus difficult to visualize that an odds ratio of 4 is equivalent to one of 0.25 if a linear scale is used. We recommend that a scale be chosen to express these quantities with equal distance above and below 1.0. This can be achieved, for example, by using a logarithmic or logit presentation scale.

Risk Difference (Absolute Risk Reduction) and Number to Treat
The risk difference is the difference between two proportions. In the above example, P − P is the risk difference. In many situations, risk difference is more meaningful than risk ratios (either relative risk or the odds ratio). Consider a low probability situation with a risk of 0.5% and another with a risk of 1%. Relative risk is 2. Yet risk difference is only 0.5%. In contrast, consider a higher-probability situation in which one probability is 50% and the other 25%. Relative risk is still 2, but risk difference is 25%. These represent the proverbial statement that “twice nothing is still nothing.” They reflect the relation between the logit scale and absolute probability (see Fig. 6-1, A), recalling that the logit scale is one of log odds.

An alternative way to express a difference in probabilities when the difference is arranged to be positive (e.g., P − P), and thus expresses absolute risk reduction, is as the inverse, 1/(P − P). This expression of absolute risk reduction is called number to treat. It is useful in many comparisons in which it is meaningful to answer the question, “How many patients must be treated by A (compared with B) to prevent one event (death)?” In our example, absolute risk reduction is 25% − 10% = 15%, and number needed to treat is 1/0.15 = 6.7. Number needed to treat is particularly valuable for thinking about risks and benefits of different treatment strategies. If it is large, one may question the risk of switching treatments, but if it is small, the benefit of doing so becomes more compelling.

Hazard Ratio
In time-related analyses, it is convenient to express the model of risk factors in terms of a log-linear function (see Box 6-5 and “Cox Proportional Hazards Regression” in Section IV): Ln(λ) = β0 + β1X1 + … + βXk, where ln is the natural logarithm and λ is the hazard function. The regression coefficients, β, for a dichotomous risk factor thus represent the logarithm of the ratio of hazard functions. Hazard ratios, as well as relative risk and the odds ratio, can be misleading in magnitude (large ratios, small risk differences) in some settings. Hazard comparisons, just like survival comparisons, are often more meaningfully and simply expressed as differences.

multivariable equations are generally reliable (see “Residual Risk” in Section VI). We compared observed survival, obtained at subsequent follow-up, with prospectively predicted survival. The correspondence was excellent in 92% of patients. However, it was poor in the rest (Fig. 6-2 and Table 6-2; see also “Residual Risk” in Section VI). A time-related analysis of residual risk identified circumstances leading to poor prediction and revealed the limitations of quantitative predictions: (1) When patients have important rare conditions that have not been considered in the analysis, risk is underestimated. (2) When large data sets rich in clinically relevant variables are the basis for prediction equations, prediction should be suspect in only a small proportion of patients with unaccounted-for conditions (see “Residual
of risk in patients with them.

No.

Predicted <

presented at time of death along horizontal axis, and according to
Kaplan-Meier life table method along vertical axis; vertical bars are
70% confidence limits (CL). Solid line and its 70% CLs represent
predicted survival. Notice systematic underestimation of survival.
Number of predicted deaths = 273 (5.7%); observed deaths =
243 (6.5%); P = .03. B, Patients stratified by presence (open squares)
and absence (circles) of rare unaccounted-for risk factors (malignancy,
preoperative dialysis, atrial fibrillation, ventricular tachycardia,
or aortic regurgitation). Otherwise, format is as in A. Note
excellent correspondence of predicted survival to observed survival
in patients without these factors, and substantial underestimation
of risk in patients with them.

Figure 6-2 Predicted and observed survival after coronary artery
bypass grafting, illustrating both ability to predict from multivariable
equations and pitfalls in doing so. A, Observed overall survival
among prospectively studied patients (n = 3720) compared with
predicted survival. Each circle represents an observed death, posi-
tioned at time of death along horizontal axis, and according to
Kaplan-Meier life table method along vertical axis; vertical bars are
70% confidence limits (CL). Solid line and its 70% CLs represent
predicted survival. Notice systematic underestimation of survival.
Number of predicted deaths = 273 (5.7%); observed deaths =
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or aortic regurgitation). Otherwise, format is as in A. Note
excellent correspondence of predicted survival to observed survival
in patients without these factors, and substantial underestimation
of risk in patients with them.

Table 6-2 Predicted and Observed Number of Deaths after
Primary Isolated Coronary Artery Bypass Grafting

<table>
<thead>
<tr>
<th>Rare Risk Factors</th>
<th>Observed</th>
<th>Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No.</td>
</tr>
<tr>
<td>No</td>
<td>3428</td>
<td>186</td>
</tr>
<tr>
<td>Yes</td>
<td>292</td>
<td>57</td>
</tr>
</tbody>
</table>

Data from Sergeant and colleagues.\textsuperscript{39} July 1987 to 1992; n = 3720.

A related use of predictive equations is in comparing
alternative therapies. Some would argue that the only believ-
able comparisons are those based on randomized trials,
and that documented clinical experiences are irrelevant and
misleading.\textsuperscript{875,877} However, many randomized trials are
homogeneous and focused and are analyzed by blunt instru-
ments, such as an overall effect. On the other hand, real-
world clinical experience involves patient selection that is
difficult to quantify, may be a single-institution experience
with limited generality except to other institutions of the
same variety, is not formalized unless there is prospective
gathering of clinical information into registries, and is less
disciplined. Nevertheless, analyses of clinical experiences can
yield a fine dissecting instrument in the form of equations
that are useful across the spectrum of heart disease for com-
paring alternative treatments and therefore for advising
patients.\textsuperscript{829} (see “Clinical Studies with Nonrandomly Assigned
Treatment” later in this section).

Parsimony versus Complexity

Although clinical data analysis methods and results may
seem complex at times, as in the large number of risk factors
that must be assessed for comparing treatment strategies
in ischemic heart disease, an important philosophy behind
such analysis is parsimony (simplicity). We have discussed two
reasons for this previously. One is that clinical data contain
inherent redundancy, and one purpose of multivariable analy-
ysis is to identify that redundancy and thus simplify the dimen-
sionality of the problem. A second reason is that assimilation
of new knowledge is incomplete unless one can extract the
essence of the information. Thus, clinical inferences are
often even more digested and simpler than the multivariable
analyses.

We must admit that simplicity is a virtue based on philo-
sophical, not scientific, grounds. The concept was introduced
by William of Ocken in the early 14th century as a concept

Risk” in Section VI for details). Except for these limitations,
multivariable equations appear capable of adjusting well for
different case mixes.

This analysis has important implications for “report card” registries used in institutional comparisons.\textsuperscript{106}
Surgeons often object to these comparisons on the basis
that risk adjustment (see Risk Adjustment in Section VI)
accounts for neither risk stratification (see Risk Stratification
in Section VI) nor rare combinations of risk factors that
defy prediction. They may be correct. Unfortunately, in
advising patients about operation, we find that these are
the very individuals whose risk is difficult to predict on
clinical grounds and for whom we wish we had good
prediction equations.

The amount of data necessary to generate new knowledge
is much larger than that needed to use the knowledge in a
predictive way. To generate new knowledge, data should be
rich both in relevant variables and in variables eventually
found not to be relevant. But for prediction, one needs to
collect only those variables used in the equation (see Risk
Adjustment in Section VI) unless one is interested in inves-
tigating reasons for lack of prediction (see Residual Risk in
Section VI).

Blunt Instruments versus Fine Dissecting Instruments

A related use of predictive equations is in comparing
alternative therapies. Some would argue that the only believ-
able comparisons are those based on randomized trials,
and that documented clinical experiences are irrelevant and
misleading.\textsuperscript{875,877} However, many randomized trials are
homogeneous and focused and are analyzed by blunt instru-
ments, such as an overall effect. On the other hand, real-
world clinical experience involves patient selection that is
difficult to quantify, may be a single-institution experience
with limited generality except to other institutions of the
same variety, is not formalized unless there is prospective
gathering of clinical information into registries, and is less
disciplined. Nevertheless, analyses of clinical experiences can
yield a fine dissecting instrument in the form of equations
that are useful across the spectrum of heart disease for com-
paring alternative treatments and therefore for advising
patients.\textsuperscript{829} (see “Clinical Studies with Nonrandomly Assigned
Treatment” later in this section).
Clinical data may be used as a form of advertising. Innovation stems less from purposefulness than from aesthetically motivated curiosity, frustration with the status quo, sheer genius, fortuitous timing, favorable circumstances, and keen intuition. With innovation comes the need to promote. However, promotional records of achievement should not be confused with serious study of safety, clinical effectiveness, and long-range appropriateness.

Of growing importance is the use of clinical information for regulation or to gain institutional competitive advantage. Using clinical outcomes data to rank institutions or individual doctors has become popular in the United States (see Risk Stratification and Risk Adjustment in Section VI). Many surgeons perceive clinical report cards as a means for punishment or regulation. What is troubling is that their use is based on a questionable quality-control model of outlier identification. Because doctors are people and not machines, this approach generates counterproductive ethical side effects, including defensiveness and hiding the truth. It hinders candid, non-accusatory (non-culpable), serious examination of medical processes for the express purpose of improving patient care (see “Human Error” earlier in this section).

Critics of clinical report cards charge that their rankings, some institutions refuse to operate on sicker patients. In several studies of community hospitals by the UAB group, it was shown that they could indeed improve their risk-unadjusted rankings by restricting surgery to low-risk cases. However, their results in such patients were often inferior to those of institutions of excellence operating on similar low-risk patients. That is, their risk-adjusted mortality was higher even for low-risk cases.

With the intense focus on institutional performance, another undesirable side effect of data analysis decreed years ago has crept back in: undue emphasis on hospital mortality and morbidity. Studies of hospital events have the advantage of readily available data for extraction, but early events may be characterized incompletely. After repair of many congenital and acquired heart diseases, early risk of mortality and morbidity. Studies of hospital events have the advantage of readily available data for extraction, but early events may be characterized incompletely. After repair of many congenital and acquired heart diseases, early risk of surgery extends well beyond the hospital stay. This has led to reflection on the effect of time frame on studies of clinical experiences. Use of intermediate-term data is likely to characterize the early events well, but requires cross-sectional patient follow-up. Long-term follow-up is essential to establish appropriateness of therapy, but it is expensive and runs the risk of being criticized as being of historical interest only.

Yet another reason for interest in clinical information is to use it for profit or corporate advantage. At present, the philosophies of scientific investigation and business are irreconcilable. One thrives on open dissemination of information, the other on proprietary information offering a competitive advantage. In an era of dwindling public resources for research and increasing commercial funding, we may be seeing the beginning of the end of open scientific inquiry.

New Knowledge versus Selling Shoes

The philosophies described so far focus on the challenge of generating new knowledge from clinical experiences. However, other uses are made of clinical data.
The second edition reflects data and outcomes from an era of largely unregulated medical care, and similar data may be impossible to gather and freely analyze when care is largely regulated. This is not intended as an opinion as to the advantages or disadvantages of regulation of health care; indeed, as regulation proceeds, the data in this book, along with other data, should be helpful in establishing priorities and guidelines.

As already noted in both the first and second editions, the last section of each chapter is on indications for operation. In the future, regulations of policymakers may need to be added to the other variables determining indications.

On the horizon is the promise that medicine will become decreasingly empirical and more deterministic.62 However, as long as treatment of heart disease requires complex procedures, and as long as most are palliative in the life history of chronic disease, there will be a need to understand more fully the nature of the disease, its treatment, and its optimal management. This will require adoption of approaches to data that are inescapably philosophical.

**CLINICAL RESEARCH**

In response to the American Medical Association’s Resolution 309 (1-98), a Clinical Research Summit and subsequently an ongoing Clinical Research Roundtable (IOM) have sought to define and reenergize clinical research.10 The most important aspects of the definition of clinical research are that (1) it is but one component of medical and health research aimed at producing new knowledge; (2) the knowledge produced should be valuable for understanding the nature of disease, its treatment, and prevention; and (3) it embraces a wide spectrum of types of research. Here we highlight only two broad examples of that spectrum: clinical trials with randomly assigned treatment and clinical studies with nonrandomly assigned treatment—both of which are interrelated with clinical effectiveness research.7

**Clinical Trials with Randomly Assigned Treatment**

Controlled trials date back at least to biblical times when casting of lots was used as a fair mechanism for decision making under uncertainty (Numbers 33:54). Solomon noted, “The lot causeth disputes to cease, and it decideth between the mighty” (Proverbs 18:18). An early clinical trial took place in the Court of Nebuchadnezzar, king of Babylon (modern Iraq). He ordered several gifted Hebrew youths (“well favored, skillful in all wisdom, cunning in knowledge, and understanding science”) to reside at his palace for 3 years as if they were his own children. He proposed to train them in Chaldean knowledge and language. Among them were Daniel and the familiar Shadrach, Meshach, and Abednego. Daniel objected to the Babylonian diet, and so proposed a 10-day clinical trial: The Hebrews would be fed a vegetarian diet with water, while the children of the king would be fed the king’s meat and wine. After 10 days, the condition of the Hebrews was determined to be better than that of the king’s children, and they received permission to continue to eat their own diet (Daniel 1:1-15).99 (This is remarkably reminiscent of the contemporary controversy surrounding carbohydrate-rich vs. protein-rich diets.)

The first modern placebo-controlled, double-blinded, randomized clinical trial was carried out in England by Sir Austin Bradford Hill on the effectiveness of streptomycin vs. bed rest alone for treatment of tuberculosis,835 although 17th- and 18th-century unblinded trials have been cited as historical predecesors.5,21,22

Clinical trials in which cardiac surgical procedures and medical therapy have been randomly assigned have made major contributions to our knowledge of treatment and outcomes of heart disease.73 Notable examples are the Veterans Administration (VA) study of CABG,912 the Coronary Artery Surgery Study (CASS) trial of CABG,93 the European Coronary Surgery Study trials,16 and the PARTNER trial of percutaneous aortic valve replacement.119 Trials of CABG vs. percutaneous coronary intervention have also been important (e.g., the Balloon Angioplasty Revascularization Investigation [BARI]).720,511

Randomization of treatment assignment has three valuable and unique characteristics:

- It eliminates selection factors (bias) in treatment assignment (although this can be defeated at least partially by enrollment bias).
- It distributes patient characteristics equally between groups, whether they are measured or not, known or unknown (balance), a well-accepted method of risk adjustment.825,874,877,87
- It meets assumptions of statistical tests used to compare end points.877

Randomized clinical trials are also characterized by concurrent treatment, excellent and complete compilation of data gathered according to explicit definitions, and proper follow-up evaluation of patients. These operational byproducts may have contributed nearly as much new knowledge as the random assignment of treatment.

Unfortunately, it has become ritualistic for some to dismiss out of hand all information, inferences, and comparisons relating to outcome events derived from experiences in which treatment was not randomly assigned.876 If this attitude is valid, then much of the information now used to manage patients with cardiac disease would have to be dismissed and ignored! Investigations concerning differences of outcome among different physicians, different institutions, and different time periods would have to be abandoned. However, moral justification may not be present for a randomized comparison of procedures and protocols that clinical experience strongly suggests have an important difference.825 (The difficulty of recruitment in BARI reflects this problem.) In fact, when Benson and Hartz811 investigated differences between randomized trials and observational comparisons over a broad range of medical and surgical interventions, they found “little evidence that estimates of treatment effects in observational studies reported after 1984 are consistently larger than or qualitatively different from those obtained in randomized controlled studies.”811 (See, however, the

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1In the United States, the Federal Council for Comparative Effectiveness Research has defined this type of research as “The conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in ‘real world’ settings.” The purpose of this research is to improve health outcomes by developing and disseminating evidence-based information to patients, clinicians, and other decision makers, responding to their expressed needs about which interventions are most effective for which patients under specific circumstances.71
rebuttal by Pocock and Elbourne.\textsuperscript{914} These findings were confirmed by Concato and colleagues.\textsuperscript{921} Nevertheless, we acknowledge a hierarchy of clinical research study designs, and the randomized trial generates the most secure information about treatment differences.\textsuperscript{937}

Trials in which treatment is randomly assigned are testing a hypothesis, and hypothesis testing in general requires a yes or no answer unperturbed by uncontrollable factors. Thus ideally, the study is of short duration, with all participants blinded and a treatment that can be well standardized. However, in many clinical situations involving patients with congenital or acquired heart disease, the time-relatedness of freedom from an unfavorable outcome event is important and can jeopardize interpretation of the trial.\textsuperscript{95} This is because individual patients assign different values to different durations of time-related freedoms, in part because differing severities of disease (and corresponding differences in natural history) affect different time frames and in part because the longer the trial, the more likely there will be crossovers (e.g., from medical to surgical therapy).\textsuperscript{915,916} Also, the greater the number of risk factors associated with the condition for which treatment is being evaluated, the greater the potential heterogeneity (number of subsets) of patients with that condition and the greater the likelihood that a yes/no answer will apply only to some subset of patients. In such situations, a randomized trial may have the disadvantage of including only a limited number of subsets. It may in fact apply to no subset, because the “average patient” for whom the answer is derived may not exist except as a computation. Trials have addressed this problem by basing the randomization on subsets\textsuperscript{96} or by later analyzing subsets by stratification (but see concerns raised by Guillemin\textsuperscript{939} or by multivariable analysis).\textsuperscript{981}

These considerations, in addition to ethical concerns,\textsuperscript{955,957,958} have fueled the debate about whether surgery is an appropriate arena for randomized trials of innovation, devices, and operations.\textsuperscript{911,929,927,934,935,937,1,29} Some argue strongly that randomization should be required at the outset of every introduction of new therapy.\textsuperscript{935} In three related articles arising from the Balliol Colloquium held at the University of Oxford between 2007 and 2009, clinicians and anesthesiologists sought to clarify the issues surrounding surgical clinical trials.\textsuperscript{941,955,957} They recognized important stages in developing a surgical technique, starting with innovation, progressing through development and exploration, to assessment and long-term outcomes. They then explore options for evaluative studies and barriers to each, including sham operations and nonoperative treatment alternatives.\textsuperscript{915} They end with an IDEAL model for surgical development (idea, development, exploration, assessment, long-term study) and the role of feasibility-randomized trials in exploration, and definitive trials in assessment, and registries in long-term surveillance.\textsuperscript{951,913}

Steven Piantadosi of Johns Hopkins University describes a number of important methodological problems with conducting successful surgical trials, however (personal communication; November 2001):

- Operations are often not amenable to blinding or use of placebos (sham operations), although there is growing acceptance of this in some cases of surgery, in part because of the huge placebo effect of surgery.\textsuperscript{983,958,912,913,916,981,900} This can introduce bias that may be impossible to control; however, thoughtful and creative study designs can often produce substantial blinding, such as of those assessing outcome.
- Selection bias is difficult to avoid. He notes that it is insufficient to compare patients undergoing operation with those who do not, no matter how similar the groups appear, unless every patient not undergoing operation is completely eligible for surgical intervention.\textsuperscript{926} Judgment is a characteristic of a good surgeon, and the better the surgical judgment, the more likely bias will enter any trial of surgical vs. nonsurgical therapy, even if it is the bias of selecting patients for the trial.
- Surgical therapy is skill-based. Therefore, any result obtained from a trial consists of the inextricable confounding of (1) procedure efficacy and (2) surgical skill.
- Surgery is largely unregulated. Every operation is different, and particularly in treatment of complex congenital heart diseases, tailoring operations to the specific anomaly is expected and often necessary for patient survival. There is little uniformity from patient to patient to provide a basis for randomizing therapy.

Given these potential obstacles to adequate evaluation of surgical procedures ever occurring, McCulloch has proposed a hybrid strategy that begins with a prospective but nonrandomized surgical study during the dissemination phase of development (phase II) that progresses to a phase III randomized clinical trial.\textsuperscript{912} During the phase II study, learning curves are determined, a likely treatment effect is identified for sample-size calculation, consensus is built, and quality measures to confirm delivery of intended operations are drawn up. Failure of these preliminary steps is perhaps what has stirred much of the controversy over the STICH trial of the Dor procedure.\textsuperscript{988,989,962}

Moses\textsuperscript{928} and others\textsuperscript{929,934,935,938,937} present the case for a balance between randomized clinical trials and observational clinical studies. However, observational studies are beset with these same problems of selection bias and skill variance; thus, not to be overlooked are the development and rapid introduction of powerful new methods for drawing causal inferences from nonrandomized trials\textsuperscript{921,929} (see “Causal Inferences” later in this section).

Clinical Studies with Nonrandomly Assigned Treatment

General Comments

Clinical studies with nonrandomly assigned treatment produce little knowledge when improperly performed and interpreted. Because this is often the case, many physicians have a strong bias against studies of this type. However, when properly performed and interpreted, and particularly when they are multinstitutional or externally validated, clinical studies of real-world experience can produce secure knowledge (see Comparative Effectiveness footnote on page 266).

This statement would be considered a hypothesis by some, a fact by others.\textsuperscript{911,914} For those who consider it a hypothesis, the hypothesis could be tested as a separate project in a large randomized trial. Hypothetically, such a trial could have two parts: (1) a trial with randomly assigned treatment and (2) a registry with nonrandomly assigned treatment (a registry usually contains many more patients than a trial). For the test, multivariable analyses would be performed of patients in the registry, with propensity adjustment or matching.\textsuperscript{921,929}
“Propensity Score” later in this section). The resulting multivariable equations for various unfavorable events would then be used to predict the now-known outcomes of the patients randomly assigned to the alternative forms of therapy. Predicted outcomes would be compared with observed outcomes (see Residual Risk in Section VI); if they were the same, the validity of the technique of properly performed and analyzed studies with nonrandomly assigned treatment would, in that instance and clinical setting, be established. If they were not the same, the reason should be investigable.

Causal Inferences

The fundamental objection to using observational clinical data for comparing treatments is that many uncontrolled variables affect outcome.\(^2\) Thus, attributing outcome differences to just one factor—alternative treatment—stretches credibility. Even a cursory glance at the characteristics of patients treated one way vs. another usually reveals that they are different groups. This should be expected because treatment has been selected by experts who believe they know what is best for a given patient. The accusation that one is comparing apples and oranges is well justified.\(^3\)

Indeed, a consistent message since Graunt is that risk factors for outcomes from analyses of clinical experience (and these include treatment differences) are associations, not causal relations.\(^4\) Multivariable adjustment for differences in outcome is valuable but not guaranteed to be effective in eliminating selection bias as the genesis of a difference in outcome (a form of confounding).\(^5\) Indeed, developers of balancing score methods claim that the difference in outcome between patients who have similar balancing scores but receive different treatments provides an unbiased estimate of the effect attributable to the comparison variable of interest.\(^6\) That is technical jargon for saying that the method can identify the apples from among the mixed fruit of clinical practice variance, transforming an apples-to-oranges comparison into an apples-to-oranges comparison.\(^7\)

Randomly assigning patients to alternative treatments in clinical trials balances both patient characteristics (at least in the long run) and number of subjects in each treatment arm. In a nonrandomized setting, neither patient characteristics nor number of patients is balanced for each treatment. A balancing score achieves local balance in patient characteristics at the expense of unbalancing \(n\). Tables 6-3 and 6-4 illustrate local balance of patient characteristics achieved by using a specific balancing score known as the propensity score (see “Propensity Score” later in this section for details on how it is derived from patient data). Table 6-3 demonstrates that patients on long-term aspirin therapy have dissimilar characteristics from those not on this therapy. Unadjusted comparison of outcomes in these two groups is invalid—an apples-to-oranges comparison.\(^8\) Therefore, multivariable logistic regression analysis (see “Logistic Regression Analysis” in Section IV) was performed to identify factors predictive of treatment received (long-term aspirin vs. not).\(^9\) The resulting logistic equation was solved for each patient’s probability of being on long-term aspirin therapy. This probability is one expression of what is known as a propensity score (in this case, the propensity to be on long-term aspirin therapy). Patients were then sorted

### Table 6-3 Selected Patient Characteristics According to Long-Term Aspirin Use in Patients Undergoing Stress Echocardiography for Known or Suspected Coronary Artery Disease\(^a\)

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>ASA</th>
<th>No ASA</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n)</td>
<td>2455</td>
<td>4072</td>
<td>.001</td>
</tr>
<tr>
<td>Men (%)</td>
<td>49</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Age (mean ± SD, years)</td>
<td>62 ± 11</td>
<td>56 ± 12</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>10</td>
<td>13</td>
<td>.001</td>
</tr>
<tr>
<td>Resting heart rate (beats · min(^{-1}))</td>
<td>74 ± 13</td>
<td>78 ± 14</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>50 ± 9</td>
<td>53 ± 7</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Data from Gum and colleagues.\(^a\)

\(^a\)Table shows that patient characteristics differ importantly, making direct comparisons of outcome invalid. As shown in original article, many other patient characteristics differed between the two groups.

Key: ASA, Long-term aspirin use; SD, standard deviation.
The most widely used balancing score is the propensity score. It provides for each patient an estimate of the probability of belonging to one group vs. another (group membership). Here we describe (1) designing the nonrandomized study, (2) constructing a propensity model, (3) calculating a propensity score for each patient using the propensity model, and (4) using the propensity score in various ways for effecting a balanced comparison.

Designing the Nonrandomized Study

The essential approach to a comparison of treatment outcomes in a nonrandomized setting is to design the comparison as if it were a randomized clinical trial and to interpret the resulting analyses as if they emanated from such a trial. This essential approach is emphasized in Rubin’s 2007 article, “The Design versus the Analysis of Observational Studies for Causal Effects: Parallels with the Design of Randomized Trials.”

As noted by Rubin, “I mean all contemplating, collecting, organizing, and analyzing data that takes place prior to seeing any outcome data.” He emphasizes by this statement his thesis that a nonrandomized set of observations should be conceptualized as a broken randomized experiment… with a lost rule for “patient allocation, and specifically for the propensity score, which the analysis will attempt to use.”

Table 6-4  Selected Patient Characteristics According to Long-Term Aspirin Use in Patients Undergoing Stress Echocardiography for Known or Suspected Coronary Artery Disease: Stratified by Propensity Score for Aspirin Use

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>Quintile I</th>
<th>Quintile II</th>
<th>Quintile III</th>
<th>Quintile IV</th>
<th>Quintile V</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>ASA</td>
<td>No ASA</td>
<td>ASA</td>
<td>No ASA</td>
<td>ASA</td>
</tr>
<tr>
<td>Men (%)</td>
<td>22</td>
<td>1092</td>
<td>194</td>
<td>1111</td>
<td>74</td>
</tr>
<tr>
<td>Age (years)</td>
<td>55</td>
<td>49</td>
<td>56</td>
<td>55</td>
<td>61</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>15</td>
<td>13</td>
<td>15</td>
<td>15</td>
<td>12</td>
</tr>
<tr>
<td>Resting heart rate (beats·min⁻¹)</td>
<td>84</td>
<td>83</td>
<td>79</td>
<td>79</td>
<td>76</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>53</td>
<td>54</td>
<td>54</td>
<td>54</td>
<td>53</td>
</tr>
</tbody>
</table>

Data from Gum and colleagues.

Table 6-5  Balance in Patient and Selection Characteristics Achieved by Unbalancing Number of Cases in Each Propensity-Ranked Group in Three Separate Studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Factor Present, n</th>
<th>Factor Absent, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-Term Aspirin Use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quintile 1</td>
<td>113</td>
<td>1192</td>
</tr>
<tr>
<td>Quintile 2</td>
<td>194</td>
<td>1111</td>
</tr>
<tr>
<td>Quintile 3</td>
<td>384</td>
<td>922</td>
</tr>
<tr>
<td>Quintile 4</td>
<td>719</td>
<td>586</td>
</tr>
<tr>
<td>Quintile 5</td>
<td>1045</td>
<td>261</td>
</tr>
<tr>
<td>Natural Selection: Preoperative AF in Degenerative MV Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quintile 1</td>
<td>2</td>
<td>225</td>
</tr>
<tr>
<td>Quintile 2</td>
<td>13</td>
<td>214</td>
</tr>
<tr>
<td>Quintile 3</td>
<td>32</td>
<td>195</td>
</tr>
<tr>
<td>Quintile 4</td>
<td>78</td>
<td>149</td>
</tr>
<tr>
<td>Quintile 5</td>
<td>162</td>
<td>66</td>
</tr>
<tr>
<td>OPCAB versus On-Pump</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quintile 1</td>
<td>40</td>
<td>702</td>
</tr>
<tr>
<td>Quintile 2</td>
<td>71</td>
<td>671</td>
</tr>
<tr>
<td>Quintile 3</td>
<td>61</td>
<td>682</td>
</tr>
<tr>
<td>Quintile 4</td>
<td>90</td>
<td>652</td>
</tr>
<tr>
<td>Quintile 5</td>
<td>219</td>
<td>524</td>
</tr>
</tbody>
</table>

Key: AF, Atrial fibrillation; MV, mitral valve; OPCAB, off-pump coronary artery bypass grafting.
construct.” For example, the investigator should ask, “Could each patient in all comparison groups be treated by all therapies considered? If not, this constitutes specific inclusion and exclusion criteria. If this were a randomized trial, when would randomization take place? One must only use variables to construct a propensity score that would be known at the time randomization would have occurred, not after that; this means that variables chosen in the propensity score analysis are not those that could possibly be affected by the treatment.

**Constructing a Propensity Model** For a two-group comparison, typically, multivariable logistic regression is used to identify factors predictive of group membership (see “Logistic Regression Analysis” in Section IV). In most respects, this is what cardiac surgery groups have done for years—find correlates of an event. In this case, it is not risk factors for an outcome event, but rather correlates of membership in one or the other comparison group of interest.

We recommend initially formulating a parsimonious multivariable explanatory model that identifies common denominators of group membership (see Multivariable Analysis in Section IV). Once this traditional modeling is completed, a further step is taken to generate the propensity model, which augments the traditional model by other factors, even if not statistically significant. Thus, the propensity model is not parsimonious. The goal is to balance patient characteristics by whatever means possible, incorporating “everything” recorded that may relate to either systematic bias or simply bad luck, no matter the statistical significance. (However, this is not to say that the addition of nonsignificant variables is done carelessly; the same rigor in variable preparation described in Multivariable Analysis in Section IV is mandatory.) It is important to use as many continuous variables as possible to represent these patient characteristics, because it produces a fine, as opposed to coarse, set of values when the propensity score is calculated.

When taken to the extreme, forming the propensity model can cause problems because medical data tend to have many variables that measure the same thing. The solution is to pick one variable from among a closely correlated cluster of variables as a representative of the cluster. An example is to select one variable representing body size from among height, weight, body surface area, and body mass index.

**Calculating a Propensity Score** Once the propensity modeling is completed, a propensity score is calculated for each patient. A logistic regression analysis, such as is used for the propensity model, produces a coefficient or numeric weight for each variable (Box 6-5). The coefficient maps the units of measurement of the variable into units of risk. Specifically, a given patient’s value for a variable is transformed into risk units by multiplying by the coefficient. If the coefficient is 1.13 and the variable is “male” with a value of 1 (for “yes”), the result will be 1.13 risk units. If the coefficient is 0.023 for the variable “age” and a patient is 61.3 years old, 0.023 times 61.3 is 1.41 risk units.

One continues through the list of model variables, multiplying the coefficient by the specific value for each variable. When finished, the resulting products are summed. To this sum is added the intercept of the model (see Box 6-5), and the result is the propensity score. Note that technically, the intercept of the model, which is constant for all patients, does not have to be added; however, in addition to using the propensity score in logit risk units as described here, it may be used as a probability, for which the intercept is necessary.

**Using Propensity Score for Comparisons** Once the propensity model is constructed and a propensity score is calculated for each patient, three common types of comparison are employed: matching, stratification, and multivariable adjustment.

The propensity score can be used as the sole criterion for matching pairs of patients (Table 6-6). Although a number of matching strategies have been used by statisticians for many years, new optimal matching algorithms have arisen within computer science and operations research. These have been motivated by the need to optimally match volume of Intranet and Internet traffic to computer network configurations. In addition, Rubin (personal communication, 2008) has suggested matching with replacement vs. the usual “greedy” matching, which removes matched patients from further consideration. Indeed, matching can be bootstrapped, creating multiple matched comparison groups over which outcome can be averaged.

Rarely does one find exact matches. Instead, a patient is selected from the control group whose propensity score is nearest to that of a patient in the case group. If multiple patients are close in propensity scores, optional selection among these candidates can be used. (Remarkably, problems of matching on multiple variables disappear by compressing all patient characteristics into a single score (compare Table 6-6 with unmatched data in Table 6-3).)

Tables 6-4 and 6-6 demonstrate that such matching works astonishingly well. The comparison data sets have all the appearances of a randomized study! The average effect of the comparison variable of interest is assessed as the difference in outcome between the groups of matched pairs. However, unlike a randomized study, the method is unlikely to balance unmeasured variables well, and this may be fatal to the inference.

Once patients are matched, it is important to diagnostically test the quality of matching. This can be accomplished visually by graphs of standardized differences (Fig. 6-3). Differences that were substantial should virtually disappear. If they do not, it is possible that interaction terms (multiplicative factors rather than additive factors) may be required.

A graph of propensity scores for the groups is instructive (Fig. 6-4). The scores for two treatments may nearly overlap, as they would for a randomized trial. On the other hand, there may be little overlap, as in Fig. 6-5, and the comparison focuses on the center part of the spectrum of propensity score where there is substantial overlap (virtual equipoise).

Outcome can be compared within broad groupings of patients called strata or subclasses, according to propensity score. After patients are sorted by propensity score, they are divided into equal-sized groups. For example, they may be split into five groups, or quintiles (see Tables 6-4 and 6-5), but fewer or more groups may be used, depending on the size of the study. Comparison of outcome for the comparison variable of interest is made within each stratum. If a consistent difference in outcome is not observed across strata, intensive investigation is required. Usually, something is discovered about the characteristics of the disease, the patients, or their clinical condition that results in different outcomes across the spectrum of disease. For example, in their study of ischemic mitral regurgitation, Gillinov and colleagues discovered that the difference in survival between those
undergoing repair vs. replacement progressively narrowed as complexity of the pattern of regurgitation increased and condition of the patient worsened (Fig. 6-6). Apparent anomalies such as this give important insight into the nature of the disease and its treatment.

The propensity score for each patient can be included in a multivariable analysis of outcome. Such an analysis includes both the comparison variable of interest and the propensity score. The propensity score adjusts the apparent influence of the comparison variable of interest for patient selection differences not accounted for by other variables in the analysis.

Logistic Regression

Sir Francis Galton, cousin of Charles Darwin, explored the relation between heights of adult children and average height of both parents (midparent height). He found that children born to tall parents were in general taller than their parents, and children born to short parents, shorter. He called this “regression towards mediocrity.” He even generated a “forecaster” for predicting son and daughter height as a function of father and mother height. It is presented in an interesting way as pendulums of a clock, with chains around two different-sized wheels equivalent to the different weights (regression coefficients) generated by the regression equation!

Today, any empirical relation of an outcome or dependent variable to one or more independent variables (see later Box 6-18) is termed a regression analysis. Several of these are described below.

**Linear**

The form of a linear regression equation for a single dependent variable \( Y \) and a single independent variable \( x \) is:

\[
Y = a + bx
\]

where \( a \) is called the intercept (the estimate of \( Y \) when \( x \) is zero), and \( b \) is the slope (the increment in \( Y \) for a one-unit change in \( x \)). More generally, when there are a number of \( x \)'s:

\[
Y = \beta_0 + \beta_1 x_1 + \cdots + \beta_k x_k
\]

where \( \beta_0 \) is the intercept, \( x_1 \) through \( x_k \) are independent variables, and \( \beta_1 \) through \( \beta_k \) are weights, regression coefficients, or model parameters (see later Box 6-13) that are multiplied by each \( x \) to produce an incremental change in \( Y \).

It would be surprising if biological systems behaved as a series of additive weighted terms like this. However, this empirical formulation has been valuable under many circumstances in which there has been no basis for constructing a biomathematical model based on biological mechanisms (computational biology).

An important assumption is that \( Y \) is distributed in Gaussian fashion (see Box 6-15), and this may require the scale of the raw data to be mathematically transformed.

**Log-Linear**

A log-linear regression equation has the following form:

\[
\ln(Y) = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \cdots + \beta_k x_k
\]

where \( \ln \) is the logarithm to base \( e \). Such a format is used, for example, in the Cox proportional hazards regression model (see Section IV). However, in studies of events (see “Logistic Regression Analysis” and Time-Related Events in Section IV), the estimation procedure does not actually use a \( Y \). Rather, just as in finding the parameter estimates called mean and standard deviation of the Gaussian equation (see Box 6-15), parameter estimation procedures use the data directly. Once these parameters are estimated, a predicted \( Y \) can be calculated.

**Model**

A model is a representation of a real system, concept, or data, and particularly the functional relationships within these; it is simpler to work with, yet predicts real system, concept, or data behavior.

**Mathematical Model**

A mathematical model consists of one or more interrelated equations that represent a real system, concept, or data by mathematical symbols. These equations contain symbols that represent parameters (constants) whose values are estimated from data and an estimating procedure.

A mathematical model may be based on a theory of nature or mechanistic understanding of what the real system, concept, or data represent (biomathematical models or computational biology). It may also be empirical. The latter characterizes most models in statistics, as depicted previously. The Gaussian distribution is an empirical mathematical model of data whose two parameters are called mean and standard deviation (see Box 6-15). All mathematical models are more compact than raw data, summarizing them by a small number of parameters in a ratio of 5 to 10 or more to 1.

**Nonlinear Equation**

When applied to mathematical models, it is an equation that can be solved directly with respect to any of its parameter values by simple mathematical manipulation. A linear regression equation is a linear model.

Occasionally the propensity score remains statistically significant in such a multivariable model. This constitutes evidence that adjustment for selection factors by multivariable analysis alone is ineffective, something that cannot be ignored. It may mean that not all variables important for bias reduction have been incorporated into the model, such as when one is using a simple set of variables. It may mean that an important modulating or synergistic effect of the comparison variable occurs across propensity scores, as noted previously (e.g., the mechanism of disease may be different within quintiles). It may mean that important interactions of the variable of interest with other variables have not been
accounted for, leading to a systematic difference identified by the propensity score. The collaborating statistician must investigate and resolve these possibilities. Understanding aside, this statistically significant propensity score has performed its intended function of adjusting the variable representing the group difference.

In some settings in which the number of events is small, the propensity score can be used as the sole means of adjusting for the variable representing the groups being compared.

Figure 6-3 Covariable balance plot before and after propensity score matching on selected covariables. Symbols depict percent standardized differences for covariables between patients in less invasive and conventional groups. Key: BMI, Body mass index; BUN, blood urea nitrogen; COPD, chronic obstructive pulmonary disease; Dysfunct., dysfunction; HTN, hypertension; LV, left ventricular; Regurg., regurgitation; TV, tricuspid valve.

Figure 6-4 Distribution of propensity scores for conventional and less invasive approaches for aortic valve replacement.

Figure 6-5 Mirrored histogram of distribution of propensity scores for conventional (bars above zero line) and less invasive (bars below zero line) approaches for aortic valve replacement. Darkened area represents matched patient pairs, showing that they cover the complete spectrum of cases but predominate in the central area (area of “virtual equipoise”).

The propensity score may reveal that a large number of patients in one group do not have scores close to patients in the other. Thus, some patients may not be matched. If stratification is used, quintiles of patients may have hardly any matches at one or the other, or both, ends of the propensity spectrum, and these remaining may not be well matched.

The knee-jerk reaction is to infer that these unmatched patients represent, indeed, apples and oranges unsuited for direct comparison. However, the most common reason for lack of matches is that a strong surrogate for the comparison group variable has been included inadvertently in the propensity score. This variable must be removed and the propensity model revised. For example, Banbury and colleagues studied blood use with vacuum-assisted venous return (VAVR) by comparing two sequential VAVR configurations with gravity drainage. Because the three groups represented consecutive sequences of patients, date of operation was a strong surrogate for group membership. Furthermore, physical configuration and size of tubing and cannulae varied systematically among groups. Thus, priming volume also was a strong surrogate for group. Neither could be used in forming propensity scores (multiple scores in this instance).

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
<th>ASA</th>
<th>No ASA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1351</td>
<td>1351</td>
</tr>
<tr>
<td>Men (%)</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60</td>
<td>61</td>
</tr>
<tr>
<td>Smoker (%)</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Resting heart rate (beats · min⁻¹)</td>
<td>77</td>
<td>76</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>51</td>
<td>51</td>
</tr>
</tbody>
</table>

Data from Gum and colleagues. Table illustrates ability of the propensity score to produce what appears to be a randomized study balancing both patient characteristics and n. Key: ASA, Long-term aspirin use.

Table 6-6 Comparison of Patient Characteristics According to Long-Term Aspirin Use in Propensity-Matched Pairs

<table>
<thead>
<tr>
<th>Patient Characteristic</th>
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<td>Men (%)</td>
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<td>76</td>
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<tr>
<td>Ejection fraction (%)</td>
<td>51</td>
<td>51</td>
</tr>
</tbody>
</table>

Figure 6-4 Distribution of propensity scores for conventional and less invasive approaches for aortic valve replacement.
If this is not the case, the analysis may indeed have identified truly unmatchable cases (mixed fruit). In some settings, they represent a different end of the spectrum of disease for which different therapies have been applied systematically.\textsuperscript{G14} Often the first clue to this “anomaly” is finding that the influence of the comparison variable of interest is inconsistent across quintiles.\textsuperscript{G14} Indeed, this emphasizes the nature of comparisons with balancing score methodology: the comparisons relate only to the subset of patients who are truly apples-to-apples. Comparing these apples to the remaining oranges with respect to outcomes is not valid. The oranges result from systematic selection of patients for one vs. the other treatment. The area of broad overlap of propensity scores, in contrast, can be thought of as the area of virtual equipoise (see Fig. 6-5).

Thus, when apples and oranges (and other “mixed fruit”) are revealed by a propensity analysis, investigation should be intensified rather than the oranges simply being set aside. After the investigations are complete, comparisons among the well-matched patients can proceed with known boundaries within which valid comparisons are possible.

**Limitations**

Some investigators tell us that balancing score methods are valid only for large studies, citing Rubin.\textsuperscript{R28} It is true that large numbers facilitate certain uses of these scores, such as stratification. Case-control matching is also better when a large group of controls far exceeding cases is available. However, we believe there is considerable latitude in matching that still reduces bias; the method seems to “work” even for modest-sized data sets.

Another limitation is having few variables available for propensity modeling. The propensity score is seriously degraded when important variables influencing selection have not been collected.\textsuperscript{D23} A corollary to this is that unmeasured variables cannot be reliably balanced. If these are influential on outcome, a spurious inference may be made.\textsuperscript{D8}

The propensity score may not eliminate all selection bias.\textsuperscript{R18} This may be attributed to limitations of the modeling itself imposed by the linear combination of factors in the regression analysis that generates the balancing score (see Box 6-5). If the comparison data sets are comparable in size, it may not be possible to match every patient in the smaller of the two data sets, simply because closely comparable patients have been “used up,” unless bootstrap sampling with replacement has been used.

Perhaps the most important limitation is inextricable confounding. Suppose one wishes to compare on-pump CABG with off-pump operations. One designs a study to compare the results of institution A, which performs only off-pump bypass, with those of institution B, which performs only on-pump bypass. Even after careful application of propensity score methods, it remains impossible to distinguish between an institutional and a treatment difference, because they are inextricably intertwined (confounded); that is, the values for institution and treatment are 100% correlated.

**Extension**

At times, one may wish to compare more than two groups, such as groups representing three different valve types. Under this circumstance, multiple propensity models are formulated.\textsuperscript{R26} We prefer to generate fully conditional multiple logistic propensity scores\textsuperscript{R28} (see “Polytomous and

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**Figure 6-6** Demonstration of changing risk across propensity score for mitral valve repair vs. replacement. Because of small numbers of patients with mitral valve replacement in quintiles III through V, these quintiles are grouped together. Patient profiles are similar in each quintile but differ across quintiles. Each symbol represents a death according to the Kaplan-Meier estimator. Vertical bars enclose asymmetric 68% confidence limits (CL); solid lines enclosed within dashed 68% CLs represent parametric survival estimates; numbers in parentheses are numbers of patients traced beyond that point. \( P \) values are for log-rank test. A, Quintile I. B, Quintile II. C, Quintiles III through V. (From Gillinov and colleagues.\textsuperscript{G14})
Ordinal Logistic Regression” in Section IV), although some believe this “correctness” is not essential.

Most applications of balancing scores have been concerned with dichotomous (yes/no) comparison group variables. However, balancing scores can be extended to a multiple-state ordered variable (ordinal) or even a continuous variable. An example of the latter is use of correlates of prosthesis size as a balancing score to isolate the possible causal influence of valve size on outcome.

Logistic regression is not the only way to formulate propensity scores. A nonparametric machine learning technique—random forests (see Classification Methods in Section VI)—can be used and has been found by Lee and colleagues to better balance groups, with reduced bias. We have formulated a generalized theorem as an extension of the work of Imai and van Dyk for propensity scores and devised a data-adaptive, random-forest nearest-neighbor algorithm that simultaneously matches patients and estimates the treatment effect from thousands of bootstrap samples, while simultaneously refining the characteristics of “true” oranges—noncomparable patients.

TECHNIQUE FOR SUCCESSFUL CLINICAL RESEARCH

Marbán and Braunwald, in reflecting on training the clinician-investigator, provide guiding principles for successful clinical research. Among these:

- Choose the right project.
- Embrace the unknown.
- Use state-of-the-art approaches.
- Do not become the slave of a single technique.
- Never underestimate the power of the written or spoken word.

In this subsection, we emphasize these principles and suggest ways to operationalize them.

Because of increasingly limited resources for conducting serious clinical research, a deliberate plan is needed to successfully carry a study through from inception to publication. Here we outline such a plan for study of a clinical question for which clinical experience (a patient cohort) will provide the data. This plan appears as a linear workflow (Fig. 6-7); in reality, most research efforts do not proceed linearly but rather iteratively, with each step being more refined and usually more focused right up to the last revision of the manuscript. As is true of most workflow, there are mileposts at which there need to be deliverables, whether a written proposal, data, analyses, tables and graphs, a manuscript, or page proofs.

Research Proposal

Because of the necessity for Institutional Review Board (Ethics Committee) oversight, but also because it is good science, every serious clinical study needs a formal proposal (Box 6-6). This proposal serves to clarify and bring into focus

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2 Although the technique described is aimed at clinical studies of cohorts of patients, many aspects apply to randomized clinical trials, retrospective clinical studies, and even laboratory research.
is to collect data for too many variables, with little thought given to how they might be used. This wastes scarce resources and compromises the quality of collecting relevant variables.

Dr. John Kirklin called this “the Christmas tree effect.”

Sample Size
For any study, a minimum sample size is needed to detect an effect reliably. For events (e.g., death), sample size is dependent on the number of events, not size of the study group (see Box 6-4).

Feasibility
Successful projects are built on ascertaining that (1) the study population can be identified reliably (ideally from electronic databases), (2) the values for variables required are either already in electronic format (but may need to be verified) or can be obtained readily by review of medical documents, (3) the sample size is sufficient to answer the question (see Box 6-4), (4) clinical practice is not completely confounded with the question being asked (one cannot compare two techniques if only one is performed; one may not be able to unravel confounding of two techniques if one surgeon performs one and another the other), and (5) institutional resources are available (one cannot assess PET scans if they are not performed). If the project is not feasible, the study should be abandoned or a long-range plan devised for prospectively obtaining and recording the needed data.

Limitations and Anticipated Problems
Every study has limitations and anticipated problems. These can be identified by a brief but serious investigation of the state of all the above. If any appear insurmountable or present fatal flaws that preclude later publication, the study should be abandoned. There are always more questions than can be addressed in cardiac surgery, so not being able to answer some specific research question is not an excuse to abandon the search for new knowledge!

Data Analysis
Details of analytic methodology should be formulated in collaboration with a statistician or other quantitative analyst (see Section IV). The surgeon-investigator often does not recognize or know the most appropriate analytic methodology. Collaboration with a statistician or other quantitative professional should reveal appropriate methodology and whether the proposed manner in which data are to be collected will meet the requirements of the methodology. Unfortunately, the surgical literature is not a good resource for determining appropriate methods.

Institutional Review Board (IRB)
Any proposal that does not use existing data already approved for use in research by an IRB requires study-specific IRB approval before any research is commenced.

Timetable and Deliverables
Develop a timetable for data abstraction, data set generation (see Fig. 6-7), data analysis, and reporting, all deliverables at various milestones in the study. If the timetable is beyond that tolerable, abandon the study. It is rare for a study to be completed in a year from start to finish. This emphasizes both the bottlenecks of research and the need for lifelong commitment. Although abstract deadlines often drive the timetable, this is a poor milepost (see “Presentation” in Section V).
the question being asked. A common mistake is to ask questions that are unfocused, or uninteresting, or overworked, or that do not target an area of importance. Marbán and Braunwald say, “Ask a bold question...about which you can feel passionate.”

Brainstorming with fellow surgeons and collaborators is essential. The first deliverable is the research question, well debated.

The next step is to define clearly the inclusion and exclusion criteria for the study group (see “Identify Study Group” in Section III). A common mistake is to define this group too narrowly, such that cases “fall through the cracks” or an insufficient spectrum is stipulated (see “Continuity versus Discontinuity in Nature” earlier in this section). The inclusive dates should be considered carefully. Readers will be suspicious if the dates are “strange”; did you stop just before a series of deaths? Whole years or at least half years dispel these suspicions. Similarly, suspicion arises when a study consists of a “nice” number of patients, such as “the first 100 or 1000 repairs.”

In defining the study group, particular care should be taken to include the denominator. For example, a study may be made of postoperative neurologic events, but it is also important to have a denominator to put these events into context. Or one may study a new surgical technique but be unable to compare it with the standard technique without a comparison group. A study of only numerators is the true definition of a retrospective study; if the denominator is included, it is a prospective or cohort study (Box 6-7).

End points (results, outcomes) must be clearly defined in a reproducible fashion. Generally, every event should be accompanied by its date of occurrence. A common failing is that repeated end points (e.g., thromboembolism, assessments of functional status) are recorded only the first or most recent time they occur. This should never be done. Techniques to analyze repeated end points are available (see Longitudinal Outcomes in Section IV).

Careful attention must be paid to the variables that will be studied. They should be pertinent to the study question (purpose, objective, hypothesis). A common failing is to collect values for too many variables such that quality suffers. This error usually arises in a reasonable and understandable way. The surgeon-investigator reasons that because the patient records must be reviewed, a number of other variables may as well be abstracted “while there.” Or realizing the full complexity of the clinical setting, the surgeon-investigator feels compelled to collect information on all possible ramifications of the study, even if it is quite peripheral to the focus of the study. This is termed the “Christmas tree effect,” meaning adding ornament upon ornament until they dominate what once was “just” a fine tree. There needs to be a balance between so sparse a set of variables that little can be done by way of risk factor identification or balancing characteristics of the group, and so rich a set of variables that the study flounders or insufficient care is given to the quality and completeness of relevant variables.

Study feasibility must then be assessed. A common failing is forgetting that if an outcome event is the end point, the effective sample size is the number of events observed (see Box 6-4). A study may have 1000 patients, but if only 10 events are observed, one cannot find multiple risk factors for those events.

It is wise at the outset to plan the data analysis. Often, for example, the setup for the analysis data set is specific to the methods of analysis. This has to be known by the data managers (see Appendix 6A).

A necessary step is review of the literature. Sifting through articles is often painful, but it should result in identifying those few key papers that are absolutely pertinent to the study. Unfortunately, the search is too often confined to recent literature, and this may result in “reinventing the wheel.”

For executing the study, some realistic time frame with deliverables should be established with collaborators. A common failing is not providing sufficient time for data verification and other aspects of data management that are the heart of a high-quality study. Actual analysis of data may consume one tenth the time of high-quality data preparation.

**Box 6-7 Retrospective, Prospective**

When clinical data are used for research, some term this retrospective research (e.g., the National Institutes of Health). Epidemiologists also perform what they call retrospective studies that bear no resemblance to typical clinical studies. Thus, confusion has been introduced by use of both the word retrospective and prospective to designate interchangeably two antithetical types of clinical study. The confusion is perpetuated by institutional review boards and government agencies that believe one (prospective), but not the other (retrospective), constitutes “research” on human subjects. The confusion can be eliminated by differentiating between (1) the temporal direction of study design and (2) the temporal direction of data collection for a study, as did Feinstein.

**Temporal Direction of Study Design**

The temporal pursuit of patients may be forward. That is, a cohort (group) of patients is defined at some common time zero, such as operation, and this group is followed for outcomes. Some call this a cohort study. It is the most typical type of study in cardiac surgery: A group of patients is operated on and outcome is assessed. Statisticians have called this a prospective clinical study design; it moves from a defined time zero forward (which is what the word prospective means).

In contrast, temporal pursuit of patients may be backward. Generally in such a study, an outcome event occurs, such as death from a communicable disease. Starting from this event (generally, a group of such events), the study proceeds backward to attempt to ascertain its cause. Feinstein suggests calling such a study a “trohoc” study (cohort spelled backwards). For years, many epidemiologists called this a retrospective clinical study design because of its backward temporal direction of study.

**Temporal Direction of Data Collection**

Increasingly, retrospective is used to designate the temporal aspect of collecting data from existing clinical records for either a cohort or trohoc study. If charts or radiographs of past patients in a cohort study must be reviewed or echocardiographic features measured, the data collection is retrospective. Feinstein has coined the term “retrolective” for this to avoid use of the word retrospective because of the previously well-understood meaning of the latter in study design. If registry data are collected concurrently with patient care, this process is surely prospective data collection. Feinstein suggests calling such data collection “prolective” data collection.
The completed formal research proposal becomes the second deliverable of a study. It is likely to be updated throughout the course of a study, and we advocate online tracking of each study, with periodic updates of the protocol as one of the tasks in project management.

Database Development and Verification

The next step for successful research is careful attention to the data themselves (see “Extract Values for Variables” in Section III). If electronically available data are to be used, every variable must be defined both medically and at the database content level (see Section II). If data are to be collected de novo, an appropriate database must be developed (see Fig. 6-7). Every variable must be in a format of one value per variable. These variables must follow a controlled vocabulary for analysis, not free text. The deliverable at this stage is a database ready for data to be collected and entered.

Data Collection

Research on existing databases for which blanket IRB approval has been secured may not require separate approval of each study. However, before any de novo data are gathered from medical records or by patient follow-up, separate IRB approval may be required.

There is generally a core set of variables (core data elements) that should be collected for each patient (Box 6-8). In many cardiac surgical settings, these data elements are stipulated by regulatory agencies (e.g., the state of New York) or surgical societies (e.g., Society of Thoracic Surgeons National Database). They include demographics (note that it is essential to record patients’ date of birth rather than age because age can be calculated from date of birth to any chosen “time zero”), the cardiac procedure and possibly clinical symptoms and status at time of operation, past cardiac medical history (particularly prior cardiac procedures), disease etiology, coexisting cardiac defects, coexisting noncardiac morbidity (e.g., diabetes), laboratory measurements known to be consistently associated with clinical outcomes, findings of diagnostic testing, intraoperative findings, support techniques during operation, and factors related to experience (e.g., date of operation).

Beyond these core variables, there will likely be a need for variables specific to a particular study. These should be identified and reproducibly defined. The danger is specifying too many variables; however, a thoughtfully compiled list adds depth to a study. Further, experienced investigators realize that in the midst of a study, it occasionally becomes evident that some variables require refinement, others collecting de novo, others rechecking, and others redefining. It is important to understand that when this occurs, the variables must be refined, collected, rechecked, or redefined uniformly for every patient in the study.

Clinical studies are only as accurate and complete as the data available in patients’ records. Therefore, cardiac surgeons and team members seriously interested in scientific progress must ensure their preoperative, operative, and postoperative records are clear, organized, precise, and extensive, so that information gathering from these records can be complete and meaningful. The records should emphasize description, and although they may well contain the conclusions of the moment, it is the description of basic observations that becomes useful in later analyses.

Verification

The first step in data verification is to enter values for each data element (variable) for 5 to 10 patients only. These reveal problems of definition, incomplete “pick lists,” missed variables, difficult-to-find variables that may not be worth the effort to locate, poor-quality variables/incomplete recording, lack of good definition, inconsistent recording, and questionable quality of observations. Once these issues are addressed, general data abstraction may proceed (see “Verify Data” in Section III).
When all values for variables are in a computer database, formal verification commences. This can take three general forms: (1) value-by-value checking of recorded data against primary source documents, (2) random quality checking, and (3) automatic reasonableness checking. If a routine activity of recording core data elements (see Section III, Data) is used, it is wise to verify each element initially to identify those that are rarely in error (these can be “spot checked” by a random process) and those that are more often in error. The latter are usually a small fraction of the whole and are often values requiring interpretation. These may require element-by-element verification.

When it is believed that data are correct (this is an iterative process with the above), they are checked for reasonableness of ranges, including discovery of inconsistencies among correlated values. For example, the database may indicate that a patient had a quadrangular resection of the mitral valve, but someone had failed to record that the posterior leaflet was prolapsing and had ruptured chordae, or the database records that a patient is 60 cm tall and weighs 180 kg; this is likely a problem of confused units of measurement (inches and pounds).

Data Conversion for Analysis
An often underappreciated, unanticipated, and time-consuming effort is conversion of data elements residing in a database to a format suitable for data analysis (see Analysis Data Set in Section III). Even if the day comes that all medical information is recorded as values for variables in a computer-based patient record (see Section II, Computer-Based Patient Record), this step will be unavoidable. Statistical procedures require data to be arranged in “columns and rows,” with each column representing values for a single variable (often in numeric format), and each row either a separate patient or multiple records on a single patient (as in repeated-measures longitudinal data analysis). Unfortunately, this conversion process may involve redundancy, such as the necessity to again document all variables and provide a key to the possible values for each.

This process nearly always involves creating additional variables from a single variable, such as a separate variable for each mutually exclusive etiology of cardiomyopathy. These polytomous variables (lists) are then converted to a series of dichotomous variables (best expressed as 0 for absence and 1 for presence of the listed value).

Some categorical variables are ordinal, such as NYHA functional classes. These may have to be reformulated as an ordered number sequence (e.g., 1-4). Variables recorded with units (e.g., weight in kilograms, weight in pounds) must be converted to a common metric.

Calculated variables are also formed. These include body surface area and body mass index from height and weight, e values (see Chapter 1) from measured cardiac dimensions, ejection fraction from systolic and diastolic ventricular volumes, intervals between date and time variables for which event indicator variables are created, and many other calculations. Because data conversion, creation of derived variables, and formation of calculated variables is time consuming and error prone, groups that conduct a large number of studies often store trusted, well-verified computer code to perform these operations on a repetitive basis.

Often information is coalesced from multiple databases, and these queries, concatenations, and joining functions transpire in this phase of the process. These otherwise arduous functions can, under some circumstances, be automated. Alternatively, a data warehouse composed of multiple disparate electronic data sources can be implemented and maintained and appears to the investigator as a single data source.

An important activity is managing sporadic missing data. If too much data are missing, the variable may be unsuitable for analysis (see “Impute Values” in Section III). Otherwise, missing value imputation is necessary so that entire patients are not removed from analyses, the default option in many analysis programs.

Data Analysis
Specific data analysis methods will be described in Section IV. Here, we simply indicate how this aspect of the research process leads to success.

First, the analysis process leads to understanding of the “raw data,” often called exploratory data analysis. This understanding is gleaned from such analyses as simple descriptive statistics, correlations among variables, simple life tables for time-related events, cumulative distribution graphs of continuously distributed variables (see “Descriptive Statistics” in Section III), and cluster analyses whereby variables with shared information content are identified.

Second, the analytic process attempts to extract meaning from the data by various methods akin to pattern recognition. Answers are sought for questions such as: Which variables relate to outcome and which do not? What inference can be made about whether an association is or is not attributable to chance alone? Might there be a causal relationship? For what might a variable associated with outcome be a surrogate?

What will be discovered is that answering such questions in the most clinically relevant way often outstrips available statistical, biomathematical, and algorithmic methodology! Instead, a question is answered with available techniques, but not the question. Some statisticians, because of insufficient continuing education, lack of needed statistical software, lack of awareness, failure of communication, or lack of time, may explore the data less expertly than required. One of the purposes of this chapter is to stimulate effective collaboration between cardiac surgeons and data analysis experts so that data are analyzed thoroughly and with appropriate methodology.

Interpreting Analyses
It is one thing for a statistician to provide a statistical inference; it is quite another for the cardiac surgeon, using that information, to draw meaningful interpretations that affect patient care.

Kirklin and Blackstone empirically found that the most successful way to embark on this interpretive phase of clinical research is to write on a clean sheet of paper the truest two or three sentences that capture the essence of the findings (and no more!). This important exercise produces an un mini abstract for a paper (whether or not it is required by a journal) and provides the roadmap for writing the manuscript (see Scientific Paper in Section V).
Communicating the Findings

A common error of the surgeon-investigator is to simply summarize the data instead of taking the important step of drawing meaningful clinical inferences from the data and analyses. He or she has not taken the vital step of asking (1) What new knowledge has been gleaned from the clinical investigation? (2) How can this new knowledge be incorporated into better patient care? (3) What do the data suggest in terms of basic research that needs to be stimulated? (4) How can I best communicate information to my local colleagues? (5) How can I best present this information to the cardiac surgical and cardiologic world at large?

Meaningful new knowledge may not be generated because the statistical inferences from data analyses are accepted as the final result. Instead, the results must be studied carefully and many questions asked. Often this will lead to additional analyses that increasingly illuminate the message the data are trying to convey. Graphical depictions are of particular importance in transforming mere numbers on computer printouts to insight. Depictions must lead beyond statistical inference to clinical inference. What have the data revealed about how to better care for patients? This question is the one best linked to the original purpose of the study. If the study has suggested ways to improve patient care, the next step is to put what has been learned into practice (see Section V).

Most studies generate more new questions than they answer. Some of these new questions require additional clinical research. Others require the surgeon-investigator to stimulate colleagues in the basic sciences to investigate fundamental mechanisms of the disease process.

Because most surgeon-investigators are part of a group, an important facet of generating new knowledge is discussing with colleagues the results, statistical and clinical inferences, and implications of a study. Multiple points of view nearly always clarify rather than obscure their interpretation.

Finally, clinical research is not a proprietary activity. Yet, too often manuscripts fail to elucidate from research. One reason may be that an abstract was not accepted for a meeting, perhaps because the data were not thoroughly digested before its submission. Although abstract deadlines may be important mechanisms for wrapping up studies, they too often stifle a serious and contemplative approach to generating new knowledge. A second reason manuscripts do not get written is that the surgeon-investigator views the task as overwhelming. Possibly he or she has not developed an orderly strategy for writing. We provide some guidance for this in Section V. A third barrier to writing is time demands on the surgeon-investigator. Usually, this results from not making writing a priority in one’s professional life. This is a decision that should be made early in one’s surgical career. If dissemination of new knowledge is a desire, then writing must be made a high-priority part of one’s lifestyle.

Section II  Information

Information is a collection of facts. The paper medical record is one such collection of facts about the health care of a patient. In it, observations are recorded (clinical documentation) for communication among healthcare professionals and for workflow (e.g., plan of care, orders). However, perhaps as much as 90% of the information communicated in the care of a patient is never recorded. The attitude of health insurers—“If it is not recorded, it did not happen”—thus represents a sobering lack of appreciation of the way information about patient care is used and communicated. However, it is also an indictment of the way medical practice is documented. Too much is left out of written records, and too many operative reports are poorly organized and incomplete. Too often this reflects the kind of imprecise thinking that gives rise to medical errors (see “Human Error” earlier in this section). If important clinical observations are not recorded during patient care, preferably in a clear, complete, and well-organized (structured) fashion, they are unavailable subsequently for clinical research.

COMPUTER-BASED PATIENT RECORD

In 1991, the IOM (Institute of Medicine) recognized the need not only for computerizing the paper medical record (as the electronic medical record [EMR]) but also for devising a radically different way to record, store, communicate, and use clinical information. They coined the term “computer-based patient record,” or CPR, and distinguished it from the EMR by the fact that it would contain values for variables using a highly controlled vocabulary rather than free text (natural language).

Two decades have passed. Still, there is no universally accepted definition of the CPR beyond that it contains electronically stored information about an individual’s lifetime health status and health care. There is no accepted information (data) model, catalog of data elements, or comprehensive controlled medical vocabulary, all of which are fundamental to developing and implementing the envisioned CPR. There is little movement to capture every health encounter in a patient-owned record; rather, data are siloed within institutions.

These issues aside, for the cardiac surgical group interested in serious clinical research, a CPR with a few specific characteristics could enormously facilitate clinical studies. Furthermore, it could transform the results into dynamic, patient-specific, strategic decision-support tools to enhance patient care.

First and foremost, the CPR must consist of values for variables, selected from a controlled vocabulary. This format for recording information is necessary because analysis now and in the foreseeable future must use information that is formatted in a highly structured, precisely defined fashion, not uncontrolled natural language. Extracting structural information from natural language is a formidable challenge and one that should be unnecessary. Second, the CPR must accommodate time as a fundamental attribute. This includes specific time (date/time stamps), inexact time (about 5 years ago), duration (how long an event lasted, including inexact duration), sequence (second myocardial infarction [MI], before, after), and repetition (number of times, such as three MIs). Third, the CPR must store information in a fashion that permits retrieval not only at the individual patient level but also at the group level, according to specified characteristics. Fourth, the CPR will ideally incorporate mechanisms for using results of clinical studies in a patient-specific fashion for decision support in the broadest sense of the term,
such as patient management algorithms and patient-specific predictions of outcome from equations developed by research.\textsuperscript{12, 14, 20} (see “Use of Incremental Risk Factors” in Section V).

There are many other requirements for CPRs, from human-user interfaces, to administrative and financial functions, to healthcare workflow, to human error avoidance systems, that are beyond the scope of the clinical research theme in this section.

**Ontology**

If medical information is to be gathered and stored as values for variables, a medical vocabulary and organizing syntax must be available.\textsuperscript{14} A technical term for this is *ontology*.

In Greek philosophy, *ontology* meant “the nature of things.” Specifically, it meant what actually is (reality), not what is perceived (see “Human Error” in Section I) or known (epistemology). In medicine of the 17th and 18th centuries, however, it came to mean a view of disease as real, distinct, classifiable, definable entities. This idea was adopted by computer science to embrace with a single term everything that formally *specifies the concepts and relationships* that can exist for some subject, such as medicine. An ontology permits sharing of information, such as a vocabulary of medicine (terms, phrases), variables, definitions of variables, synonyms, all possible values for variables, classification and relationships of variables (e.g., in terms of anatomy, disease, healthcare delivery), semantics, syntax, and other attributes and relationships.

An ontology for all of medicine does not yet exist. Efforts to develop a unified medical language, such as the Unified Medical Language System (UMLS) of the National Library of Medicine, are well underway and becoming increasingly formalized linguistically as ontologies.\textsuperscript{15}

Ontology is familiar to clinical researchers, who must always have a controlled vocabulary for values for variables, well-defined variables, and explicit interrelations among variables. Without these, there is no way to accurately interpret analyses or relate results to the findings of other investigators. However, a clinical study is a microscopic view of medicine; scaling up to all of medicine is daunting.

Perhaps, then, the simplest way of thinking about an ontology for the researcher is as dictionaries of variables and values and their organizational structure, and some mechanism to develop and maintain them. These attributes have collectively been called *metadata* (data about data) or a *knowledge base*, and metadata-base or knowledge-base management systems, respectively.\textsuperscript{21}

**Information (Data) Model**

An information (data) model is a specification of the arrangement of the most granular piece of information according to specific relationships and the organization of all of these into sets of related information. The objective of an information model is to decrease entropy—that is, to decrease the degree of disorder in the information and thereby increase efficiency of information storage and retrieval (performance).

**Object-Oriented Information Model**

In 1993 at UAB, John Kirklin led a team effort to develop a CPR that would be ideal for clinical care as well as clinical research.\textsuperscript{21} The first step was an attempt to develop an object-oriented information model. These efforts failed. In object technology, only a few formal relationships can be established easily. Failure of the object data model was attributed to the realization that in medicine, “everything is related to everything” on multiple hierarchical (polyhierarchical) levels. Indeed, medical linguistics forms a semantic network.\textsuperscript{51}

**Relational Information Model**

The most ubiquitous information model in business, the relational database model, was found to be even more unsuitable as a medical information model,\textsuperscript{17} just as it is now being found to be unsuitable in complex, rapidly changing, multidimensional businesses such as aircraft building and repair. In relational database technology, variables are arranged as columns of a table, sets of columns are organized as a table, individual patients are in rows, and a set of interrelated tables constitute the database. However, in medicine, information is multidimensional. A given value for a variable must carry with it time, who or what machine generated the value, the context of obtaining the value (“documentation”), format or units of measurement, and a host of attributes and relationships—indeed ontology—that give the value meaning within the context of healthcare delivery. Simply storing a set of values is insufficient. Furthermore, when data must be analyzed, information relevant to the values, such as described earlier, may importantly affect the analysis and must be present even if it seems ancillary. The relational data model also poorly represents and retrieves sequences (in which retention of order is vital) and is difficult to maintain for complex data, because every change (addition, subtraction) in data structure requires the database to be updated.

Popularity of the relational model among clinical researchers stems from its simplicity in handling a microscopic corner of medical information. As soon as a new topic is addressed or new variables must be collected, the typical behavior of the research team is to generate a new specific database. Rarely do these multiple, independent, and to some extent redundant databases communicate with one another across studies. This attests to the inappropriateness of such a simplistic data model for a CPR, and even for a busy cardiac surgery research organization.\textsuperscript{18}

**Semistructured Information Model**

A different kind of information model emerged from an important conference at UAB of leaders in the development of several different types of database as part of the CPR project. After review of the strengths and profound limitations of various information models, a novel approach was suggested by Kirklin and then formalized. He proposed that all information that provided context and meaning to a value for a variable be packaged together. He envisioned that such a complex data element should be able to reside as an independent self-sufficient entity.\textsuperscript{21} (In computer science terminology, this would be called a completely flattened data model.)

This idea has several meritorious implications. First, an electronic container for a collection of complex data elements could consist of a highly stable, totally generic repository for a CPR because it would be required to possess no knowledge of content of any data element. It could therefore manage important information storage and retrieval functions, implement data encryption for privacy and
confidentiality, store knowledge bases used to construct the complex data elements and retrieve them, maintain audit trails, and perform all those functions of database management systems that are independent of data content. The second implication is that as medical knowledge increases, new entries would be made in the knowledge-base dictionaries. These would be updated, not the database structure. Not only would this case database maintenance, it would enforce documentation in the knowledge base. The third implication, and the one most important for clinical research, is that no a priori limitations would be placed on relations; they could be of any dimensionality considered useful at the time. These data elements were retrieved for analysis. Thus, the electronic container is a single variable value-pair augmented with contextual documentation and capable of being modified as new or more knowledge accrues.

Essential characteristics of such an information repository are:

- Self-documentation at the level of individual values for a variable (complex data element)
- Self-reporting at the time of data element retrieval and potential
- Self-displaying in a human-computer interface
- Self-organizing

The latter is an important attribute for future implementation of what might be called “artificial intelligence” features of a CPR. These may be as simple as self-generation of alerts, solution of multivariable equations for decision support at the individual patient level, or intelligent data mining for undiscovered relations within the information. B42

About 1995, at the time these ideas were being developed at UAB, similar thinking was going on among computer scientists at Stanford University and the University of Pennsylvania, arising from different stimuli. B71,M17 They termed an information model of complex data elements that carried with them all attributes intended for self-documentation, self-reporting, and self-organizing semistructured data. This phrase meant that the data elements were fully structured, but no necessary relation of one data element to another was presupposed. The culmination of these efforts was a database for storing complex data elements called Lore M17 and a novel query language for retrieving complex data elements called Lorel. A1

In the 1990s, it was recognized that the information structure suggested by Kirklin and the University of Pennsylvania and Stanford computer scientists could be conceptualized as a directed acyclic graph (Fig. 6-8). At that time, another entity was also rapidly coming into existence with similar properties, but of global proportions: the World Wide Web (WWW, or simply the Web). A Web page is analogous to a complex data element, with an essential feature being that it is self-describing, so it can be retrieved. The Web is the infrastructure for these pages. It has no need to be aware of Web page content. The subject matter has no bounds. Not surprisingly, then, the tools developed for retrieving semistructured data were quickly adapted to what has become known as search engines for the Web. Like Dr. Kirklin’s vision of complex data elements, information retrieved by a search engine can become related in ways never envisioned by the person generating it, because full structure is imposed only at the time of retrieval, not at the time of storage.

In 1998, the Lore scientists realized that the information model for semistructured data could be implemented in XML (extensible markup language). XML is a textual language for information representation and exchange, largely developed for document storage and retrieval but adaptable to values for variables. D6,G16

At least on a conceptual basis, we believe a CPR can be formulated using a semistructured information model that will facilitate clinical research by not imposing restrictions at the time of storage, as relational and object models do.

Subsequently at Cleveland Clinic, investigators have been both harnessing and developing “Semantic Web” tools for data storage and manipulation, in part within the framework of the World Wide Web Consortium (W3C) and in part through ontologies built by Douglas Lenat of Cycorp. B42 W3C is an international community that works with the public to develop Web standards. It is developing a suite of technologies that build on standards associated with the World Wide Web and provide a formal model for representing information in a manner that emphasizes the meaning of terms rather than their structure. B32 It is a vision of how the existing infrastructure of the Web can be extended in such a way that machines can interpret the meaning of data involved in interactions over the Web.

This particular collection of standards is commonly referred to as Semantic Web technologies. They are built on a graph-based data model known as the Resource Description Framework (RDF), as well as a framework for describing conceptual models of RDF data in a particular domain known as the Ontology Web Language (OWL). It also includes a standard querying language called SPARQL.

RDF captures meaning as a collection of triples consisting of components analogous to those of an elementary sentence in natural language: subject, verb, object. Typically, terms in these sentences are resources identified by Uniform Resource Identifiers (URIs). URIs are global identifiers for items of interest (called resources) in the information space of the Web. B32 Collections of RDF triples constitute an RDF graph.

Many requirements outlined by the IOM as crucial for CPR systems are addressed by using RDF as a data format for patient record content. In particular, our ability to link with other clinical records can be facilitated when RDF is used in this way. B32 Use of URIs as syntax for the names of concepts in RDF graphs is the primary reason for this. The meaning of terms used in a patient record (as well as the patient record itself or some part of it) can be made available over the Web in a (secure) distributed fashion for on-demand retrieval.

A judicious application of Semantic Web technologies can also lead to faster movement of innovation from the research laboratory to the clinic or hospital. B32 In particular, it is envisioned that use of these technologies will improve productivity of research, help raise quality of health care, and enable scientists to formulate new hypotheses, inspiring research based on clinical experience. B41

TIME

The ability to manage that ubiquitous attribute of all medical data—time—is not part of any widely available information retrieval system (generally called query languages). Some proposals have been tested in a limited fashion, such as the
Figure 6-8 Comparison of relational information model with a semistructured one presented as a directed acyclic graph. A, Relational. Tables are related by ID and source. Note that second table is many-to-one; that is, many postoperative echocardiograms were performed on one patient. B, Semistructured. (From Jonathan Borden, www.jonathanborden-md.com).

Tzolkin system developed at Stanford University, but the software is not generally available. The reason for needing to consider time is readily apparent. Whenever we think about retrieving medical information along some time axis (e.g., sequence, duration, point in time), new logical relations must be generated to obtain reasonable results. For example, if we ask for all patients younger than 80 years who have undergone a second coronary artery bypass operation followed within 6 months by an MI, a number of time-related logical steps must be formulated. What is meant by patients younger than 80? Younger than 80 when? At the time of initial surgery, second surgery, MI, or at the time of the inquiry? The sequence of coronary artery bypass grafting (CABG) must be ascertained from data elements about each procedure a patient has undergone. Information about the MI and its relation to the date of the second CABG must be retrieved. The process is even more complex if only approximate dates are available.
Perhaps a growing interest pertaining to the time axis in business may stimulate development of better tools for managing queries related to time in medical information.

Section III  Data

Data consist of organized information. We add the following further constraints.

First, data consist of values for variables. These values have been selected from a list of all possible values for a variable, and this list is part of a constrained vocabulary. Natural language processing is too primitive at present to allow values to consist of free text, and that will not change in the foreseeable future. Our exploration with linguistics experts of the needed lexical parsing rules to determine from dictated medical notes whether a person experienced a hospital death after cardiac operation produced multiple pages of daunting logic. In part, the complexity arises because of the richness of language that includes euphemisms, synonyms, and misspellings; in part it is because one must also identify negating (“did not expire”), adjudicate probabilities (“may have died”), and examine indirect evidence (no mention of death in available dictated notes, but an autopsy was reported).

Second, data consist of values for variables that have been accurately and precisely defined both at the level of the database and medically. One of the important benefits of multicenter randomized trials, concurrent observational studies, or national registries is that these activities require establishing agreed-upon definitions at the outset. Coupled with this is often intensive and ongoing education of study coordinators and other data-gathering personnel about these definitions, exceptions, and evolution of definitions and standards. There is a mechanism to monitor compliance with these definitions and standards throughout the study, and the same should hold true for any registry. However, a mechanism to ensure similar adherence to definitions is essential even for individual clinical studies. Further, documentation must be in place to identify dates on which changes in definition have occurred, and these must be communicated to the individuals analyzing the data (generally, indicator variables are created that “flag” cases for which definitions of an individual variable have changed). The rigor of establishing good definitions is considered distasteful by investigators who are impatient to collect data, but it is essential for successful research. It is also somewhat of an iterative process, which is why we suggest extracting data on the basis of initial definitions for a few patients scattered over the entire time frame of the study, then refining the definitions. One must also be aware of standards developed by national and international groups of cardiac surgeons and cardiologists assembled for this purpose.

Third, data consist of values for variables that have been organized, generally using a database management system, into a database or data set(s) suitable for analysis. There is an essential translation step in going from even organized information into data in a format compatible with the analytic technique to be employed. For example, if one is analyzing survival after a cardiac surgical procedure, one must define “time zero,” construct the interval from time zero to occurrence of the event of interest from date-time data, generate an indicator variable for whether by the end of follow-up a patient has or has not experienced the event, impute values for additional variables if some of the data are known only inexactly, and manage the problem of possible missing values for some of these variables (see Time-Related Events in Section IV). These details will not be part of the medical information system but must be created at the time of analysis (see “Analysis Data Set” later in this section). This is because at the present time and for the foreseeable future, data analysis procedures presume that data will be organized in a fully structured format, generally a relational one (tables with columns for each variable and rows for each separate observation, which may be a single patient or multiple measurements for a single patient). It is our view that the fully structured organization of data, probably in relational database format (see “Relational Information Model” in Section II), should be imposed only at the point of extraction of values for variables from information (often called the “export” phase in a process termed rectangularization). This allows the input of data to be semistructured (see “Semistructured Information Model” in Section II), maximally flexible, and with few imposed organizational constraints (outside of retrievability), so that relations among variables are imposed by the research question being asked and not by a priori database constraints.

INFORMATION TO DATA

An idealized, linearized perspective on the process of transforming clinical information to data suitable for analysis requires three broad steps (see Fig. 6-7): (1) formulating a clinical research proposal that leads to identifying a suitable study group, (2) gathering proposed variables and values that lead to an electronic data set, and (3) manipulating the values and variables to create a data set in a format suitable for analysis. This is a linear process in theory only. In reality, it contains checks that cause the investigator to retrace steps.

Identify Study Group

The clinical research proposal (see Box 6-6) provides detailed specifications for the study group of interest. The medical specification must be translated into a formal query, generally using a query language that will be used to identify patients in the study group. Query engines include the now-familiar Bing and Google, and the search engines of the National Library of Medicine, including PubMed. For data managers familiar with relational databases, the Structured Query Language (SQL) is a universal query language.

It is frequently true that electronic sources of registry data do not narrow the study group as much as desired. This may require investigating a larger group of candidate patients and selecting by medical records review those who meet the study specifications.

If the semistructured information model is adopted (see “Semistructured Information Model” in Section II) as we advocate, then at the present time, experts in query languages specific to this type of information must be consulted. However, because such information is stored in the same format as Web documents, the increasing sophistication, accuracy, and usability of Internet search engine technology will simplify this process.

The end result of a query is identification of a group of patients (or candidate patients) for the study. The major
checks here are whether the patients indeed meet criteria for inclusion and exclusion and whether a sufficient number of patients (or a sufficient number of outcome events, as will be found in subsequent steps; see Box 6-4) are retrieved for a meaningful analysis.

**Extract Values for Variables**

A source, or sources, for obtaining values for the set of variables specified in the clinical research proposal must now be identified for the study group (see Fig. 6-4 and Box 6-6). Currently these are contained either in some electronic format (e.g., hospital information system) or in the paper record.

**Export from Electronic Information Sources**

If some or all the variables specified are in electronic format, sources must be identified and a query made for patients in the study to extract values for the variables. This often time-consuming step is facilitated by three factors. First, at the time the information system is created, procedures can be built in to ease extracting, formatting, and exporting values for variables. This is particularly feasible in a so-called metadata-driven system, in which “data about data” drives not only the data entry process but the data extraction process as well.\(^\text{621}\)

It is also particularly feasible for relational databases that are electronically linked (e.g., portals) to the analysis system. Second, “standard” groups of core data elements can be identified that form the basis for at least a major portion of the variables needed for most studies. The advantage of this strategy is that queries can be assembled carefully and refined over time. Third, successful, accurate ad hoc queries can be stored so that when the same variables are again specified, these queries can be reused.

Often more than one electronic data source must be used. In this case, values for variables in common may need to be adjudicated if they do not match in value or in variable nomenclature. Ultimately, unique variables must be joined into a common database.

**Extract from Medical Records**

Even if the majority of information is available electronically, there are nearly always some variables new to the study that must be gathered from paper records if a CPR is not available. A more arduous process must be put into place for extracting data from original documents.\(^\text{33}\) A precise methodology is necessary for assembling information to prevent repetitious handling of both the patient’s record and the extracted information, as well as to ensure complete and accurate data retrieval while preserving the patient’s privacy and confidentiality.\(^\text{4}\)

All information should be recorded in clearly defined, objective terms. There may be a preference for using descriptive terms that have been clearly defined (e.g., absent, trivial, mild, moderate, severe). Alternatively, numeric coding may be used,\(^\text{367,33}\) with each numeral clearly defined. Pedal pulses, for example, may be recorded as 0, 1, 2, 3, or 4, with 4 indicating normal. Either method is equally rigorous as long as values are picked from a controlled vocabulary.

Accuracy of data entry is improved by recording only primary information (e.g., date of birth, date of operation) and not indices derived or calculated from them (e.g., patient age at operation, body surface area). Such indices can later be calculated quickly and reproducibly by computer. Data should also be coded in a way that is simple and self-documenting (using words or phrases from a constrained list of possible values for a variable, sometimes called “pick lists”).

A key concept is to record core data elements that can be logically combined in multiple ways to form derived variables (see Box 6-8). For example, for analysis one may want to use only the variable “current smoker.” If this were the variable gathered primarily, one would be unable later to derive other data about smoking, such as pack-years, duration of smoking, or when a previous smoker quit. Core data elements would instead relate to dates of smoking and intensity, from which all others could be derived.

The process of gathering data is the most time-consuming step in a study. It is not unusual for it to consume months or years of work. Even if electronic sources of information are used, if values for variables were not entered at the point of care, the expense can be enormous. This is why the CPR, as the repository of all patient data and patient care workflow, is essential to increase the efficiency of clinical research.

For many institutions, identifying patients using a simple registry (e.g., Society of Thoracic Surgeons Database) and extracting more detailed ancillary data for a specific study is the cost-effective method for clinical research. Although review of the medical record in this way is often considered a thankless chore, it has the benefit of an investigator gaining valuable in-depth insight into the patient cohort that is generally not captured by typical “case report forms” or routine registry capture. Indeed, the clinical importance of the research and the clinical inferences and practical recommendations coming from the research are often greatly enhanced by careful review of all or at least a substantial sampling of the medical records.

**Verify Data**

No matter what method of data export or extraction is used, experience dictates that one or more iterative data verification steps must be inserted before any analyses are performed. This process is long and tedious and can be boring. It usually reveals many errors, but it also allows review of each patient’s record to detect missed information. Data are then checked for reasonableness, a process greatly aided by computer. This can be accomplished quite simply by looking at the maximum, minimum, and average of each variable (although sometimes more sophisticated univariable analyses must be done, as described later in this section under Descriptive Data Exploration) by making simple scatter plots of related variables (e.g., age, height, and weight form a smooth scatter plot against one another), cumulative distribution plots of

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\(^1\)Regulations regarding patient privacy and confidentiality are pertinent to how clinical data can be used for research. Some generalities can be made, however. First, during analysis of data, informative patient identifiers are unnecessary and should be eliminated from the analysis data set. Second, those who must verify data values for medical records, perform patient follow-up, and join disparate databases will need patient identifiers to accomplish these tasks. Because these activities take place within the confines of an institution, it is generally agreed at the present time that use of patient identifiers is appropriate under the purview of an institutional review board (IRB). Third, communication with patients by IRB-approved mailed questionnaires or IRB-approved telephone scripts must begin with obtaining patient consent. Fourth, communication with medical professionals about follow-up status or documentation of events requires patient consent. Fifth, databases should conform to regulatory (Health Insurance Portability and Accountability Act [HIPAA]) standards.
Follow-up

Time-related events occurring after hospital discharge are often extracted opportunistically simply from clinic visit records rather than by systematic patient contact. Patients not appearing for clinic visits are said to be untraced. This is an unacceptable method of follow-up.

Even with systematic methods, however, some patients cannot be traced, and in the United States, privacy and confidentiality regulations are making this task increasingly difficult. It has been demonstrated that untraced adult patients have a high probability of being dead. In contrast, in the UAB experience, untraced infants usually were doing well; their parents, generally young and often highly mobile, have simply dropped contact with the pediatric cardiologist. Either way, a high prevalence of untraced patients potentially introduces bias into the time-related analysis, leading to overestimating or underestimating survival or freedom from other events, and reduces effective sample size.

Follow-up may be active (direct patient contact) or passive (use of government death indices). In either case, most institutions require IRB (ethics committee) approval of the follow-up process, and patient consent at each contact as well.

It is possible that the movement toward IRB reform may remove some of the variability in IRB handling of follow-up studies. In addition, patients, like families, can be invited to consent for follow-up by a centralized group, such as has been employed by the Congenital Heart Surgeons Society. Yet another interesting development is PatientsLikeMe (www.patientslikeme.com), a highly monitored and sophisticated Web-based research site focused primarily on neurologic diseases with moment-to-moment updates of real-world side effects of medications. It is uncertain how representative the sample of patients might be, but it illustrates our experience that with rare exceptions, patients want to be contacted. PatientsLikeMe has found that with rare exceptions, patients want to be contacted by opportunities the sample of patients might be, but it illustrates our experience that with rare exceptions, patients want to be contacted.

Active Follow-up

Active follow-up means that patients or their families are contacted directly by mailed questionnaire, telephone, or electronic means (e-mail, Internet). Active follow-up is essential for discovering time-related events and longitudinal clinical condition, perhaps with the exception of vital status, which may be available from government sources. Active follow-up data, and particularly the date of last active follow-up, must be kept separate from any augmentation of these data from passive sources. If a patient is found to have died, nearest relatives are contacted in a sensitive, sympathetic fashion to document the circumstances of death and ascertain all other pertinent cardiac events that occurred between the date of last active contact and death.

There are two general methods of active follow-up: anniversary and cross-sectional.

Anniversary Method In the anniversary method, the patient is contacted yearly on the anniversary of his or her entry into the study (or periodically if not yearly) or is given a set of forms to send to the investigators on the anniversary of entry. This method is ideal for sampling the time-varying condition of the patient (e.g., functional status, freedom from angina, growth and developmental patterns). It has the added advantage of maintaining yearly contact with the patient, an important consideration in a mobile society. It has also been
demonstrated that nonlethal morbid events such as thromboembolism and hemorrhage after heart valve replacement are forgotten unless there is at least yearly contact.\textsuperscript{B52} Yearly active contact also makes it more likely patients will report events to their physicians during the course of the year.

**Cross-sectional Method** In the cross-sectional method, a specific follow-up inquiry of the patient cohort is initiated on a specific calendar date (called the common closing date), with the goal of obtaining the status of all patients at a specific instant in time. In practice, of course, finite time is necessary to conduct the follow-up. For example, a cross-sectional follow-up may be initiated on August 1 and questionnaires returned over the ensuing 2 months. During this time, telephone calls may be made to nonresponders or those whose questionnaires have been returned as undeliverable.

Two techniques are then used to manage the cross-sectional data. The best method is to choose a common closing date. In the example stated, this would be August 1, the date follow-up began. For this method, the status of the patient, including all events observed, is that as of the common closing date. For patient condition (longitudinal data), a decision must be made about condition as of the closing date. This can be made clear on the follow-up form or via the telephone script. Alternatively, all events reported during follow-up are used, with the date of follow-up taken as the date the questionnaire was signed or the telephone call completed. This method, called date of last report,\textsuperscript{B13} was suggested by the Mayo Clinic group; we do not recommend it.

Note that if a patient responds to the questionnaire but shortly thereafter experiences an event and contacts those performing the follow-up study, the new information is recorded but disregarded. Restriction to initially reported events emphasizes a property of active follow-up: it is systematic. In contrast, any other method, be it physician office visits or voluntary contact, is opportunistic and nonsystematic. The problem with nonsystematic follow-up is that it captures numerators but not the denominator of a patient cohort, so analyses of time-related events are distorted.

**Goodness of Follow-up** In performing active follow-up, particularly in cross-sectional follow-up studies conceived after considerable experience has accumulated, every effort should be made to contact every patient in as short a time as possible.\textsuperscript{B54} Special assistance may be required to achieve a high level of follow-up under these circumstances. In the past, we advised using cross-reference indices to former neighbors or contact of relatives and former physicians, churches, and other agencies.\textsuperscript{B54} However, in the United States this is now prohibited.

There is no perfect way to describe and quantify goodness of follow-up. Traditionally, the mean and standard deviation of follow-up duration, including either all patients or only living patients, are given, as well as total patient-years of follow-up. Various percentiles of follow-up are also useful (see “Descriptive Statistics” later in this section), such as the 10th, 50th, and 90th. Alternatively, the percentage of patients traced beyond certain intervals (e.g., 5, 10, 15 years) may be given. We then recommend stating what percentage of patients have not been traced beyond hospital discharge (lost to follow-up) and how many could not be contacted by active follow-up at the latest inquiry.

Grunkemeier and Starr have described a patient-year method for estimating goodness of follow-up based on observed vs. potential follow-up duration.\textsuperscript{G32} For each patient, the duration of potential follow-up is computed (this is the interval from study entry until death or, for the patient still alive at follow-up, common closing date or response date, anniversary date, or analysis date, depending on the type of follow-up study performed). The measure of goodness of follow-up is the ratio of total observed follow-up duration to total potential follow-up duration.

Neither of these methods of reporting adequately indicates the degree of information lost by incomplete follow-up. The traditional reporting method may be overly optimistic, and the Grunkemeier and Starr method has the same drawback as all patient-year methods in that it reflects loss of information accurately only when the hazard function for the event is reasonably constant. For example, if a patient has been traced for 10 years but has been lost for the past 5 years, the contribution to the goodness of follow-up statistic would be the same as that of five individuals who were lost just after study entry (e.g., after hospital discharge) 1 year ago. If the hazard function is steeply declining in the first year (as it often is), then is very low after 10 to 15 years, the information lost by failure to trace the five recent patients is greater than the information lost by failure to trace further the patient with a follow-up duration of 10 years.

It may be possible to devise a better expression of goodness of follow-up. For example, if a parametric estimate of the cumulative hazard function is made, the difference in potential vs. observed cumulative hazard experienced (expressed as a percentage) may better account for the time-related loss of information. However, the important thing is to expend great effort to obtain complete follow-up information.\textsuperscript{B54} Failure to trace a substantial number of patients, however expressed, makes even the most sophisticated analysis suspect.

**Follow-up Instrument** The follow-up instrument may be a simple questionnaire mailed to the patient (with one or two remailings followed by telephone contacts to nonresponders). If so, it is wise to not exceed a single sheet in length, relying on the telephone or personal contact to obtain more details if events have occurred. Alternatively, the inquiry may be completely by telephone, using well-trained individuals, a script, and a form that is filled out during the conversation.

Patients rarely resent being followed up; to the contrary, periodic follow-up is useful not only in detecting medical trends in individual patients who may need attention, but also in generating good will between the patient and the medical system.

**Passive Follow-up** If vital status is the only outcome of interest, date of death may be obtainable from government vital statistics offices or a death registry. In passive follow-up, only death and date of death (which may be approximate) are identified, not whether each individual in the study is alive or dead at the time of inquiry.\textsuperscript{T1} Usually there is a lag between death and reporting, so methods must be employed to determine the status of living patients at any given time. At Cleveland Clinic, investigators have available a large registry of patients who are actively followed. When passive follow-up is used, patients known by active follow-up to be dead or alive are purposely included. It is then determined when most of these actively followed patients were identified as dead by the passive government death indices. A common closing date is thereby selected for all passively followed patients in the study.
 Manipulate Variables and Values

To interpret patient information meaningfully, an index time for study entry must be established for every patient. The reason is the central place of date-time in medicine. In a system of longitudinal data entry at the time of patient care, past, present, and future are defined in terms of this index time. For surgeons, fortunately, this is often the time of an operative procedure. It is more difficult in medical situations to define, say, onset of disease; often, date of diagnosis or patient encounter is used. Once index time for study entry has been determined, then, using dates for each data element, one can determine if there have been previous events, such as MRIs, how many of these have occurred, and the interval from the most recent to the index time. All items in what we commonly think of as “past medical history” are defined in terms of this index time for study entry.

One of the most common requirements is to compute intervals between dates. For example, the age of a patient at index time is calculated from index time and date of birth. Follow-up intervals are similarly computed from dates. A common error is attempting to manually calculate intervals between dates and index time. This is rarely accurate and should be done by computer.

Indicator variables are always required (an exception is described in Classification Methods in Section VI). These may simply be the translation of a variable whose value has been coded as YES or NO into the numbers 1 and 0, respectively. A cardinal rule to avoid ambiguity, human error, and misinterpretation is that the computer variable name of an indicator variable must always be the one indicated by a YES or 1. Thus, in forming an indicator variable from a primary variable called SEX with values of MALE and FEMALE, one would name the indicator variable MALE with values of 0 for female and 1 for male. An indicator variable called SEX or GROUP is ambiguous and should rarely be used as an analysis variable, because it is not self-documenting.

Another common requirement is to form multiple indicator variables from a single variable containing values from a non-ordered list. These list variables often are represented by a set that allows selection of multiple items from the list. Typical list variables are diagnoses or type of operation. A non-ordered (polytomous) list variable is not interpretable in many types of data analysis (the exception is mutually exclusive lists, for which polytomous methods are useful; see “Polytomous and Ordinal Logistic Regression” in Section IV and Classification Methods in Section VI). Generally, a variable useful for data analysis from such list variables must take on at least one of three values: 0 (NO), 1 (YES), or blank (MISSING). However, in many cases the medical pick list can be so long that in general clinical practice, only positive findings are recorded and all the rest (e.g., thousands of possible diagnoses) “dismissed” (Kirklin called these “dismissal lists”).

When it comes to data analysis, however, we often need indicator variables for all list items that identify more than YES (or 1). Generally, the assumption is made that if a list item is not selected, the patient did not have that condition or procedure. However, it is possible that he or she did, but the list item was added recently and so was not collected at index time; (2) the data abstractor could not find the item, forgot to look for it, or was distracted and did not return to find it; or (3) the item was recorded in a previous clinical record that was not retrieved by the criterion used to gather the electronic data set.

Such ambiguities can be avoided to some extent for a particular discipline by gathering important data elements using individual variables. For example, one may wish to have unambiguous information on the comorbidities diabetes (and its treatment); preoperative dialysis for chronic renal failure; history of prior MI (perhaps with date or a count of the number experienced); history of cerebral vascular accident, carotid artery, and often peripheral arterial disease; chronic pulmonary disease, and the like. Rather than making them items in a long list of variables, create individual variables whose values of YES or NO must be explicitly entered. An alternative is to have multiple missing value indicators, representing by default “not yet found,” but then including the extremes of “pending” and “completely absent,” “don’t know,” “lost chart,” “illegible,” “invalid response,” “refused to answer,” and “not applicable” (e.g., child relation of parent fields to which the answer is NO, or all smoking history variables for a person who never smoked).

Screen and Scrub

As intervals and indicator variables are created, data screening is performed. Negative intervals are found, and dates or times corrected in original sources. Impossible combinations of variables may be found, such as a “normal” aortic valve said to have a 100-mmHg gradient and valve area less than 1 cm². Parent-child relations are verified, particularly if the database has inadvertently not been set up properly to manage such relations. For example, specifying an aortic valve prosthesis should be a child variable of a parent variable for “aortic valve replacement.”

Inconsistencies are reported to the investigation team for resolution, and the iterative process is repeated. This process is often discouraging to the unknowledgeable investigator who assumes that all data (particularly those personally extracted) are flawless.

1In a hierarchical data structure, a parent variable (or node) is one level higher and directly associated with one or more child variables (or nodes). Thus, “duration of smoking” is a child variable to the parent variable “history of smoking.” If history of smoking is positive, then duration is a child node associated with that positive response. Likewise, CABG is a child node of “cardiac procedures,” which itself is a child node of “therapeutic interventions.”
Just as important as improving accuracy of the data set is evaluating the quality of each variable by this screening and scrubbing process. One may find that information is too often unavailable in medical records to trust the variable, and it is dropped. One may also find that interpretation of the clinical condition has been so variable that the values gathered are not reproducible. Either a better surrogate has to be found or the data element must be dropped from further consideration.

If an electronic repository of information is maintained by a research enterprise, it is important that corrections discovered in the information anywhere along the way be fed back to the original database and the data re-exported. In this way, database quality will be constantly improved. Ideally, the change in the primary data will be documented (audit trail).

**Impute Values**

In any study, there are likely to be values that have not been recorded. Most statistical procedures eliminate entire observations (e.g., patients) for which any data requested for analysis are missing. In medical data analysis, however, one is more likely to introduce bias by eliminating all data on an entire patient than by substituting a value for the missing data that can be shown not to importantly bias the analysis. The process is called **missing value imputation**.

Although the literature on managing missing data is extensive, much of it is directed toward survey investigations in which entire survey instruments have not been returned. The general directive for such data is to eliminate records for nonresponders. In clinical research, missing data are most commonly sporadic or systematic (block missing) for some specific time segment (e.g., missing magnetic resonance imaging data before the introduction of that technology). These common types of missing data should be managed in a different way from that of surveys.

**Sporadic Missing Values**

For sporadic values missing in a small proportion of patients, it is reasonable to substitute (impute) the mean value for all patients with non-missing data (called noninformative imputation). Thus, if 5% of patients are missing values for ejection fraction, the mean value is substituted.

If there are at least five outcome events associated with patients having sporadic missing values for a variable, a dichotomous (0,1) missing value indicator is created and forced into all models in which the primary variable is incorporated. If the indicator variable is not statistically significant, it is likely that the imputation has been noninformative with respect to outcome. If it is significant, the indicator variable both adjusts for this and serves as a warning that additional work must be done, such as use of informative imputation.

**Informative imputation** capitalizes on redundancy in medical information. A multivariable equation is generated (see Multivariable Analysis in Section IV) for the variable of interest, but using only patients for whom values are not missing. A value is predicted from this equation for the patient with the value missing, and this is the imputed value. Missing value indicators are just as germane for informative as for noninformative imputation.

Yet another strategy is **multiple imputation**. Briefly, a set of randomly chosen values is used for imputing missing values for each patient and analysis is performed, followed by another set of values and analysis. This process may be repeated as many as 200 to 1000 times, and the many analyses summarized. More commonly, an initial investigation data set is constructed and used for preliminary model building (see Multivariable Analysis in Section IV). This is followed by applying that preliminary model to additional imputed data sets (5 to 10) and aggregating the results.

When to impute missing values by whatever method is chosen turns out to be important: transform, then impute. As noted in “Calibration” under “Risk Factor Identification” in the Section IV discussion titled Multivariable Analysis, the scale of continuous variables may have to be transformed to meet model assumptions (linearizing transformations). It is important that transformations first be performed, followed by missing value imputation, as documented by von Hippel.

**Systematic Missing Values**

Systematic missing values occur under two conditions that can be managed similarly. First, a value may be inapplicable. For example, in a study of mitral valve surgery, values for various repair techniques are inapplicable to patients receiving a prosthesis. Second, some test may come into use part way (in calendar time) through a study, or information may not have been collected about some variable until a certain calendar date. For such patients, we suggest that the missing data be managed as “interaction terms.” By this we mean that systematic missing values be set to zero (0). Then a missing value indicator is generated—1 for patients with systematic missing values and 0 otherwise. Both variables are linked in all analyses. This makes interpretation of the models realistic, although it is a strategy that is computationally close to noninformative missing value imputation. A drawback is that the missing value indicator may become an unrecognized surrogate for temporal trends in the data if the block missing data are concentrated among patients early in the study.

**Organize Variables for Analysis**

Once the aforementioned steps have been achieved, often iteratively, the result is a final data set in the format needed for analysis. However, one further step remains: organizing variables deemed suitable for analysis in a medically meaningful way. The reason for this is the importance we place on informed data analysis. Those analyzing the data must “know the data” just as the investigator knows the data. Not every variable has equal importance for analysis. For example, quantitative ejection fraction is “better data” than a qualitative assessment of left ventricular function on a coarsely graded scale; creatinine level at surgery contains more data than a diagnosis of renal failure; individual components of leaflet morphology in atrioventricular septal defect contain higher information content than Rastelli type.

Not every variable is of equal reliability, but medical information tends to be redundant, so more reliable surrogates should be sought and analyzed. Many variables are highly correlated and may be of equal reliability, such as height, weight, body surface area, and body mass index (indeed, the latter two are calculated from the former two). Therefore, if such variables are equally associated with an outcome, one may arbitrarily select the most reliable or easily measured representative of that concept (in this example, body size).

The data management team, in collaboration with the investigator, must then compile a final list of analyzable variables. These should be grouped in a medically meaningful fashion that aids informal data analysis. A suggested
grouping might be as follows, although it will vary from study to study:

- Demographics (age, sex, socioeconomic position, size)
- Symptoms (functional status, angina class)
- Ventricular function (ejection fraction, number of previous MIs, interval from last infarction to surgery)
- Pathophysiology and etiology (grade of mitral valve regurgitation, etiology of valvar regurgitation)
- Coronary artery anatomy and disease (degree of left main disease and that of each coronary system, dominance)
- Other cardiac comorbidity (previous cardiac operations, atrial fibrillation)
- Noncardiac comorbidity (smoking history, creatinine, pulmonary disease, diabetes, albumin level)
- Preoperative management (preoperative intraaortic balloon counterpulsation for hemodynamic instability, intravenous nitroglycerin and heparin for unstable angina)
- Cardiac procedure (coronary artery bypass grafting, bilateral internal thoracic artery grafts, quadrangular resection of mitral valve)
- Support techniques (duration of aortic clamping, use of warm substrate-enhanced induction cardioplegia, duration of circulatory arrest)
- Experience (date of operation, surgeon)
- Outcome, in-hospital events (length of postoperative stay, occurrence of various complications, hospital death)
- Outcome, time-related events (all-cause mortality, interval from surgery to death or censoring)
- Longitudinal data (echocardiographic findings after valve operations, NYHA functional class)
- Missing value indicator variables
- Interaction terms (organized according to above schema)

A practical way to implement this organizational structure is to isolate programming code in the form of a computer macro that contains the list of available variables for analysis and a place for those analyzing the data to insert code for imputing missing values, transforming the scale of variables, forming additional indicator variables, and performing other useful data manipulations. This strategy guards against human error in data analysis by isolating to a single location all data manipulation useful for all analyses.

DESCRIPTIVE DATA EXPLORATION

After the analysis data set has been constructed, data are explored by producing simple descriptive tables (sorting and tallying) and simple statistics about continuous variables, scatter plots of variables, and other exploratory data analyses. To understand this process, some appreciation of numeric data is necessary.

Numbers

Accuracy and Precision

Because both calculators and computers express numbers to many digits (Box 6-9), it is necessary to know a set of rules for compaction and expression (display) of numeric data. The format in which a numeric value is expressed has implications. The number 493, for example, implies that the \textit{truth} is somewhere between 492.5 and 493.5 (accuracy), and that the scatter in repeated measurements of the number (precision) is no greater than that explicitly expressed (Box 6-10). The number 492.8 implies that the result is somewhere between 492.75 and 492.85, and 492.76 implies that the result is somewhere between 492.755 and 492.765. This last numeral to the right (right-most digit) explicitly indicates that the accuracy is much greater and the precision much less than when the number is 493.

Rounding

In computation and computer storage, all available digits of numbers displayed or recorded by measuring devices should be retained. It is only at the last step of numeric presentation that numbers are rounded (Box 6-11). In presenting numeric information, numbers should be rounded in such a way as to reflect their precision or reproducibility, although consistency within tables is also important.

Tabular Presentation

Numbers are often presented in tabular form that indicates distribution of data between the extremes of a continuous variable (e.g., patient age). Such tables should be prepared so that positioning of any point along the continuous variable can be unambiguously determined. In this text, intervals between extremes of a continuous variable are indicated by symbols of inequality (Table 6-7). This method of presentation of tabular information is mathematically conventional (Box 6-12) but not conventional for medical publications, where ambiguity often abounds.

Descriptive Statistics

Descriptive statistics are numbers used to summarize values for a specific variable recorded for a group of patients (sample; nomenclature is given in Box 6-13), such as age, presence or absence of coronary artery disease, and NYHA functional class. Variables fall into two broad categories for which different methods and expression of summarization are appropriate: (1) \textit{categorical} and (2) \textit{continuous}.

Categorical variables take on a small number of values. If they take on just two (e.g., YES, NO), they are called \textit{dichotomous} variables. If they have values that are ordered (e.g., none, mild, moderate, severe), they are called \textit{ordinal} variables. If they are just a list (e.g., type of valve prosthesis), they are called \textit{polytomous} variables.

Continuous variables take on a theoretically limitless number of values, although these values may have natural constraints (e.g., age, which cannot be negative). Their degree of granularity may vary (e.g., age may be calculated in whole years in adults, but in days or even hours [higher granularity] in neonates).

Categorical Variables

Dichotomous

Descriptive statistics for dichotomous categorical variables include simple counts (i.e., a count of the number of times the variable was YES [or 1] or NO [or 0]): How many cases were performed? How many men and women were in the study? How many patients died after operation? Summary counts are of limited value, however, because they do not reflect the size of the sample. Therefore, a summary statistic can be formulated that normalizes the counts to a standard denominator, commonly 100 (percent). This is a probability parameter estimate, so it not only reflects
Accuracy versus Precision

**Accuracy**
Absence of systematic error of measurement (bias) from the “truth.” It is an expression of “rightness.”

**Precision**
Ability to provide the same answer in repeated measurements. It is an expression of “exactness.”

These terms are often interchanged, but in data analysis they are not synonymous. Repeated measurements of PO2 in a blood gas machine may have a great deal of scatter on repeated readings (imprecise), but their average value may reflect faithfully the true PO2 (accurate). Another blood gas machine may yield PO2 with little scatter in repeat readings (precise), but may be uncalibrated, so the readings are inaccurate (biased). There is often a trade-off between accuracy and precision in medical measuring instruments.

Another way to express this number is as the sum of 4 + 30 + 200 + 1,000.

To the right of the decimal point, the first place is called the tenths (1/10) place, the second the hundredths (1/100) place, and the third the thousandths (1/1000) place. Thus, in 0.1234, the 4 is in the tenths place, 3 in the hundredths place, 2 in the thousandths place, and 1 in the ten-thousandths place. Another way to express this number is as the sum of 0.0004 + 0.02 + 0.1.

**Decimal Place**
In the decimal system, decimal place is the position of digits immediately to the right of the symbol designating the decimal point. Location of the decimal point reflects the scale of measurement and is unrelated to significant digits.

**Significant Digit**
Digits of the decimal form of a number beginning with the leftmost nonzero digit and extending to the right, with the implicit implication that all digits to the right are significant digits. That is, they are warranted either by inherent properties of the measuring device used to generate the numbers or by statistical properties of a collection of such numbers.

**Scientific Notation**
A method of expressing (displaying) numbers from 1 to 9, followed by a decimal point, the remaining significant digits, if any, multiplied by a power of 10. For example, 0.00037 in scientific notation is $3.7 \times 10^{-4}$, where $10^{-4} = 0.0001$. In general, the numeric value, here 3.7, is called the mantissa, 10 is called the radix, and $-4$ is called the exponent.

**Leading Zero**
Zero placed before a decimal point that is not considered a significant digit. It is generally used (1) when it is implied that a nonzero significant digit could replace it, or (2) to separate a negative sign (−), a positive sign (+), or a plus or minus sign (±) from the decimal point. Increasingly, numbers that are constrained to the range 0 to 1, such as probabilities (including $P$ values), are expressed (displayed) without a leading zero.
**Box 6-11 Rounding Numbers**

Certain generally agreed-upon conventions for rounding numbers exist, although they are not easily found in print.

**Step 1: Determine the Number of Digits to Save**

This is suggested by precision of the measuring instrument for individual numbers and by the standard error of the mean value or proportion associated with a series of numbers (see Box 6-12). For the latter, the place of the first significant digit of the standard error is found, and the mean or proportion is then rounded to that place. The same place is saved in confidence limits. If the standard error is also being expressed, one additional place is saved in it (because the usual expression of the standard error is a form of shorthand, and saving the extra place helps in using the standard error to calculate confidence limits).

**Step 2: Look for Exceptions**

Exceptions to Step 1 are as follows: (1) if the first significant digit of the standard error is 1, then one additional place may be saved; (2) for percentages with a floor of 0% and ceiling of 100%, if the percentage is between 0% and 10% or between 90% and 100%, keep at least 2 significant digits; and (3) within a single contingency table, consistency in saving digits is desirable, so all numbers may be rounded to the place indicated by the majority of the numbers. In medical data, two significant digits (see Box 6-9) usually suffice.

**Step 3: Round**

Round the number by removing digits from its right side that falsely suggest a high degree of precision or accuracy. This is done as follows:

- If the digit in the first place beyond (to the right of) the digit to be rounded is greater than 5, add 1 to the right-most digit to be retained and drop all other digits to its right. This is called “rounding up.”
- If the digit in the first place beyond the digit to be rounded is less than 5, simply drop it and all other digits to its right. This is called “rounding down.”
- If the digit in the first place beyond the digit to be rounded is exactly 500 … 0, add 1 to the rightmost digit to be retained if the last significant digit is odd (i.e., 1, 3, 5, 7, 9), and leave the digit to be rounded as is if it is even (i.e., 0, 2, 4, 6, 8). This rule results after rounding in a rightmost digit that is always an even number.

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**Table 6-7 Use of Symbols of Inequality: Illustration with \( P \) Values and Their Interpretation**

<table>
<thead>
<tr>
<th>( P )</th>
<th>Interpretation of Null Hypothesis</th>
<th>Inferences About the Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>.05</td>
<td>Almost certainly not true</td>
<td>Unlikely to be due to chance</td>
</tr>
<tr>
<td>.05</td>
<td>.1</td>
<td>Probably not true</td>
</tr>
<tr>
<td>.2</td>
<td>Possibly not true</td>
<td>Possibly not due to chance</td>
</tr>
<tr>
<td>.2</td>
<td>Nearly certainly true</td>
<td>Likely to be due to chance</td>
</tr>
</tbody>
</table>

*Each \( P \) value can be unambiguously located in one of the four lines of the table. The top line contains all \( P \) values less than .05. The fourth, or bottom, line contains all \( P \) values greater than or equal to .2. The second line embraces all \( P \) values greater than or equal to .05 but less than .1. A small sample size also could account for this \( P \) value.

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**Box 6-12 Inequalities**

- Less than; \( 3 < 4 \) means “3 is less than 4.”
- Greater than; \( 5 > 3 \) means “5 is greater than 3.”
- Less than or equal to; systolic blood pressure \( \leq 130 \) means systolic pressure is “less than or equal to 130.”
- Greater than or equal to; diastolic blood pressure \( \geq 80 \) means diastolic pressure is “greater than or equal to 80.”

**30 \( \leq x < 40 \)**

The number represented by \( x \) is greater than or equal to 30 (i.e., 30 is less than or equal to \( x \)) but is less than 40. Note that \( x \) is strictly less than 40 (39.999...), not exactly equal to 40. This statement is unambiguous, whereas the statement that “\( x \) is between 30 and 40” is ambiguous because it is unclear whether 30 or 40 (or both) is included by the word *between*.

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the counts represent mutually exclusive categories. A list of types of prosthesis used is likely to be mutually exclusive (a patient can fall into only one category), but a table of complications is unlikely to be so (a patient can experience more than one complication). In presenting lists, all categories should be represented, including number of missing values and whether some categories have been coalesced (e.g., under “other”).

List variables are often useful for analysis if they are mutually exclusive (see “Polytomous and Ordinal Logistic Regression” in Section IV). Otherwise, the list should be decomposed into a set of dichotomous variables for each category.

**Continuous Variables**

The other broad category of variables is continuous, for which each patient in a study (sample) may have a different value (e.g., age, weight, ejection fraction). Thus, the raw data are rarely published, because each patient or subject in a study is likely to be unique in regard to continuous variables, making any tabular presentation unwieldy unless the number of patients and number of variables are small. Summarizing statements may be made of the raw data by one of several techniques.

A commonly used summarization of raw data is a simple table with patients grouped into “nice” ordered categories. A histogram is a plot of such a table (see Fig. 6-9, A). Another method of constructing a simple table is to sort patients into several groups of equal number, even if the width of the range of values in each group is different. Because the number of such groups was originally 10, these are called *decile tables*.

Yet another alternative is to divide patients into *percentiles*, stating the value of the variable at these percentiles as follows. Patients or subjects are first sorted by (generally) increasing magnitude of the variable under consideration (e.g., by increasing age). Then the number (or more commonly the proportion) of patients with values less than or equal to each value is calculated. For example, if there are 21 patients and each is a different age at operation, patients are first sorted.
Box 6-13  Words

Piantadosi, Kirklin, and Blackstone provided a glossary of statistical terms in the first edition of Pearson and colleagues' Thoracic Surgery.13

**Population**
The entire set of things with specified attributes. For example, the population of patients with ischemic heart disease encompasses everybody with that disease, not only at the present time, but anyone in the past or future.

**Sample**
One or more things with specific attributes belonging to a population. Thus, my next patient, or a group of patients I have operated on with ischemic heart disease, represents a sample of the population of such individuals.

**Proportion**
A proportion is a part compared with the whole. Specifically, it is the number having some attribute value of interest, divided by the number in the sample. Ten deaths among 30 patients is a proportion of 0.3.

**Percent**
Percent is a part compared with the whole, normalized to a sample size of 100. It is calculated by multiplying a proportion by 100.

**Parameter**
A constant used to characterize some attribute of a population. One generally uses a sample of patients to estimate such constants. These constants are commonly (but not always) designated by letters or symbols in mathematical equations called models (see Box 6-5).

**Variable**
An attribute about a thing that can take on different values from one thing to another. For example, systolic blood pressure is a variable because its value differs from patient to patient. The word *parameter* is often used incorrectly when the word *variable* is meant.

**Prevalence, Incidence, Rate**
*Prevalence*, *incidence*, and *rate* are often used interchangeably. Perhaps common usage should prevail (it rarely leads to confusion), but from the standpoint of correct usage, these are not interchangeable terms. We prefer selecting the specific word whose technical definition matches the context.

**Prevalence**
Frequency of occurrence of some factor, characteristic, event, or incident in a group. Of the three words being considered, it is the least commonly used but the most commonly meant! For example, if 78% of patients are men, the prevalence of males in the sample is 78%; we would not use the phrase, “The incidence of males was….“ Similarly, hospital mortality may be 1%. That is the *prevalence*, or occurrence, of hospital mortality. We would not use the phrase, “Hospital mortality rate was…“ or “Incidence of hospital mortality was….“ The word *occurrence* is often a suitable substitute for *prevalence*.

**Incidence**
Frequency of occurrence *per unit of time*. It is expressed on a scale of inverse time (cases per year, deaths per year) or *rate* of occurrence. The prevalence of mortality across time is expressed as survival; the incidence of mortality is expressed by the hazard function.

**Rate**
Quantity per unit time. Speed is a rate: km · h⁻¹; cardiac output is a blood flow rate: L · min⁻¹. In the context of events, *rate* is synonymous with *incidence*. The hazard function is a rate (mortality · year⁻¹) and incidence.

How, then, can we rephrase such common expressions as the following?
- Incidence of hospital mortality was…
- Hospital mortality rate was…
- Five-year survival rate was…

We could write “Prevalence of hospital mortality was…..” However, in most instances, the words *prevalence*, *incidence*, and *rate* are superfluous. It is better to just write “Hospital mortality was…..” or “Five-year survival was…..”

Box 6-14  Parametric versus Nonparametric

**Nonparametric**
A statistical method that summarizes data in specific ways and by specific procedures that do not use either an empirical or biomathematical model (see Box 6-5). A median value in the distribution of values for age is a nonparametric estimate. Kaplan-Meier survival estimates are nonparametric estimates.

**Parametric**
A statistical method that summarizes data in terms of either an empirical or biomathematical model (see Box 6-5). Numeric estimates of the constants in these models are called *parameter estimates*. Coefficients of a regression equation are parameters (see Box 6-5), as are mean and standard deviation.

**Parameter Estimates**
Parameters in mathematical models (see Box 6-5) are placeholders for numeric values. When the parameters take on specific values, the model becomes an *equation* that can be solved—for example, for an individual patient’s risk. These numeric values are called *parameter estimates*. They are *estimates* because they are based on a finite sample of data. Just as a mean value (a parameter estimate) is associated with uncertainty proportional to both the standard duration (another parameter estimate) and effective sample size, so any parameter estimate is associated with uncertainty.

Parameter values are estimated by means of statistical theory and procedures. The estimation process may be complex or as simple as counting and dividing.
from youngest to oldest. No patient is younger than the youngest one (0/21, 0%, or minimum); 1/21 are as young or younger than the youngest (4.8%), and for these data, this is also the 5th percentile; 2/21 (9.5%) are as young or younger than the second youngest patient, and this is also the 10th percentile. The middle value of age, that of the 11th patient in this list, is called the median or 50th percentile. All (21/21, 100%) are as young or younger than the oldest. A cumulative distribution plot, produced easily by computer but laboriously by hand, presents all the raw data in this percentile format (see Fig. 6-9, B).

Alternatively (and more commonly), a value is found below which a stated proportion of patients have that value or a lesser one (100 times that proportion is the percentile). For example, the median is the 50th percentile. This means that half the patients have a value for the continuous variable below the median, and half have values greater. For consistency, one might also state the 15th and 85th percentiles, as they correspond to 70% confidence limits (CLs; see “Confidence Limits [Intervals]” in Section IV). More commonly, 25th and 75th percentiles (quartiles) or 10th and 90th percentiles are used, which summarize the middle 50% of data.

This method of summarizing data is called nonparametric (see Box 6-14). Beyond such simple counting (percentages and percentiles), more abstract methods are often brought into play to describe continuous data. The methods have in common a process whereby raw data on a sample of patients are used to estimate values of parameters of mathematical equations. The most familiar of these is the arithmetic average, or mean, which is estimated as the summation of all values of the continuous variable (e.g., age, pulmonary artery pressure) divided by the number of people or observations (n). The rationale for using the arithmetic average is that it provides an estimate of the central tendency of the data and a characteristic of the population studied. If the data are distributed perfectly symmetrically in the form of a bell-shaped curve, the arithmetic average is exactly at the midpoint of the data range (Fig. 6-10). It is also the most frequently occurring number (mode), with half the patients above it and half below (median).

The derivation of averages, or means, was begun by astronomers centuries ago. They thought that the scatter in their data was from observational error or imprecision, and they used means, or averages, in an attempt to obtain true values (accuracy). Later, Gauss discussed and described the normal distribution curve, which is estimated as the summation of all values of the continuous variable (e.g., age, pulmonary artery pressure) divided by the number of people or observations (n). The rationale for using the arithmetic average is that it provides an estimate of the central tendency of the data and a characteristic of the population studied. If the data are distributed perfectly symmetrically in the form of a bell-shaped curve, the arithmetic average is exactly at the midpoint of the data range (Fig. 6-10). It is also the most frequently occurring number (mode), with half the patients above it and half below (median).

The mean is the easiest statistic to calculate. Unfortunately, it is not a robust measure of central tendency. If many infants and only one or two adults are in a study, average age is greatly exaggerated by the few adults. A more robust measure of central tendency is the median. Whether or not the sample data are distributed in a Gaussian-type bell-shaped curve (see Fig. 6-10 and Box 6-15) may be tested by such statistics as the Shapiro-Wilk W statistic for small n (e.g., 50 or less) and the Kolmogorov-Smirnov D statistic for larger samples. The skewness of the data (rightward or leftward asymmetric tail) and their kurtosis (unusual peakedness of the distribution of values) are also tested.

Thus, in addition to an estimation of the population mean, some measure of dispersion (variance, spread, scatter) of values is needed. One such measure is the standard deviation, the name of the second parameter of the Gaussian distribution equation (see Box 6-15). It refers to variability from subject to subject or variability of individuals within the sample and is used to determine whether an individual is “within limits of normal.” Standard deviation is necessary for comparison statistics. For example, an individual’s standard deviation from the mean regarding a particular measured variable (commonly called z) is often useful. This is calculated from the difference between the measurement for the individual and the mean normal value divided by the standard deviation. A z may be negative or positive and has no units (see “Standardization of Dimensions” under Dimensions of Normal Cardiac and Great Artery Pathways in Chapter 1).

Standard error is a measure of the reliability with which the population mean is estimated from the sample mean, and it is needed for comparing one group with another. It is more appropriately (but infrequently) called the standard deviation.
### Box 6-15 Gaussian Distribution

The equation of the bell-shaped Gaussian (normal) distribution curve is:

\[
y = \frac{1}{\sigma \sqrt{2\pi}} e^{\frac{-(x-\mu)^2}{2\sigma^2}}
\]

where:
- \( \pi \) is a constant, approximately 3.1415927…, pi
- \( e \) is a constant, approximately 2.7183…, the base of the natural logarithms
- \( \sigma \) is a parameter that represents the standard deviation of the variable
- \( \mu \) is a parameter that represents the mean of the variable \( x \)
- \( y \) represents the probability of occurrence of a particular value of \( x \)

Because in medicine normal has several unrelated meanings, we have used the more technical term Gaussian.

#### Standard Deviation versus Standard Error

Standard deviation is the Gaussian distribution parameter representing the scatter or deviation of individual values from the mean. It is a descriptive statistic, the inflection point of the Gaussian distribution (see Fig. 6-10, B).

Standard error is the standard deviation of the mean, an estimate of the precision of the mean (see Box 6-15). Unlike the standard deviation, which is similar in value for large and small samples of data, the standard error decreases as approximately the square root of \( n \) increases.

Because the Gaussian curve is symmetric around the mean, the two parameters of the Gaussian distribution are expressed by the shorthand mean \( \pm SD \), where SD is 1 standard deviation. This means 68.3% of values for patient age fall between (mean – SD) and (mean + SD). This is one instance, not common in statistics, where the shorthand \( \pm \) is used instead of confidence limits (see Box 6-16).

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of the mean and is obtained simply by dividing the standard deviation by the square root of \( n \) (see Box 6-15).

Other methods are available for summarizing skewed data. One is to resort to a purely nonparametric (i.e., without equations, coefficients) description (e.g., using the median and its various percentiles). Another is to transform the data into a more normally distributed variable. For example, a logarithmic transformation is often useful; the resultant mean is called the geometric mean.

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### Section IV Analyses

**HISTORICAL NOTE**

Analysis, as expressed by Sir Isaac Newton, is that part of an inductive scientific process whereby a small part of nature (a phenomenon) is examined in the light of observations (data) so that inferences can be drawn that help explain some aspect of the workings of nature.

Philosophies underpinning methods of data analysis have evolved rapidly since the latter part of the 19th century and may be at an important crossroad. Stimulated in large part by the findings of his cousin Charles Darwin, Sir Francis Galton, along with Karl Pearson and Francis Edgeworth, established at that time what has come to be known as biostatistics. Because of the Darwinian link, much of their thinking was directed toward an empirical study of genetic versus environmental influence on biological development. It stimulated development of the field of eugenics (human breeding) and the study of mental and even criminal characteristics of humans as they relate to physical characteristics (profiling). The outbreak of World War I led to development of statistics related to quality control. Sir Ronald Fisher formalized a methodological approach to experimentation, including randomized designs. The varying milieu of development led to several competing schools of thought within statistics, such as frequentist and Bayesian, with different languages and different methods. Formalization of the discipline occurred, and whatever the flavor of statistics, it came to dominate the analytic phase of inferential data analysis, perhaps because of its empirical approach and lack of underlying mechanistic assumptions.

Simultaneously, the discipline of biomathematics arose, stimulated in particular by the need to understand the growth of organisms (allometric growth) and populations in a quantitative fashion. Biomathematicians specifically attempt to develop mathematical models of natural phenomena such as clearance of pharmaceuticals, enzyme kinetics, and blood flow dynamics. These continue to be important today in understanding such altered physiology as cavopulmonary shunt flow. Many of the biomathematical models came to compete with statistical models for distribution of values for variables, such as the distribution of times to an event.

Advent of the fast Fourier transform in the mid-1960s led to important medical advances in filtering signal from noise and image processing. The impetus for this development came largely from the communications industry, so only a few noticed that concepts in communication theory coincided with those in statistics and mathematics.

As business use of computers expanded, and more recently as genomic data became voluminous, computer scientists developed methods for examining large stores of data (see footnote 1, p. 253). These included data mining in business and computational biology and bioinformatics in the life sciences. Problems of classification (e.g., of addresses for automating postal services) led to such tools as neural networks, which have been superseded in recent years by an entire discipline of machine learning.

In the past quarter century, all these disciplines of mathematics, computer science, information modeling, and digital signal processing have been vying for a place in the analytic phase of clinical research that in the past has largely been dominated by biostatistics. Specifically, advanced statistics and algorithmic data analysis have conquered the huge inductive inference problem of disparity between number of parameters to be estimated and number of subjects (e.g., in genetics, hundreds of thousands of variables for \( n = 1 \)). Advanced high-order computer reasoning and logic have taken the Aristotelian deterministic approach to a level that allows intelligent agents to connect genotype with phenotype. It may be rational to believe that the power of these two divergent approaches to science can be combined in such a way that very “black box” but highly predictive methods can be explored by intelligent agents.
report the logical reasons for a black-box prediction.31 Fortunately for those of us in cardiac surgery, we need not be threatened by these alternative voices, but rather can seize the opportunity to discover how each can help us understand the phenomena in which we are interested.

OVERVIEW

This section highlights (1) the important statistical concept of dealing with uncertainty, illustrating it with CLs and P values, (2) the increasingly important signal processing concept, multivariable analysis, illustrating it with logistic regression of early postoperative events; and (3) analysis of time-related and longitudinal events, which we present in terms of biomathematical concepts. In Section VI, other specialized methods are highlighted, including some that are only peripherally related to serious clinical research but importantly affect cardiac surgeons.

UNCERTAINTY

Publication of an experience with mitral valve repair in 438 patients, among whom 8 (1.8%) died in the hospital, is in isolation a record of past achievement. Assuming honest reporting, there is no uncertainty about this result, but in and of itself, except for inviting applause or criticism, it has only historical value. Yet most persons expect past experience to be useful in predicting what can be accomplished in the present or the future, or in comparing outcome with that of other surgical options or continued medical therapy (see “Nihilism versus Predictability” in Section I). That is, they recognize the future is uncertain, but they are not nihilists; they assume there is continuity in nature (see “Continuity versus Discontinuity in Nature” in Section I). There are well-tested theories and methods that quantify the uncertainty of inferring from the past the probable results in the future (assuming nothing changes), expressed as a degree of uncertainty. Quantifying the degree of uncertainty is a major part of making results of past experience truly useful.

Point Estimates

Point estimates usually represent the central tendency of a set of numbers that describe the characteristics or state of a sample (e.g., group of patients). The previously mentioned 1.8% hospital mortality is a point estimate. So are the mean value of age in a group of patients and percent survival (survivorship) 1 or 20 years after an operation.

Such numbers are generally derived from a study of a sample (see Box 6-13) of all members of a population (e.g., everyone everywhere undergoing mitral valve repair). Yet the clinical study is nearly always performed to generalize beyond the sample examined.

Generalizing from a sample to the population is fraught with uncertainty. For example, recorded, unrecorded, or unrecognized patient characteristics may occur at a different frequency in the sample than in the population (including your future patients). Surgeons use expert clinical judgment in decision making, and this introduces selection bias into the sample. There is well-recognized variance in institutional policies, processes, procedures, skill, and experience that influences outcome in ways that are difficult to dissect and confounded inextricably with both outcomes and interpretation of outcomes. These all suggest that inferences from sample point estimates alone are unlikely to be predictive of results in either the population or future samples.

Despite this admonition over the past quarter century, we have observed fewer and fewer cardiac surgery publications that accompany point estimates with a measure of uncertainty. Although it is speculation, the cause may be in part the complexity of programming the present generation of advanced programmable calculators and handheld computers to generate CLs “on the fly” as one reads journal articles.

Confidence Limits (Intervals)

CLs, the extremes of a confidence interval (Box 6-16), are the fundamental statistics that quantify the uncertainty of point estimates. It is not the underlying data that are uncertain (e.g., how many hospital deaths occurred in a well-defined group of patients), but inferences about the future based on known data from the past.

For example, if there was one hospital death in three operations for postinfarction VSD, the proportion of hospital deaths (hospital mortality) was 0.33 (1/3, 33% hospital mortality). This was the mortality in that experience, looking at it solely as a record of achievement. Likewise, if 10 deaths occurred among 30 such operations, or 100 occurred among 300, the mortality was also 33%. Intuitively, there would be more confidence that the risk in an entire population, not just in the small sample studied, was near 33% on the basis of the experience with 300 operations than on the basis of three operations. Yet, also intuitively, one suspects something has been learned about the risk in an entire population from only three operations. For example, the true risk cannot be exactly 0% or exactly 100%.

Historical Development

The questions “What is the risk of repair of postinfarction VSD in general?” and “Is risk with the method of repair I used higher or lower than that with the method another surgeon is using?” are similar to questions put to Galileo about the nature of chance, and particularly games of chance, by 17th-century gamblers.33,34 From those questions emerged the Laws of Chance, now known as the theory of probability.33 These laws are believed to apply to all things that can have more than one possible result; things with exactly one result are the limiting case of this theory, having a probability equal to 1, or certainty. More and more scientists believe that all natural phenomena, including those of the physical world, behave in accordance with the theory of probability.37,39

Box 6-16 Confidence Limits, Confidence Intervals

Confidence Limits

Numbers at the two extremes of an interval that encompasses a stated percentage of the variability of a point estimate. In this book, we use confidence limits (CL) rather than confidence intervals (CI) to avoid confusion with cardiac index (CI), a familiar abbreviation used by cardiac surgeons.

Confidence Interval

Interval encompassing a stated percentage of the variability of a point estimate.
Events and phenomena of cardiac surgery can also be considered to behave in accordance with this theory.

Galileo showed that there is variability in sample point estimates. To illustrate, if the risk of death in the entire population of patients undergoing repair of postinfarction VSD by a given method is 33%, and samples of 3 patients are taken repeatedly, 0 deaths among the 3 would be experienced in 30% of samples, 1 death in 44% of samples, 2 deaths in 22% of samples, and 3 deaths in 4% of samples. In larger samples, results are less variable. For example, with samples of size 300, although the number of deaths experienced may still be quite variable, the proportion dying will be 30% to 36% in 70% of samples taken.

Because of this random variability in the sample estimates of risk, it is impossible to estimate the population parameter (see Box 6-13) with certainty (i.e., to know the risk in the entire population) from sample information. However, the pattern of variability in repeated sampling is well understood, and in most situations it is possible to derive a formula to calculate the range of values that would contain the parameter for a specified percentage (e.g., 70%) of samples taken.

Users of CLs should be aware that this range of values for all proportions except 0.5 (50%) is asymmetric, in contrast to standard deviations, which are symmetric. Thus, we must report both the point estimate (probability) and lower and upper CLs.

As the sample size increases and more information becomes available, width of the confidence interval decreases (i.e., a more precise estimate is obtained). With a more precise estimate, the investigator is less uncertain where the population parameter lies, or in other words, what the “true” risk is. With a less precise estimate, the investigator is more uncertain.

### Computational Methods

A number of methods have been developed to calculate CLs for proportions. Bootstrapping is a generalized method for obtaining CLs for any statistic. The original sample of data is randomly sampled in such a way that the patient can be sampled again (sampled with replacement) and form a data set equal in size to the original. Because of replacement, some patients will appear more than once in this bootstrap sample, and others will not appear at all. The point estimate (e.g., hospital mortality) is estimated in this sample. Then another sample is drawn in the same fashion, and this process is repeated as many as 1000 times. All the point estimates from each sample are sorted from smallest to largest, as in forming a cumulative frequency distribution (see Descriptive Data Exploration in Section III). The “best” estimate of the point estimate is the median value (50% above and 50% below). If 70% CLs are desired, then the 15th percentile is the lower CL and the 85th percentile is the upper limit (if 68.3% limits are desired, the numbers would be approximately the 16th and 84th percentiles). Approximating formulae are used in most statistical packages.

### What Level of Confidence?

Any desired CL can be derived, such as 50%, 70%, 90%, 95%, or 97.5%. Choice of CLs to be expressed (called the confidence coefficient) depends on (1) use to be made of them, (2) consistency, or (3) convention, in that order of preference.

Most often in cardiac surgery, CLs are used as scanning tools to aid predictions and comparisons, either of proportions or time-related depictions (see “Scanning Tool” later in this section). If great certainty is desired in the inference that there is a difference between two proportions of time-related depictions, 95% confidence intervals may be chosen for the comparisons. If only moderate certainty is required that the evident difference is a true difference and would be found in larger samples, 50% confidence intervals might be chosen.

Most situations in cardiac surgery seem to lie somewhere between these extremes, so use of 70% CLs for most comparisons is reasonable. The interval is relatively narrow (specific), and although it is reasonably certain that lies within the CLs, there is a 15% chance it will be higher and a 15% chance it will be lower.

Seventy-percent CLs (actually 68.3%) are equivalent to 1 standard deviation (SD), and 95% CLs are consistent with 2 SDs. For consistency, if other numeric estimates are presented to 1 SD, 70% CLs should be used, and if 2 SDs are presented, 95% CLs should be used. We emphasize consistency because we believe surgeons should become familiar with using CLs as a scanning tool; to use a tool effectively, it is helpful to be consistent among all measures of uncertainty. Conventionally, many statisticians use 95% CLs, even in the context of using 1 SD for most everything else, and 50% limits for nonparametric statistics. This makes no sense and is simply a habit, not a product of reflective thinking about the inferences or about consistency.

In numeric presentation of differences, such as difference in survival curves (see Box 6-3), 90% CLs are equivalent in comparative inference to individual 70% CLs, a largely empirical finding. The reason is that a one-sided confidence interval of a difference between two estimates is narrower than the sum of the 70% upper and lower CLs that just touch. This narrowness is compensated for by use of somewhat wider CLs (90%) of the difference.

### Scanning Tool

Overlapping or nonoverlapping of CLs around two or more point estimates can be used as a simple and intuitive scanning method for determining whether the difference in point estimates is unlikely to be due to chance alone. Delimit the effect, and because they are accompanied by the magnitude of the effect, there is no confusion between statistical significance and magnitude of the effect, as there may be if P values are used (see “P Values” later in this section). When CLs are not overlapping, the difference is unlikely to be due to chance alone.

Because the phrase “nonoverlapping CLs suggests with a stated degree of uncertainty that a difference exists” is cumbersome, the phrase evident difference may be used to express the same idea (Appendix 6B). Nonoverlapping CLs are easily visualized in a nomogram in which the CLs are displayed around the point estimate expressing the association between variables. Within this context, it can be said with a stated degree of uncertainty that the effect of the independent variable compared with a baseline value becomes evident at the
point at which the CLs just separate. However, in contrast to evident differences in a contingency table, this point is not easily seen in a nomogram, and it does not appear in an equation. The point at which evident differences appear in equations can, however, be calculated mathematically (see Appendix 6B).

We stress that comparing CLs in this way is a scanning tool. The classic method using \( P \) values involves computing the difference between the two proportions and testing the hypothesis that the difference is zero. Experience with scanning and \( P \) value methods has taught that when the lower 70% CL of one estimate just touches the upper 70% confidence of the other, the \( P \) value for the difference is between .08 and .1; when similar 95% CLs just touch, the \( P \) value is about .01.

**\( P \) Values**

The phrase “statistically significant,” generally referring to \( P \) values, has done disservice to the understanding of truth, proof, and uncertainty. This is in part because of fundamental misunderstandings, in part because of failure to appreciate that all test statistics are specific in their use, and in part because \( P \) values are frequently used for their effect on the reader rather than as one of many tools useful for promoting understanding and framing inferences from data.\(^{6,5,13,58}\) In fact, \( P \) values are deemed by some to be unnecessary statistics and not worth the risk of misinterpreting or misusing them. They prefer CLs.\(^{56}\)

**Definition**

In the context of hypothesis (or significance) testing, the \( P \) value is the probability of observing the data we have, or something even more extreme, if a so-called null hypothesis is true.\(^{6,53}\) (Box 6-17).

Historically, hypothesis testing is a formal expression of English common law. The null hypothesis represents “innocent until proven guilty beyond a reasonable doubt.” Clearly, two injustices can occur: a guilty person can go free or an innocent person can be convicted. These possibilities are termed **type I error** and **type II error**, respectively (see Box 6-17). Evidence marshaled against the null hypothesis is called a test statistic, which is based on the data themselves (the exhibits) and \( n \). The probability of guilt (reasonable doubt) is quantified by the \( P \) value or its inverse, the odds \([1/(1/P)]−1\) (see Box 6-3).

Had the originators been raised under a different judicial system, perhaps a different pattern for testing hypotheses might have arisen. Specifically, the system does not judge how innocent a person is (the “alternative hypothesis”; see Box 6-17), nor does it test for equivalence, a very important matter for comparing pharmaceuticals and even alternative surgical therapies.\(^{6,5,12,5,4,7,4,51,8}\)

Some statisticians believe that hypothesis or significance testing and interpretation of the \( P \) value by this system of justice is too artificial and misses important information.\(^{5,3,6,5,2}\) For example, it is sobering to demonstrate the distribution of \( P \) values by bootstrap sampling. Furthermore, the magnitude of the \( P \) value is dependent on two factors: magnitude of difference and sample size. These individuals would prefer that \( P \) values be interpreted simply as “degree of evidence,” “degree of surprise,” or “degree of belief.”\(^{6,7,5}\) We agree with these ideas and suggest that rather than using \( P \) values for judging guilt or innocence (accepting or rejecting the null hypothesis), the \( P \) value itself should be reported as degree of evidence.

### Box 6-17 Hypothesis (Significance) Testing

#### Statistical Hypothesis

A claim about the value of one or more parameters. For example, the claim may be that the mean for some variable (e.g., creatinine) is greater than some fixed value or some value obtained under different conditions or in a different sample of patients.

#### Null Hypothesis

A claim that the difference between one or more parameters is zero or no change (written \( H_0 \)). It is the claim the investigator is arguing against. When a statistician infers that there is “statistical significance,” it means that by some criteria (generally a \( P \) value), this null hypothesis has been rejected. Some argue that the null hypothesis can never be true, and that sample size is just insufficient to demonstrate this fact. They emphasize that the magnitude of \( P \) values is highly dependent on \( n \), so other “measures of surprise” need to be sought.

#### Alternative Hypothesis

This is the “investigator’s claim” and is sometimes called the study hypothesis. Usually the investigator would like the data to support the alternative hypothesis.

#### Test Statistic

A number, computed from the distribution of the variable to be tested in the sample of data, that is used to test the merit of the null hypothesis.

#### Type I Error

Rejecting the null hypothesis when it is true (false negative). The probability of a type I error is designated by the Greek letter alpha (\( \alpha \)).

#### Type II Error

Not rejecting the null hypothesis when it is false (false positive). The probability of type II error is designated by the Greek letter beta (\( \beta \)).

Calculating the \( P \) Value

All methods for calculating \( P \) values have in common one or more point estimates, some measure of variability for each, some comparison statistic related to the point estimates (e.g., the difference or a ratio), an estimate of the variability of the comparison statistic, and size of the groups.

The test to be used is selected. This must be appropriate for the comparison. It is crucial that a biostatistician familiar with the data and desired comparison be the one to select this test and interpret the results. In general terms, this demands that a specific distribution of the difference or ratio be selected. From the difference or ratio, some measure of its variability, \( \sigma \), and \( n \), a number is computed for the particular distribution selected, called the test statistic (see Box 6-17). There are a number of test statistics, which means there are a number of prescribed, defined, specific methods (tests) for calculating the test statistic. The statistician selects the test statistic to be used on the basis of the fit of the data to the assumptions underlying the test.
The magnitude of the computed test statistic among the hypothetically determined distribution of values for the test chosen is determined. The area under the distribution curve (proportion of the total area) occupied by more extreme values of the test statistic is the $P$ value, a number ranging from 0 to 1.

In the case of many test statistics, a family of distribution curves exists, and to determine the $P$ values, one of these must be selected. The selection is based, more or less, on the sample size ($n$). By “more or less,” we mean that some information content in the $n$ may already have been “used up” in other calculations in the process and may not be available for computation of the $P$ value. What is left, called degrees of freedom, determines the distribution curve selected.

The phrases one-tailed $P$ value and two-tailed $P$ value are commonly used. Which is appropriate depends on the research hypothesis being tested. When the hypothesis relates to differences in either direction (“different from zero”), a two-tailed $P$ value is used; when it relates to differences in only one direction (“less than,” for example), a one-tailed $P$ value is used. A two-tailed $P$ value is always the same as or larger than a one-tailed $P$ value. Generally, in the work described in this book, two-tailed $P$ values are used.

Use of Expressions of Degree of Uncertainty

Whether one uses CLs or $P$ values, a decision must be made concerning the degree of certainty desired in the inference that $A$ is different from $B$. Some have a slavish attachment to a certain $P$ value, such as .05, or a certain width of CLs, such as 95%, as the yardstick for all situations. Sir Ronald Fisher wrote, “No scientific worker has a fixed level of significance at which from year to year, and in all circumstances, he rejects hypotheses; he rather gives his mind to each particular case in the light of his evidence and his ideas.”

This discussion would be unnecessary if all sample sizes were moderately large and the number of events ample, providing adequate power (information content) for all computations (see Box 6-4). In many clinical investigations, a large sample is simply not available, yet important decisions must be made on the basis of the inference generated. Then the cost of making a wrong decision based on an analysis, and the risk of overlooking or not finding a relation between two variables that in fact exists, plays importantly in the decision regarding what $P$ value to use (see Table 6-7 and Box 6-17). The greater the cost, the smaller the $P$ value demanded.

An apparent contradiction to the foregoing discussion is the setting of so-called humongous databases of hundreds of thousands or millions of patients. In this setting, the dependence of $P$ values on $n$ becomes glaringly apparent. Essentially in every comparison, no matter how small the clinical difference, $P$ values are small. “All null hypotheses are false.”

In this circumstance, other measures of surprise must be devised for testing differences that take into account the magnitude of the difference.

**MULTIVARIABLE ANALYSIS**

The Necessity

Surgeons have intuitively understood that surgical outcome, such as hospital mortality, may be related to a number of explanatory variables, such as renal and hepatic function. However, when presenting a risk factor analysis of outcome for a group of patients, two reactions are heard, often from the same critic: (1) “Your analyses are much too complex, far beyond the comprehension of ordinary cardiac surgeons,” and (2) “This is a very complex, multifactorial situation, and you have not begun to take all the things that could have influenced outcome into consideration.” This contradiction reflects the cognitive structure of the human mind, as discussed in Section I. On the one hand, we perceive, understand, and store in our brains simplified models of reality; on the other hand, our conscious minds recognize that “things are often less simple than they seem.”

To complicate matters, we generally know neither the cause nor the causal sequence that leads to a surgical failure, and that is what we want to know to make progress toward preventing future failures. The cause may in fact be buried in the clinical record and the data we have extracted therefrom, but we do not know this is true and suspect we are ignorant of the real cause. Extensive cautionary literature on surrogate endpoints for clinical trials and how they can lead us astray fuel this anxiety (Fig. 6-11). We need, perhaps, to be reminded that public health recommendations based on crude risk factors for the plague were effective in halting it and preventing its recurrence for 200 years while the causative organism and vector were being discovered.

Faced with hundreds, perhaps thousands, of variables, the investigator seeks to find simple or dominant or stratospheric comprehension of the data. He or she wants to discover the wood, not necessarily the trees (or branches and leaves, for that matter). Multivariable analysis (Box 6-18) is a set of methods for considering multiple variables simultaneously and for (1) identifying those that by some criteria are associated with an outcome, (2) estimating the magnitude of each variable’s influence in light of all others, (3) quantifying the degree of uncertainty of those estimates, and (4) revealing the relation among the set of variables so identified while (5) dismissing others either as noise or as so correlated with other variables associated with outcome that they either do not contribute further information or are so lacking in information (sparse) that their association cannot be determined.

**Historical Note**

Fisher understood the relation of outcome to possibly multiple explanatory variables when he wrote that the behavior of a sample could be considered characteristic of the population only when no subsets within the population behaved differently. Yet the use of these ideas in a formal way in medicine emerged only during the last half of the 20th century. This is because multivariable analysis, particularly of events after cardiac procedures and more especially time-related outcomes, involves considerable computational power. The mathematical models are nonlinear (see Box 6-5), so solving for their parameters is (1) an iterative process—that is, a series of systematically directed mathematical steps that
follow an algorithm or plan to find the best value of the coefficient and its variability by gradually closing in on it, and (2) a mathematical process in which computations for explanatory variables are performed simultaneously. Because the computational challenge is considerable, use of multivariable analysis had to await development of computers.

The first use of multivariable analysis to identify risk factors for outcome events in humans was probably the Framingham epidemiologic study of coronary artery disease.\textsuperscript{520} Two papers are landmarks in this regard. In 1967, Walker and Duncan published their paper on multivariable analysis in the domain of logistic regression analysis, stating that “the purpose of this paper is to develop a method for estimating from dichotomous (quantal) or polytomous data the probability of occurrence of an event as a function of a relatively large number of independent variables.”\textsuperscript{W2} Then in 1976, Kannel and colleagues coined the term “risk factors” (actually “factors of risk”), noting that (1) “a single risk factor is neither a logical nor an effective means of detecting persons at high risk” and (2) “the risk function…is an effective instrument…for assisting in the search for and care of persons at high risk for cardiovascular disease.”\textsuperscript{K3} In 1979, the phrase “incremental risk factors” was coined at UAB to emphasize that risk factors add in a stepwise, or incremental, fashion to the risk present in the most favorable situation.\textsuperscript{K9}

Before the advent of multivariable analysis, stratification of the values of one or more potential risk factors was often used to search for association of risk with outcome. Although this is still of interest as a scanning method, it has serious disadvantages, including (1) loss of information by coarseness of stratification and (2) possibly erroneous inferences from the necessarily arbitrary nature of stratification. These dangers were well summarized by Kannel and colleagues, who stated that “while there is some convenience in dichotomizing a continuous variable like blood pressure into high and low, one would prefer some method to take into account the exact value.”\textsuperscript{K3}

Figure 6-11  Success and failure of surrogate end points. Success: Setting that provides greatest potential for surrogate end point to be valid. Failure: Four reasons for failure of surrogate end points. A, Surrogate is not in causal pathway of disease process. B, Of several causal pathways of disease, intervention affects only pathway mediated through surrogate. C, Surrogate is not in pathway of intervention’s effect or insensitive to its effect. D, Intervention has mechanisms of action independent of disease process. Dotted lines represent mechanisms of action that might exist. (Redrawn from Fleming and DeMets.\textsuperscript{F2})
Carrier of Risk Factors: Underlying Mathematical Model

Multivariable analysis as described by the Framingham investigators requires a model (equation) that relates a placeholder for explanatory variables (generally one or more of the model parameters) to the dependent (outcome) variable. The equation may be a completely linear one; for these, iterative techniques are not required, but the computations are large and for all practical purposes require a computer. The general term for such a model is a regression equation (see Box 6-5).

Logistic multivariable regression analysis is a special type of nonlinear model that can be used as a prototype to understand the nature of the relation of risk factors to outcome in a medically rational fashion. Fig. 6-1, A illustrates the relation between the absolute probability of an event on the vertical axis and an expression of risk measured in logit units along the horizontal axis. The horizontal axis is the one related to risk factors. The relation is sigmoidal (S-shaped). Notice that an increment of risk along the horizontal axis, if far to the left or right of the curve, is not associated with a perceptible increase or decrement in probability. However, a small increment near 0 logit units is associated with a large change in probability.

To illustrate, imagine two patients. One is a strapping football player who is mugged on his way to a pharmacy late at night. He is stabbed in the abdomen, and his inferior vena cava is lacerated. Fortunately, a trauma center is nearby, and he is rushed to surgery. His anxious parents arrive at the hospital about an hour after the incident and want to know, “What are his chances, doctor?” Let us say that the injury moves the football player’s risk two units to the right on the logit scale. Before the incident, this robust individual was near the center of the logit curve, say at −1 logit units, before the incident. Two logit units of acute risk greatly increase his probability of hospital mortality.

A week later, the second patient, a frail, elderly diabetic man, is walking to the same pharmacy for his insulin when he is stabbed in the abdomen, and his inferior vena cava is lacerated. He too is rushed to the trauma center and into the operating room. An hour later, his anxious daughter arrives at the hospital and wants to know, “What are his chances, doctor?” The fragile patient may already have been sitting near the center of the logit curve, say at −1 logit units, before the incident. Two logit units of acute risk greatly increase his probability of hospital mortality.

These anecdotes emphasize that the models underlying risk make good medical sense. They reflect what we mean by a robust patient, a fragile patient, and an unsalvageable patient. They reflect the reality that the identical risk factor may operate with respect to absolute risk differently, depending on the presence or absence of other risk factors.

Risk Factor Identification

Given a mathematical model to carry risk factors (see Box 6-5), the next task is risk factor identification. It requires (1) screening of candidate variables for suitability in the analysis, (2) calibrating continuous and ordinal variables to outcome, (3) selecting variables related to outcome, and (4) presenting results in the format of incremental risk factors.

Screening

Screening candidate variables has two purposes: (1) to determine whether there are sufficient data (see Box 6-4) to be suitable in the analysis and (2) to understand a variable in relation to other candidate variables. Because for outcome events the effective sample size for analysis is the number of events, not the number of patients, a variable may not be suitable for analysis when it represents a subgroup of patients with too few events to evaluate. This represents a limitation of the study, not of methodology. Indeed, one is generally happy with a therapy associated with few events; however, it then makes sense that risk factors cannot be identified.

We do not screen variables to discover which ones relate individually to outcome. It is a common practice of many groups to ignore variables that are not univariately associated with outcome. However, there is a long history of occurrence of lurking variables (Box 6-19 and Fig. 6-12) that are found to relate to outcome only when (1) other variables that mask their importance are accounted for in the analysis or (2) they are suitably transformed (or coupled with nonlinear rescaling of themselves), indicating a complex association with outcome.

It is valuable to determine the pairwise correlation of variables. This will help one understand why many variables may be associated with outcome, but only a few are selected as risk factors. Medical data are highly redundant, sharing a great deal of information.

Calibration

Continuous variables contain unique values for each patient and so are particularly valuable in analyses. For unclear reasons (statisticians uniformly decry the practice), many investigators stratify continuous variables into two or a few arbitrary categories, throwing away valuable information. This flies in the teeth of a fundamental philosophy of data analysis: continuity in nature (see “Continuity versus Discontinuity in Nature” in Section I). Furthermore, to better understand the phenomenon we are studying, it is important to determine the shape of the relation of continuous variables (e.g., age, birth weight, creatinine) to outcome.

Box 6-19 Lurking Variables

Lurking variables are those found to relate to some outcome or dependent variable (see Box 6-5) only after (1) other variables masking their importance are taken into account either by multivariable analysis or matched-type analyses (e.g., using balancing scores) or (2) the lurking variable (if continuous or ordinal) is properly rescaled (e.g., transformed) so that complex relations are revealed, such as higher risk of mortality at both old and young age.

Fig. 6-12, A shows survival in patients after exercise stress testing stratified according to long-term aspirin use.

Apparently there is no relation to survival. However, Table 6-3 shows that there are multiple differences in patient characteristics between these two groups of patients, with those taking aspirin being older, for example. Indeed, in multivariable analysis, the moment age is taken into account, a beneficial effect of long-term aspirin is revealed. Fig. 6-12, B shows survival in propensity-matched pairs of patients (see “Clinical Studies with Nonrandomly Assigned Treatment” in Section I). The lurking benefit of long-term aspirin use is clearly revealed.
However, the scale on which a continuous variable has been measured or expressed may not coincide with the outcome. Therefore, the appropriate calibration of the variable to outcome must be discovered. One method to accomplish this is to examine various linearizing transformations (Fig. 6-13). However, the “perfect” transformation of scale may not coincide with the best one after other factors have been considered in a multivariable model. Thus, we rely on graphical methods, as in the figure, to obtain a set of similar transformations, and then include all transformed variable candidates in the selection process to be described. A promising offshoot of nonparametric machine learning techniques, such as random forests technology, is the generation of risk-adjusted coplots that can suggest the shape of the relationship of these continuous variables with risk (Fig. 6-14).

**Variable Selection**

A seminal contribution of the Framingham Study investigators was the idea that in the absence of identified mechanisms of either disease or treatment failure, useful inferences for medical decision making, lifestyle modification, and programmatic decisions about avenues of further research can be gleaned by nonspecific risk factor identification. A direct consequence of the idea, however, is that for any set of potential variables that may be associated with outcome, there is no unique set of risk factors that constitute the best common denominators of disease or treatment failure. Therefore, different persons analyzing the same data may generate different sets of risk factors.

As a consequence, multivariable identification of risk factors has become an art that depends on expert medical knowledge of the entity being studied, understanding the goals of the research, knowledge of the variables and how they relate to the study goals as well as to one another, identification of the quality and reliability of each variable, and development of different, often sequential, analysis strategies appropriate to each research question. Not all these issues of art or expertise will disappear, but there are substantial aspects of multivariable analysis that are yielding to science.
Figure 6-14  Risk-adjusted coplot demonstrating shape of relationship of continuous variables at risk. A, Blood urea nitrogen (BUN) and 5-year survival with coplots of treadmill exercise time and peak oxygen consumption ($\text{VO}_2$) using less smoothing. B, Preoperative creatinine and risk of postoperative atrial fibrillation for white and black patients. Note the nonlinear U-shaped relationship.

<table>
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<th>peak $\text{VO}_2$ (mL/kg/min)</th>
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<th>15</th>
<th>20</th>
<th>25</th>
<th>30</th>
<th>35</th>
<th>40</th>
</tr>
</thead>
<tbody>
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<td>80</td>
<td>0</td>
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<td>80</td>
<td>0</td>
</tr>
<tr>
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<td>40</td>
<td>70</td>
<td>10</td>
<td>40</td>
<td>70</td>
<td>10</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
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<td>80</td>
<td>0</td>
<td>40</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>Adjusted probability</td>
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<td>0.3</td>
<td>0.35</td>
<td>0.4</td>
<td>0.45</td>
<td>0.5</td>
</tr>
<tr>
<td>Preoperative creatinine level (mg·dL$^{-1}$)</td>
<td>0</td>
<td>2</td>
<td>4</td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A3,L6

Nafteil, of UAB, in an important 1994 letter to the editor of the Journal of Thoracic and Cardiovascular Surgery, addressed nine aspects of multivariable analysis that contribute to obtaining different models (sets of risk factors). He called these “steps and decisions that may influence the final equation”:

- Differing statistical models. For example, if time-related events are being modeled, results using a Cox proportional hazards model (see “Cox Proportional Hazards Regression” later in this section) will differ from those using a multiphase nonproportional hazards model (see “Parametric Hazard Function Regression” later in this section).
- Differing approaches to missing data (see “Impute Values” in Section III).
- Differing approaches to minimal information (see Box 6-4).
- Differing approaches to correlated data. Variables with similar information content should be chosen for maximal insight by the clinical investigator, not necessarily the statistician.
- Differing coding of data. Some may pay more attention than others to linearizing transformation of continuous variables, to whether continuous or ordinal variables should be dichotomized or in other ways collapsed, or to management of interaction (multiplicative) variables.
- Differing approach to apparently incorrect data. Variables with similar information content should be chosen for maximal insight by the clinical investigator, not necessarily the statistician.
- Differing variable selection methods and $P$-value criteria. This area is undergoing complete change through introduction of machine learning algorithmic methods.\cite{561} Even with new methods, however, a criterion must be arbitrarily established to differentiate what is signal from what is noise ($P$ values, for example).
- Differing computer resources. Although even desktop computers rival the computational capacity of large-scale computers of a decade ago, computer-intensive methods may require large networks of computers.
- Differing appreciations of the science. Unless data analysts work collaboratively with the surgeon-investigator, analysis may be uncreative. One cannot divorce the underlying clinical science from data analysis.

In all these areas but one, new knowledge has been generated that is beginning to differentiate inadequate techniques from reasonable techniques and optimal techniques. That one area remaining is “differing variable selection methods,” and it is an important one.

Part of the challenge is that variables may be thought to be risk factors because they are associated with a small $P$ value, and other factors may be thought not to be risk factors because of larger $P$ values, but both opinions may be erroneous (type I and type II statistical errors, respectively; see Box 6-17). There is therefore a need for a method that balances these two types of error. Closely coupled with this is the need for a statistic that measures the reliability with which a risk factor has been identified. Because one is analyzing only a single set of data rather than many sets of data about the same subject, determining this reliability has been elusive.

There is new thinking about what risk factor identification is. In thinking anew, we leave traditional statistical methodology out of the picture, and risk factor identification becomes an attempt to find signal (risk factors) in noise (other candidates). Important advances in pure mathematics (logical analysis)\cite{53,54} and machine learning (algorithmic analysis)\cite{561} are proving valuable for such diverse signal detection challenges as handwriting identification, genomic identification, and now risk factor identification. These techniques are
Chapter 6  Generating Knowledge from Information, Data, and Analyses

Bootstrap bagging belongs to a class of new methods that has developed over the past 30 years. In 1983, an astonishing article entitled “Computer-Intensive Methods in Statistics” appeared in the popular scientific literature. Its authors, Persi Diaconis and Bradley Efron from Stanford University, indicated that “most statistical methods in common use today were developed between 1800 and 1930, when computation was slow and expensive. Now, computation is fast and cheap…. The new methods are fantastic computational spendthrifts…. The payoff for such intensive computation is freedom from two limiting factors that have dominated statistical theory since its beginnings: the assumption that the data conform to a bell-shaped curve and the need to focus on statistical measures whose theoretical properties can be analyzed mathematically.”

Efron and his group demonstrated that random sampling with replacement from a data set to create a new data set, resampling to produce perhaps thousands of new data sets, and combining the information generated from these many data sets can produce robust and accurate statistics without assumptions. His group called this technique bootstrapping, after the expression “pulling yourself up by your own bootstraps,” because it reflected the fact that one could develop all the statistical testing necessary directly from the actual data simply by repeatedly sampling them (see footnote 7, p. 296).

These techniques have been applied to entire analytical processes, including multivariable analysis. In fact, one still has to pay attention to appropriate models, missing data, variable considerations, correlated variables, appropriate strategy, and so forth, that remain part of a disciplined, informed approach to the data. However, the variable selection process is bootstrapped.

In practice, a carefully crafted set of variables is formulated that will be subjected to simple automated variable selection, such as forward stepwise selection, whereby the most significant variables are entered one by one into a multivariable model. Specific $P$ value criteria for entering and retaining these variables are specified. Then a random bootstrap sample of cases is selected, generally of the same sample size as the original $n$. A complete automated analysis is performed, and its results are stored. Then another random bootstrap set of cases is drawn from the original data set, and analysis is performed. This resampling of the original data set, followed by analysis, continues perhaps hundreds and even thousands of times, then the frequency of occurrence of risk factors among these many models is summarized. Frequency of occurrence generally stabilizes after about 100 bootstrap analyses. The many models are also analyzed by cluster techniques to detect closely related variables that in the final model will be represented by the most commonly occurring representative. All this information is used to select variables for the final multivariable model.

Of interest, the variables identified for every bootstrap data set are usually different, a sobering revelation. However, it becomes evident that some variables never are selected and others are seldom selected; these constitute “noise.” Variables that appear in 50% or more of models are claimed to be reliable and are considered “signal” for inclusion in the final model.

This phenomenon is illustrated in Table 6-8 and Fig. 6-15. Fifteen variables were selected from among many being analyzed for the late hazard phase of death following mitral valve repair or replacement for degenerative disease. In analysis of the first bootstrap sample, 8 of these 15 variables were selected (only 5 were ultimately found to be reliable risk factors). By 100 analyses, although every variable had been identified as a risk factor in at least 2 analyses, 5 variables dominated the analyses (we considered these reliable risk factors), 8 rarely appeared, and 2 appeared in 22% to 32% of analyses.

What happens in bootstrap bagging is similar to what is seen in signal averaging, such as in visual evoked potentials. Noise becomes canceled out, and signal becomes amplified. In the same way, many variables appear rarely in models, but a few show up time and time again (see Fig. 6-15). One can therefore express the reliability of identification of a given risk factor.

Bootstrap bagging, although demanding a huge number of computer cycles, removes much of the human arbitrariness from multivariable analysis and provides another important statistic: a measure of reliability of each risk factor. Thus, increasingly we have been reporting not only the magnitude of the effect, its variance, and its $P$ value, but also its bootstrap reliability. The technique appears to provide a balance between selecting risk factors that are not reliable (type I error) and overlooking variables that are reliable (type II error).

Machine learning technologies, often used to avoid the issue of variable selection, are being harnessed in interesting ways by either embedding traditional parametric models (which are emphasized in this chapter) or extending nonparametric analytic strategies. For example, results of traditional variable selection are highly dependent on the order in which variables are entered or eliminated. One can instead imagine forming thousands of bootstrap models with clusters of randomly chosen variables forced into each, and aggregating the results. One can apply learning theories to model development. One can examine “variable importance” (often revealing that many variables actually degrade predictive power). Splitting algorithms can be averaged to reveal the most common splits (Fig. 6-16). Research in variable selection is extremely brisk, and important new methods are developing quickly.

Verification

The ideal verification of a multivariable analysis is to demonstrate its accuracy in predicting results of a new set of patients,

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Footnote 7: Sampling with replacement: Imagine a data set having 869 patients and 30 variables. A uniform random number generator produces at random a number between 0 and 1 (the numbers chosen at random are, in the long run, equally likely across that range). The random number is multiplied by 869, and the product is rounded to the nearest integer from 1 to 869. All the variables and their values for the patient with that observation number are copied to a new data set. Importantly, the patient is not removed from the original data set and is available to be selected at random again. This is what is meant by “sampling with replacement”; the patient is chosen but not removed from the possibility of being chosen again.

In bootstrapping, random selection continues until a new data set is built with the same $n$ as the original. However, because patients were never removed from the original data set, the new data set contains many duplicate observations and does not contain on average 37% of patients who were never chosen. When hundreds or even thousands of such data sets are built by this sampling with replacement mechanism, it is rare that any two are alike; it is also extremely rare that one of the data sets will, by chance, have the exact composition of the original data set (each patient selected only once).
Table 6-8  Frequency of Occurrence (%) of Variables Selected in Bootstrap Analyses of the Late Hazard Phase of Death after Mitral Valve Repair or Replacement for Degenerative Disease

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>5</th>
<th>10</th>
<th>55</th>
<th>100</th>
<th>250</th>
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<td>16</td>
<td>12</td>
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<td>BUN</td>
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<td>76</td>
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<td>Hypertension</td>
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<td>6</td>
<td>6</td>
<td>5</td>
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<td>Peripheral arterial disease</td>
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<td>0</td>
<td>4</td>
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<td>4</td>
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<td>Smoker</td>
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Key: BUN, Blood urea nitrogen; NYHA, New York Heart Association.

preferably extramurally. Another popular method, if the data set or number of events is large, is to split the data set randomly into training and testing data sets. Modeling is performed on the former and verification on the latter. Whether this is an efficient and effective strategy has been debated. One of the first applications of bootstrapping was to address this issue by generating multiple training and testing sets. Within the domain of the primary multivariable analysis itself, there are, as it were, internal validity diagnostics. For example, in linear regression (see Box 6-5), a measure of explained scatter is the \( r^2 \) value (square of the familiar correlation coefficient). It is desirable that the value of \( r^2 \) be high (closer to 1 than 0); however, if a model is overdetermined by having in it either too many factors or surrogates for the outcome-dependent variable, a high \( r^2 \) may be spurious.

In logistic regression (see “Logistic Regression Analysis” later in this section), there are a number of diagnostic tools available. One of the earliest was the decile table, often attributed to Hosmer and Lemeshow but used much earlier by the Framingham investigators and others. By solving the multivariable equation for each patient, patients are ordered with respect to their estimated probability of experiencing an event. They are then stratified in up to 10 groups (thus “decile”), and within each group the estimated probabilities summed. This sum represents expected events; it is compared with observed events in each decile. The Hosmer-Lemeshow statistic is a general test of the differences between observed and predicted events.

Borrowing from classification theory, which deals with false and true positives and false and true negatives, an analysis of sensitivity and specificity can be performed, varying the cut point from 0 to 1 of what probability is considered predictive of an event’s occurring. The number of correctly predicted events (true positives) divided by the number of true positives plus false negatives is sensitivity. The number of correctly predicted nonevents (true negatives) divided by the number of true negatives plus false positives is specificity. A graph of 1-specificity on the horizontal axis and sensitivity on the vertical axis is then constructed—the receiver operating characteristic (ROC) curve (Fig. 6-17). The area beneath this curve is a measure of goodness of fit. (Harrell and colleagues called this the c index of concordance.) It varies from .5 to 1. A concordance index between .8 and .9 is desirable for prediction purposes.

In addition, for all varieties of multivariable models, a number of regression diagnostic procedures are used, including formal testing of goodness of fit, identification of observations that particularly influence the results, and analysis of residuals (difference between observed and predicted values) in linear regression.

A validation technique that holds future promise is “out-of-bag” (OOB) prediction error assessment. As noted earlier in this section, a bootstrap sample or average does not
select about a third of patients. These nonselected patients are known as the OOB sample. A model developed on the two thirds of data can be applied to the OOB sample, and prediction error calculated.

Presentation

A multivariable parametric model analysis generates an enormous amount of information, including:

- The structure of the model and estimates of parameters related to that structure
- A list of risk factors identified
- Magnitude of association of each risk factor with outcome as adjusted for all other variables in the model (these multipliers may be expressed either as the parameter estimates themselves—called model coefficients—or as some reformatted relative risk expression; see Box 6-3)
- Direction of each relation, positive or negative
- Uncertainty of the associations, generally expressed as standard deviations of the coefficients
- A statistical score on which a \( P \) value is based
- \( P \) values

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**Figure 6-15** Example of automated variable selection by bootstrap aggregation (bagging). Fifteen variables labeled A through O are depicted as potential predictors of death after mitral valve surgery. In column A, analyses of five bootstrap samples are shown. Tall bars indicate the variable was selected at \( P < .05 \), and gaps represent variables not selected. In all cases, variables A and D were selected, but otherwise analyses appear to be unique. Panel B shows a running average of these five analyses. Variables A, D, I, and J were selected more often than others. Panel C shows averages of 10, 50, 100, 250, and 1000 bootstrap analyses. Notice that no variable was selected 100% of the time, and all 15 were selected at one time or another. But if we consider variables appearing in 50% or more analyses as reliable risk factors, variables A, C, D, I, and J fit that criterion of “signal” and the rest are “noise.” (From Blackstone and colleagues.\(^{842}\))
Figure 6-16 Use of random forests for variable selection. **A,** Example of a random tree. A bootstrap sample of patients from original data set is used to create a random tree. At the root node, a random set of variables are chosen to be candidates, and the most predictive variable for survival among those is identified. Node levels are numbered based on their relative distance to top of tree (i.e., 0, 1, 2). Splitting of nodes to create trees continues until terminal nodes have a few distinct events (e.g., deaths). **B,** Illustration of minimal depth of a variable in a random tree from a 2000-tree forest. Highlighted are three top variables: peak VO₂ (violet), blood urea nitrogen (BUN, aqua), and exercise time (tan). Depth of a node is indicated by numbers 0, 1, 2, 3-8. Minimal depths are 0, 1, 2 for exercise time, peak VO₂, and BUN, respectively.
Figure 6-16, cont’d  

C, Illustration of six random trees from a 2000-tree forest. Three most important variables among these trees are color coded blue for treadmill exercise time, violet for peak \( \dot{V}O_2 \), and green for serum BUN.  

D, Minimal depth (variable importance) from random survival forests analysis. Dashed blue line is threshold for filtering variables: all variables below line are predictive. Diameter of each circle is proportional to forest-averaged number of maximal subtrees for that variable. (From Hsich and colleagues.)
Incremental Risk Factor Concept

An incremental risk factor is a variable identified by multivariable analysis that is associated with an increased risk of an adverse outcome (surgical failure). Surgical failure may be an event, such as early postoperative stroke, and risk is expressed in terms of probability. It may be a time-related event, and risk is expressed in terms of a shorter interval to the event, such as premature death. It may be a longitudinal outcome, and risk is expressed as increased prevalence, higher grade of failure, or elevated or lowered quantitative level. In the context of other simultaneously identified factors, the magnitude (strength) and certainty (P value) of an incremental risk factor represent its contribution over and above those of all other factors. Thus, it is incremental in two ways: (1) with respect to being associated with increased risk and (2) with respect to other factors simultaneously incorporated into a risk factor equation.

There are a number of possible interpretations of an incremental risk factor, all of which should be assessed in drawing inferences:

- Incremental risk factors are variables that reflect increased difficulty in achieving surgical success. This original definition addressed the reality of surgical complexity. Complexity may be expressed in terms of morphologic features (e.g., atrioventricular septal defect). It may also relate to duration of operation (e.g., longer myocardial ischemic time); to both the operation and components of it; to presence of associated cardiac or noncardiac diseases; to demographics (e.g., young age, low birth weight, gender, socioeconomic position); or to conditions that increase difficulty of access (reoperations) or add a potential for complication (e.g., religious preference that precludes administration of blood products, administration of thrombolytics shortly before operation).

- Incremental risk factors are common denominators of surgical failure. The Framingham originators of the risk factor concept were initially disappointed that they did not discover mechanistic (deterministic) causes of heart disease, only weak associations. These weak associations are what we call common denominators. They are general factors associated with increased or decreased risk of an outcome. Sufficient data (see Box 6-4) are necessary to keep them from becoming identifiers of specific patients.

- Some incremental risk factors reflect disease acuity. Need for emergency or urgent operation in patients with severely impaired functional status, such as NYHA class IV or V (the latter designating severe hemodynamic instability or cardiogenic shock), low pH, or short interval from MI to ruptured ventricular septum, represent risk factors that increase acuity.

- Some incremental risk factors reflect immutable conditions that increase risk. These include extremes of age or body size, genetic disorders, gender, and race.

- Some incremental risk factors reflect influential coexisting noncardiac diseases that shorten life expectancy in the absence of cardiac disease. These include chronic renal disease, diabetes, malignancies, arteriosclerosis, and infectious diseases.

- Incremental risk factors are usually surrogates for true, but unmeasured or unrecognized, sources of surgical failure. It is tempting to misinterpret associations as causes. Studies of surrogate end points to decrease sample size for randomized clinical trials are instructive.

A set of numbers indicating quantitative interrelation of all parameter estimates in the model (the variance-covariance matrix)

Bootstrap reliability of each risk factor identified

Figure 6-17 Illustration of receiver operating characteristic (ROC) curves. These are for renal failure after either coronary artery bypass grafting or cardiac valve procedures in 15,844 patients operated on at Cleveland Clinic from 1986 to 2000. Three ROC curves are shown. One is based on preoperative laboratory measurements alone, the second on extensive clinical data alone, and the third combines the two. Diagonal dashed line is the line of random prediction.

There is some controversy about which of these nine sets of numbers should be reported in a manuscript. It may be sufficient for understanding the relations to simply list the risk factors and place in an appendix some of the numeric data. If the model is intended to be used for prediction, including CLs, the entire list must be reported or provided electronically, as has been done for Society of Thoracic Surgeons National Cardiac Database models.

None of the nine, however, directly addresses the way a final multivariable model is formulated to reveal incremental risk factors (see “Incremental Risk Factor Concept” later in this section). The incremental risk factor concept was developed to facilitate medical interpretation of a multivariable analysis. Any dichotomous risk factor in a multivariable analysis can be complemented to allow it to have a positive sign. This is desirable because we think of variables in the model as risk factors, and usually we consider risk to be increasing (positive value) with increasing value of the risk factor. Generally, continuous and ordinal variables cannot be formulated this way, so we recommend that each of these be accompanied by an indication of the direction of greater risk (younger age, lower ejection fraction, greater functional impairment, higher bilirubin).

Incremental Risk Factor Concept

This is desirable because we think of variables in the model as risk factors, and usually we consider risk to be increasing (positive value) with increasing value of the risk factor. Generally, continuous and ordinal variables cannot be formulated this way, so we recommend that each of these be accompanied by an indication of the direction of greater risk (younger age, lower ejection fraction, greater functional impairment, higher bilirubin).
They demonstrate a number of circumstances under which such surrogates may be misleading (see Fig. 6-11). On the other hand, if unknown cause and measurable surrogate are strongly mechanistically linked, interim neutralization of the surrogate may neutralize the cause (Appendix 6D). The Framingham investigators classified most risk factors as rather general, insensitive, but useful surrogates for underlying mechanisms.  

- Incremental risk factors may be spurious associations with risk. One of our motivations to base risk factor identification on algorithmic methods such as bootstrap bagging is that in simulations, these methods balance very nearly 50:50 the probability of overlooking a risk factor and identifying a spurious association.

- An incremental risk factor may be a cause or mechanism of surgical failure. It is difficult to establish a causal mechanism outside the scope of a randomized, well-powered, and well-conducted generalizable clinical trial. This is due to confounding between selection factors influencing treatment recommendations and decisions and outcome. Balancing score methods (e.g., propensity score) attempt to remove such confounding and approach more closely causal inferences (818) (see “Balancing Scores” in Section I).

In addition, we must acknowledge that “association,” “cause,” and “mechanism” may simply be levels of granularity in the pathway of cause to effect. As more becomes known at the molecular level, it may be assumed that at that level of fine granularity, a clear understanding of mechanisms may emerge. However, a macroscopic event such as death or a complication after a cardiac operation may not be completely understood by knowledge of the many individual events taking place at the microscopic level, which probably interact in a complex fashion.

- Some incremental risk factors reflect temporal experience. The “learning curve” idea is intended to capture variables relating to experience of the surgical team, but also those representing temporal changes in approach or practice (e.g., addition of retrograde cardioplegia to myocardial management, preservation of chordae in mitral valve replacement). It is more helpful to identify specific temporal changes in management as separate variables than to lump them into a “date of operation” variable. To do so may require initially suppressing date of operation in the analysis to allow entry of such identifiers of management changes.

- Some incremental risk factors reflect quality of care and, as such, “blunt end” ramifications of institutional policies and practices, healthcare systems, and national and political decisions. Just like temporal experience, however, it is more helpful to identify the specific factors reflected in institutional variance than simply to state that some institutions are high risk and others low risk. If these can be identified and institutions no longer enter an analysis as risk factors, it becomes important to quantify their frequency of occurrence in each institution. If the prevalence is high, and if associations are strongly linked to mechanisms of failure, then institutional protocols to lower the prevalence are warranted. Although quality of care is measured by outcomes, factors influencing it are identified in risk factor assessment and serve as important information for quality monitoring, quality improvement, quality comparison, and assessment of strategies implemented. (Institutional variance is addressed in more detail under Risk Stratification in Section VI.)

- Incremental risk factors reflect individual patient prognosis. They cannot be used to identify which patient will suffer a surgical failure, but they can be used to predict the probability of failure. Surgeons make recommendations and decisions every day that reflect conscious or unconscious assessment of probabilities. Patient selection requires weighing the probabilities of risks and benefits (value) of intervention vs. nonintervention or an alternative management strategy. Indications for operation is the same. Analysis of clinical experience transforms generalities of patient selection and indication guidelines into quantitative probabilities for an individual patient’s characteristics (see “Decision Making for Individual Patients” in Section V).

**EARLY EVENTS**

**Method of Expression**

Early mortality is often expressed as hospital mortality, which includes all deaths that occur after operation but before hospital discharge. The disadvantage of using hospital mortality is that the relatively high but rapidly declining early phase of risk after cardiac operation nearly always extends beyond the hospital period, often out to 3 months and occasionally 6. The degree of extension, even after such safe operations as CABG, appears to increase as risk factors increase. Thus, hospital mortality underestimates the true early risk of operation and gives an incomplete picture of this measure of quality of care. It also covers a variable time period.

An alternative is to use 30-day mortality, but this requires patient follow-up, either active (and expensive) or passive (and delayed). The hybrid of these, operative mortality, is all hospital deaths plus those that occur in the first 30 days. Actually, the most appropriate way to depict early mortality (or any other outcome event) after a procedure or decision is in a time-related manner beginning at time zero (see Time-Related Events later in this section).

If simple percentages are used, at least the confidence intervals around that percentage have to be stated (see Uncertainty earlier in this section), and ideally some information about characteristics of the patient group. Often the patient group is stratified in some manner to demonstrate the effects of heterogeneity of risk factors on outcomes.

**Logistic Regression Analysis**

Logistic regression is used for multivariable analysis of hospital outcomes (events) that are dichotomous (yes/no).

**Historical Note**

The logistic equation was introduced by Verhulst between 1835 and 1845 to describe population growth in France and Belgium. Thus, it belongs to a large class of growth equations. The logistic equation is the simplest of these, resulting in a symmetric S-shaped curve when plotted (see Fig. 6-1, A). The model reappeared in the work of Pearl and Reed at Johns Hopkins University in 1920. They recognized the
pattern of an autocatalytic reaction in the characteristic pattern of the logistic equation for populations; this was earlier suspected by Pearl in 1909 from his reflections on the relation of these curves to organic laws of change. The equation is characterized by an initial phase of increasingly rapid chemical conversion catalyzed by the products produced, followed by a decelerating phase as reactants are consumed (e.g., hydrolysis of ethyl acetate to acetic acid and ethyl alcohol).

Also at Johns Hopkins University during the late 1920s, Berkson and colleagues found that the logistic equation represented kinetics between enzymes and certain substrates. Later at the Mayo Clinic in the 1940s, Berkson found a logistic relationship between dosage of drug and proportion of small experimental animals killed (bioassay). In his studies, the outcome variable was a probability. Unlike population or biochemical kinetics in which not only the rate but also the initial (base) level and the final (asymptotic, limiting) level must be estimated, when the logistic equation is used to estimate the probability of an event, values are constrained within a base of 0 and asymptotic level of 100% (or unity), simplifying the equation and leaving a single parameter to estimate from the data, z.

In 1955, Berkson dubbed the units of the logistic nomogram logit units, parallel to the probit units of another method of bioassay. Thus, certain aspects of the nature of population behavior, enzyme kinetics, lethality of drugs, and risk factors for human outcomes found common ground in this fundamental logistic expression. The logistic equation was made multivariable in the 1960s by Cornfield and colleagues and Walker and Duncan, as described under Multivariable Analyses earlier in this section.

Logistic Regression Equation
Multivariable logistic regression generalizes the discriminant analysis of Fisher by embedding it within the logistic equation. Thus z, the logistic parameter expressed in logit units, is assumed to be related to a logit-linear combination of incremental risk factors (see Box 6-5):

\[ z = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_k x_k \]  

(6.1)

where \( \beta_0 \) is the intercept term (logit units when all \( x = 0 \)), \( x_i \) through \( x_k \) are the numeric values for the independent variables, and \( \beta_i \) through \( \beta_k \) are coefficients, estimated from the data, that translate the values of the independent variables (see Box 6-18) to logit units. Logit units are related to probabilities \( P \) by the logistic relationship:

\[ z = \ln \left( \frac{P}{1-P} \right) \]  

(6.2)

where \( \ln \) is the natural logarithm. This form of the logistic equation makes clear why “log” is part of its name. Notice, also, that \( z \) is a function of the ratio of \( P \), the probability of an event, and \( 1-P \), the complementary probability of the event’s not occurring. This ratio is the odds ratio (see Box 6-3), and Equation 6-2 is referred to as log odds. Equation 6-2 is not computationally applicable to raw clinical data for which \( P \) is exactly 0 or 1 for each patient (e.g., analysis of a dichotomous variable like mortality; see Box 6-5). Thus, the computational form is a nonlinear equation obtained by exponentiating Equation 6-2:

\[ P = \frac{1}{1+e^{-z}} \]  

(6.3)

where \( P \) is the estimated probability using the maximum likelihood principle, and \( e \) is the base of the natural logarithms. In practice, the dependent variable is a dichotomous variable with value 0 (no event) or 1 (event), and the independent variables are potential incremental risk factors (see Box 6-18). In this form, no restrictions are made on the distribution of the risk factors \( x_i \); they may be any mix of continuous, dichotomous, or ordinal variables.

Polymorphic and Ordinal Logistic Regression
Polymorphic Logistic Regression
The “event” whose probability is being calculated does not always take the simple form of 0 and 1; sometimes it is a list of possible dichotomous outcomes. Consider hospital mortality. It may occur in a multiplicity of modes (e.g., acute cardiac failure, death from hemorrhage, death in renal failure). The data may need to be analyzed for more than one mode of death. Such analysis leads to the coding of multiple so-called competing events (bioassay), alive, acute cardiac failure, death in renal failure, and so forth. These are unordered lists of modes of death for which polymorphic logistic regression might be considered.

One option for polymorphic variables is to analyze each event category independently, determining its incremental risk factors using logistic regression for dichotomous outcomes as previously described. It is important to note that for such analyses, the entire data set is used.

Another option is to analyze each variable in the same fashion as time-related competing risks (see “Competing Risks” under Time-Related Events later in this section). The assumption is that all items in the list are independent. As in temporal competing risks analysis, patients experiencing events in any other category are eliminated (e.g., all patients dying in other modes) in these separate analyses. Thus, the data set used to analyze each event in the list contains all patients experiencing each successive event in the list. The entire data set is not used. The analysis is performed and the results interpreted as a conditional probability; that is, the probability of an event of one type, conditional on the absence of another type (e.g., the probability of cardiac death given the absence of any other mode of death.)

An important feature of this type of conditional probability analysis is that event categories must be strictly mutually exclusive. This means that a patient can be assigned only one mode of death, for example. If one were analyzing morbid events such as hospital complications, this should be the earliest occurring complication (in which case one would normally use time-related techniques, of course). This introduces a certain arbitrariness into the analysis. Furthermore, if one adds another category of morbid event to the list, the probabilities of the remaining new ones will not be the same, because the “denominator” (all those not experiencing an event) plus the patients in each successive category will change.

On the other hand, if one then uses the logistic regression equation to predict the occurrence of each event category, the method of conditional probability guarantees these will add to 100% (including the category “no event”) as long as the same risk factors are used for each analysis, and approximately so if a different set is used. This property of polymorphic logistic regression, then, distinguishes it from ordinary logistic regression. In ordinary logistic regression in which
Figure 6-18 Illustration of ordinal longitudinal outcomes. Diagram illustrates the assumption that aortic regurgitation across stented bovine pericardial aortic valve prostheses progresses from grade 0 to grade 1+, then to grade 2+, and finally to grades 3+ and 4+. (Redrawn from Blackstone.823)

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the entire patient sample is used for each event, it is unlikely that the probabilities for a list of events will add to 100%.

This leads us to reflect that ordinary logistic regression examines an event in isolation of any other kind of event. It is ideal for answering the question, “What is the nature of this outcome phenomenon?” Polytomous logistic regression, by considering the entire list of events that make up a more global event (e.g., death, complications), answers the question, “What are the probabilities of each kind of event conditional on none of the others occurring?” All these will add up to the total probability of the overall event.

Although used in data analysis by others before them, Hosmer and colleagues described the equations and programmed the software for performing a multiple (polytomous) logistic regression simultaneously on multiple events.829 and these algorithms are incorporated into the most modern logistic regression computer software. Generally, all items in the polytomous list are analyzed simultaneously, with multiple streams of the same set of risk factors. This allows assessment of the sometimes complex interplay of risk factors among the various list items.

An important limitation of polytomous logistic regression is that the number of risk factors must be such that the category with the fewest events does not become overdetermined. When there is wide difference among the categories in number of events, perhaps one or two orders of magnitude, this can limit the model considerably, permitting little insight into the most commonly occurring category and jeopardizing the least commonly occurring. Some coalescence of categories may be necessary.

Assumptions of polytomous logistic regression include noninformative censoring (just as for time-related events)—that is, occurrence of one item in the list is unrelated to the possible occurrence of another, had the first not happened first. In cardiac operations, in which multiorgan system failure often leads to death, independence of modes of death such as from renal failure or hepatic failure is hard to accept.

**Ordinal Logistic Regression.** A generalization of logistic regression is to an ordinal response (dependent) variable such as NYHA functional status after operation.828,829 The logistic equation, by means of multiple intercept terms, then predicts the probability for each ordinal level, all of which sum to 100%. We have found the widest application of this method in examining repeated assessment of time-related patient status (NYHA class or degree of regurgitation of a cardiac valve after repair),831 so this topic is discussed in more depth under Longitudinal Outcomes later in this section.

The primary assumption of ordinal logistic regression is that there is an orderly relation between increasing risk and increasing ordinal level of the outcome variable.832 Patients “flow,” as it were, into states of greater severity, and states of lesser severity empty (Fig. 6-18). This assumption may be violated, so testing the proportional odds assumption is mandatory during analysis. The most common reason for violation of the proportional odds assumption is too few patients in some categories. This requires coalescence of categories until the proportional odds assumption is met.

A practical note is that a naive solution of an ordinal logistic equation generates cumulative probabilities. What one generally is interested in is the actual probabilities of each level of the ordinal variable. These must be obtained by subtraction and the CLs calculated for each such conditional probability.

**Diagnostics.** Upon completion of a logistic regression analysis, it is important to perform a variety of diagnostics to determine the quality of the results obtained.821 Pregibon has presented a number of helpful logistic regression diagnostics.816 Harrell has incorporated a number of diagnostics into his R-based package.812 These substantially extend more typical Hosmer-Lemeshow diagnostics.

**TIME-RELATED EVENTS.** The interval between an intervention such as a cardiac procedure and an unfavorable outcome event such as death is of obvious importance.

The usual outcome events considered, such as death, are called terminating events; that is, they can occur only once. Other morbid events, such as thromboembolism and transplant rejection, may occur a number of times and are called repeated morbid events.828 Yet others are not dichotomous events but events associated with a severity scale; these are called weighted morbid events. Terminating, repeated, and weighted events have in common one attribute or assumption: They occur instantly in time distant from some starting time (e.g., cardiac operation).

Depictions of time-related events have been called by many names that reflect their origin in the discipline from which they arose (economics, government, industrial reliability testing, biologic sciences).831 In this book, estimates based on counting theory alone (nonparametric estimates, see Box 6-14) are termed actuarial estimates or life-table estimates, for which there is strong historical precedence.831 These terms do not imply for us the specific theoretical underpinnings or method of calculation, of which there are many.
Historical Note

The word actuarial comes from the Latin actuarius, meaning “secretary of accounts.” The most notable actuarius was the Praetorian Prefect Domitius Ulpianus, who produced a table of annuity values in the early 3rd century AD. This table continued to be used in Europe into the early 19th century. With emergence of both definitive population data and the science of probability, modern actuarial tables arose, produced first by Edmund Halley (of comet fame) in 1693. He was motivated, as was Ulpianus, by economics related to human survival, because governments sold annuities to finance public works. Workers in this combined area of demography and economics came to be known as actuaries in the late 18th century. Importantly for this discussion, the methodology of the actuary varied widely. In the 19th century, the actuary of the Alliance Assurance Company of London, Benjamin Gompertz, developed mathematical models of the dynamics of population growth (birth and death) to characterize survival. This model-based, completely parametric (equations with constants estimated from data) methodology (see Box 6-14) was substantially different from the simple empirical counting methodology (nonparametric) of Halley.

In the more than 300 years since Halley, a multitude of methods have been developed (and often reinvented) in actuarial science, demography, statistics, industry, and medical science. They all have the common goal of estimating the distribution of intervals between a designated time zero and occurrence of an event. In medicine, an ad hoc direct method of survival estimation was developed in which nth-year survival (e.g., 5-year survival) excluded all patients whose follow-up interval was less than n years. Life tables constructed in this fashion were not guaranteed to be monotonically decreasing, nor did they use all patients with all available information for each time-related estimate.

The direct method highlights a unique problem with time-related events data: incomplete (not missing) data (Box 6-20). Rarely are we patient enough to observe a group of patients until all have died. Rather, at a given point in time we know the duration of survival for some patients and therefore have complete data with respect to vital status; for others we know only that they are still living after a certain interval of time. We know something (they have not died within that interval), but information about when they will eventually die is incomplete. A method was needed to use both complete and incomplete data; we call this censored data (see Box 6-20).

In 1950, Berkson and Gage published their landmark medical paper on the life-table (actuarial) method for censored data, which they stated was no different from that used by others as early as at least 1922. Estimates of percent survival and censoring were made at arbitrarily determined intervals (e.g., yearly), although the original papers Berkson cites also address a method of generating a new estimate at every unique death interval that went unrecognized even after the work by Kaplan and Meier.

In 1952, Paul Meier at Johns Hopkins University and, in 1953, Edward Kaplan at Bell Telephone Laboratories submitted to the Journal of the American Statistical Association a new method for survival analysis, the product-limit method, that used more of the data. Estimates were generated at the time of each occurrence of an event. Furthermore, the basis for the estimates was grounded in sound statistical theory.
and assumptions, such as the effect of informative censoring. Much of the development was in the field of medicine.

Important developments also took place in industrial reliability. Wayne Nelson\textsuperscript{66} at General Electric developed a method for analyzing time-related events in the \textit{cumulative hazard function} rather than the survivorship domain (see "Fundamentals" under Time-Related Events later in this section) because he was interested in the rate at which events occurred (hazard function). The estimation procedure differed, therefore, from that of Kaplan and Meier, but the two methods converge as the number of events increases (see "Repeated Events" and "Weighted Events" later in this section). Importantly, by not "thinking" in the probability domain but rather the hazard function domain, he extended his method to repeated events, and then extended this further to weighted events.\textsuperscript{N7,N8} He called the latter \textit{time-related cost functions}, recognizing that recurrence of the same event, such as a machine repair, may be associated with different costs. (We have used this, for example, to analyze the grade of medical impairment from repeated episodes of thromboembolism following heart valve replacement.\textsuperscript{B27,B28})

Fundamentals

Time-related events are those presumed to occur at an instant in time after a defined starting time. Time of occurrence generally differs from patient to patient. Information about occurrence of the event and when it occurred is obtained by patient follow-up, as detailed under "Follow-up" in Section III.

Essential Data

Successful analysis of time-related events requires answers to three fundamental questions:

- What is the event?
- When is time zero?
- Who is at risk?

\textbf{Event} Defining the \textit{event} for an analysis may be straightforward, such as death from any cause. Events that are not uniformly fatal are called \textit{nonterminating} or \textit{morbid events}. Examples include brain abscesses, reoperations, and development of angina. A clear, uniformly applied definition of the event is vital and has two components: (1) It defines an \textit{uncensored} patient who experiences the event, and (2) it defines a \textit{censored} patient who at some point in time becomes untraced as regards the event.

Caution must be exercised in considering the time-relatedness of some events. For example, degeneration of a xenograft heart valve is a time-related \textit{process}, not an event. Timing of reoperation for structural valve deterioration of a xenograft, therefore, depends on the rate of a process, the patient’s response to that process, and medical decision making. Processes that can be measured at multiple times are best studied by the methods described under \textit{Longitudinal Outcomes} later in this section.

\textbf{Time Zero} The moment a patient becomes at risk of experiencing the event of interest is called \textit{time zero} (Fig. 6.19). For patients who undergo interventions such as a cardiac procedure, time zero is often the time of the procedure. Under many circumstances, however, defining time zero is not so simple. For example, it is not easy to date the

![Figure 6.19: Right-censored time-related-events data. Conceptual graph of incomplete data in a group (cohort) of patients followed after operation cross-sectionally (see Follow-up in Section III). A, Calendar date is along horizontal axis, and each patient enters at a different date, ordered from earliest date of operation to most recent, top to bottom. Systematic active follow-up has a common closing date. Patients still alive at follow-up are depicted by arrowheads indicating that they will continue to be followed. Terminated lines are deaths. B, Patients are now aligned at \textit{time zero}, when operation was performed. They have also been sorted from shortest interval to longest (called \textit{rank order}). Patients who are still alive are depicted by lines with arrowheads. Time of their death is unknown and in the future, but we at least know they have lived as long as is indicated by the length of their follow-up line. This is called \textit{incomplete data} with respect to death, or \textit{censored data}. Because the arrow of time is presumed to proceed from left to right, data are called \textit{right censored}. The four lines that terminate without an arrow are deaths. C, Basic counting needed to estimate survival. Along the left is number of patients at risk; at time of shortest follow-up, all eight patients were at risk. Number decreases progressively as patients either die or are no longer traced. On right is the count of deaths at that interval (here, as is usually the case, the number is 1).
onset of ischemic heart disease, although it may be easy to identify the date of a first MI.

At Risk Patients remain at risk of experiencing the event from time zero to either the occurrence of the event or the time at which they no longer can experience the event (censoring; see Box 6-20). Defining who is at risk demands thought. For example, if the event is reoperation for bioprosthetic structural valve deterioration, then patients receiving a mechanical prosthesis are never at risk. This distinction may not be obvious to a statistician asked to analyze structural valve deterioration unless the surgeon-investigator explains it in detail. In this example, patients receiving a bioprosthesis also become no longer at risk of this event the moment the bioprosthesis is explanted for other indications. They are permanently censored at that point. Note that if a repeated morbid event is being analyzed, such as transplant rejection or thromboembolism, patients continue to remain at risk after each occurrence of the event until they are censored by death, end of follow-up, or, for these examples, retransplantation or removal of the valve prosthesis.

Granularity of Time
The basic data required for the simplest time-related analyses are (1) the interval from time zero to either occurrence of the event or censoring (usually the interval to end of follow-up) and (2) an indicator variable specifying that the event occurred (uncensored) or did not (censored). Granularity of this interval is important, particularly for parametric models (see “Parametric Survival Estimation” later in this section). The shorter the interval from time zero to the event, the finer the granularity required. In cardiac surgery, calculating the interval for a patient dying on the day of operation or experiencing a complication may require use of clock time (hours and minutes) of time zero (generally the first time that an attempt is made to wean the patient from cardiopulmonary bypass or that the operation is declared to be completed) and clock time of death or the complication. When the interval is long, simply subtracting the calendar date of the event from that of surgery is sufficiently granular.

Time-to-Event Model
There are two distinctly different ways to think about time-related events, and this difference must be understood for effective communication between the surgeon-investigator and the statistician. First, time-to-event data may be thought of as simply the distribution of intervals to an event (martingale or counting theory). This will be the framework with which most statisticians are familiar. Second, time-to-event data may be thought of in terms of the mathematics of mass transport from one state (e.g., alive) to another (death) (Markov process theory). This is the framework more familiar to a surgeon, who has training in such mass transport phenomena as diffusion, heat transfer, blood flow, and other dynamic transport processes involving rates.

Distribution Framework (Counting Process) Intervals to event are thought of like any other continuous, positive-valued variable. They can be expressed as a cumulative distribution graph (see Fig. 6-9, B), just like age. The only nuance is that by convention, the graph is turned upside down (its complement) so that it starts at 100% and falls as the interval lengthens. This is called the survivorship function. A common alternative expression for a cumulative distribution function is its slope (derivative), the probability density function, which is analogous to an ordinary histogram (see Fig. 6-9, A). Typically this function is not useful in survival analysis. What is useful is the ratio of the probability density function to the survivorship function (the conditional probability density function), because it represents the risk of the event in patients who have not yet experienced it. This ratio is the hazard function in survival analysis.

If \( S(t) \) is the survivorship function across time \( t \), \( b(t) \) the probability density function, and \( \lambda(t) \) the hazard function, the following mathematical equations express the above relations:

\[
b(t) = \frac{\partial S(t)}{\partial t} \tag{6-4}
\]

where \( \partial S(t)/\partial t \) is the slope (derivative) of \( S(t) \), and:

\[
\lambda(t) = b(t)/S(t) \tag{6-5}
\]

Mass Transport Framework (Hazard Function) A force of mortality called the hazard function, or \( \lambda(t) \), transports patients from the state of being alive, \( S(t) \), to the state of death \( F(t) \) (Fig. 6-20). This framework of thinking was initially suggested by John Graunt in the mid-1600s.\(^{6,23}\) Exactly the same equations, 6-4 and 6-5, hold for this dynamic process.

Useful Mathematical Relations
The area beneath the hazard function accumulates exposure to risk across time and is called the cumulative hazard function, \( \Lambda(t) \):

\[
\Lambda(t) = \int_0^t \lambda(u)du \tag{6-6}
\]

This relation yields other useful relationships:

\[
S(t) = e^{-\Lambda(t)} \tag{6-7}
\]

where \( e \) is the base of the natural logarithms, and

\[
-\ln[S(t)] = \Lambda(t) \tag{6-8}
\]

where \( \ln \) is the natural logarithm. Thus, the cumulative hazard function is easily calculated from estimates of \( S(t) \), and its slope reflects the shape of \( \lambda(t) \).

Nonparametric Survival Estimation
The nonparametric Kaplan-Meier method\(^{24}\) is the most commonly used method for estimating the survivorship function in medicine, although a number of others have been
Each Kaplan-Meier estimate incorporates the number of patients experiencing an event since the last event occurred and the number of patients at risk in that interval, taking into account censoring (see Fig. 6-19, C). Computing Kaplan-Meier survival estimates is relatively straightforward. The basic idea is to first calculate the probability of surviving (being event-free) in the interval since the last event occurred (the ratio of events, generally 1, to number at risk). This probability is then multiplied by the probability of surviving up to that time, a product called a conditional probability. This successive multiplication of individual probabilities by preceding ones is what gave rise to the generic description of this method, the product-limit method. It also guarantees that the estimates of survival decrease monotonically.

As can be imagined, at the longest intervals, few patients remain at risk and individual survival estimates make large jumps. For example, if four patients are alive and one dies, the probability of survival in that interval is only 75%. This phenomenon results in systematic bias downward, underestimating the survivorship function. This is called the completion effect.

Each Kaplan-Meier estimate has an expressed degree of uncertainty. Often this is reported as the standard error (essentially the 68% symmetric confidence intervals). Preferably, however, the degree of uncertainty is expressed using asymmetric confidence units. When plotted, a symbol positioned on the horizontal axis at the time of each event and on the vertical axis at the Kaplan-Meier estimate graphically displays the information (Fig. 6-21, A).

There is controversy about (1) whether or not Kaplan-Meier estimates should be connected and (2) if they are connected, in what fashion. If parametric estimates are also generated, the obvious solution is to compare nonparametric and parametric estimates, with nonparametric estimates unconnected (Fig. 6-21, B). If this is not the case and connection is desired, most statisticians connect estimates with a horizontal straight line at the level of the previous estimate. This is technically called “zero order” interpolation with a left step. It can be proven that this practice is the worst possible means of connecting estimates. Therefore, some statisticians connect the estimates by straight line segments (first-order interpolation), as did Berkson and Gage, but others use yet higher-order interpolation methods that approach the smoothness of parametric estimates. Kaplan-Meier and other nonparametric life-table estimates are not “raw data” (descriptions of actual events). The time of death actually “happened,” but the proportion, or percentage, is a computation and thus an estimate.

**Parametric Survival Estimation**

Unlike nonparametric survival estimation that arose from the theory of counting, model-based or parametric survival estimation (see Box 6-14) arose out of biomathematical considerations of the force of mortality, the hazard function. Unlike survival, which depicts prevalence of an event (or freedom therefrom) across time, the hazard function depicts the rate of occurrence, or incidence, of an event across time (see Box 6-13).

**General Comments**

During the Great Plague, John Graunt assumed a constant risk of mortality (the mortality rate or force of mortality). He called it the hazard function after a technical term for a form of dicing that had, by the mid-17th century, come into common usage to mean “calamity,” much as “crap shoot” has taken on the connotation of the losing throw in craps. Because a constant hazard rate presumes a mathematical model of survival, his was a parametric method. Graunt’s colleague, William Petty, believed instead that the hazard rate was age related (time varying).

Thereafter, the hazard function essentially disappeared from the medical world until the 1980s, although it remained in use in industry and in government depictions of population behavior. This is possibly because the hazard function, unlike the survivorship function, appears to have no well-understood statistical counterpart, as do the Kaplan-Meier estimator and death density function. It may also be related to the difficulty of understanding intuitively a series composed of almost an infinite number of instantaneous estimates of risk to the easily perceived accumulated risk expressed as freedom from the event. Also, the inherently mathematical nature of the hazard function makes it difficult and
forbidding to many physicians whose statistical collaborators may not have thought to introduce it to them in terms of biochemical reaction rates or other familiar physiologic rates. For those who need a visceral sense of the hazard function, think of its magnitude in terms of the sudden change from a sense of well-being to one of danger when screeching tires are heard close by.

Linearized Rate The most common expression of hazard is the linearized rate. It was linearized rates that John Graunt used when exploring risk factors for the plague. A linearized rate means the hazard function is constant across time. The analogy is radioactive decay: a constant rate of decay leads to exponential decrease in radioactivity. Likewise, a constant hazard leads to an exponentially decreasing survivorship function. When hazard is constant, the cumulative hazard is linearly increasing: \( A(t) = at \); that is, it increases linearly with increasing time with constant hazard slope \( a \). Then \( S(t) = \exp(-at) \), where \( \exp \) is the exponential function, and thus survival decreases exponentially.

The linearized rate is easily computed by simply counting the number of events and dividing by the total follow-up time of a group of patients:

\[
\hat{\lambda} = \frac{n_d}{\sum t_i} \tag{6-9}
\]

where \( \hat{\lambda} \) is estimated constant hazard, \( n_d \) is number of events, \( n \) is total number of patients, and \( t_i \) is individual \( i \) time to the event.

Importantly, if there are multiple events per patient, such as thromboembolic events, all occurrences are counted. CLs of linearized rates are also easily calculated (see “Repeate Events” later in this section). However, there are a number of different, although roughly equivalent, formulae for these CLs. For example, Cox and Oakes present a simple formula:

\[
\text{SD} \left[ \ln(\hat{\lambda}) \right] = \frac{1}{\sqrt{n_d}} \tag{6-10}
\]

and the upper CL of \( \hat{\lambda} \), \( \hat{\lambda}^+ \), is:

\[
\hat{\lambda}^+ = e^{\ln(\hat{\lambda}) + z\sqrt{n_d}} \tag{6-11}
\]

and the lower CL, \( \hat{\lambda}^- \), is

\[
\hat{\lambda}^- = e^{\ln(\hat{\lambda}) - z\sqrt{n_d}} \tag{6-12}
\]

where \( z \) is the confidence coefficient (1 for 68% CL, 1.96 for 95% CL), and \( e \) is the base of the natural logarithms.

Time-Varying Rate Although linearized rates have frequently been used for cardiac surgery data, particularly by regulatory agencies, it is uncommon for hazard to be constant. Rather, cardiac procedures, perhaps more than many other therapies, impose on patients a time-related course composed of highly variable and sometimes rapidly changing instantaneous risks of death modulated by multiple risk factors of varying strength and times of influence. Certainly the hazard function is greater 1 hour after operation than it is 1 week, 1 month, or 1 year after operation. Thus, a great deal of practical importance is attached to the time-varying hazard function after operation.

Visual examination of life-table depictions of events after cardiac operation in cohorts of well-followed patients reveals simple, smoothly time-varying patterns (see Fig. 6-21). These patterns suggest that the intervals between events are closely spaced immediately after the operation (usually time zero) and become more widely spaced in the hours and days that follow. Some days, weeks, or even months later, they merge into a sparse, random spacing of events. If follow-up evaluation is extended considerably, the time interval between events may again begin to shorten, representing accelerated risk. Nevertheless, under most circumstances, the majority of patients are free of the event even after many years, making censoring prevalence high in the cardiac surgical setting.

The stereotypical patterns observed in analysis of several thousand life tables of freedom from an unfavorable outcome event after cardiac operation led the UAB group, at the urging of D.R. Cox, to believe that a mathematical model for time-related events could be developed. In this development, it was thought likely that risk factors for late-occurring events would differ at least in strength, if not qualitatively, from those in the acute phase of recovery after operation, and that their prevalence might be different in different time frames. Further, the ability to graph patient-specific risk and survival estimates became increasingly important to development of new knowledge in cardiac surgery. Finally, these depictions required CLs. Therefore, the UAB group introduced a hazard function modeling method that produced not only time-related freedom from an event but also time-varying risk (hazard function) for an event, complete with CLs. The method is analogous to using a prism to decompose white light into its various colors. It decomposes time-varying hazard into as many as three simple additive hazard phases as shown in Fig. 6-22 (a more generalized method would allow more than three phases for unusual situations as has been done for longitudinal outcomes described later in this section).

The mathematical model is as follows:

\[
A(t, x) = \sum_{j=1}^{k} \mu_j(x, \beta_j) \cdot G_j(t, \Theta_j) \tag{6-13}
\]

where \( A(t,x) \) is the cumulative hazard function, \( \mu_j(x,\beta_j) \) is a function of risk factors for the \( j \)th phase, \( G_j(t,\Theta_j) \) is a shaping function unique for each phase, and \( \Sigma \) is the sum of the individual components (phases) \( 1 \) through \( k \). Such a formulation places Equation 6-13 into the class of mixture distributions and competing risk models (see “Competing Risks” later in this section), with each hazard phase competing for the event.

The shaping functions \( G_j(t,\Theta_j) \) are based on a collection of biomathematical models of risk that were assembled into generic expressions. They permit great flexibility in shape of the short- and long-term hazard. Shape of the early hazard phase of short-term risk originated as an assembly of a large number of nested mathematical models describing biochemical reactions, ecology, and population growth. The early hazard function can begin at infinity after time zero, it can start at zero and peak, or it can start at a finite value and decline from there. Shape of the constant hazard phase, as its name implies, is a constant value (horizontal line) across time. Shape of the late hazard function is based on a
generalization of the Weibull model of risk used widely in industrial settings.\textsuperscript{10}

Although early and late hazard phases can have several of their shaping parameters estimated, in practice they usually reduce from four down to one or two parameters, resulting in simple, special-case forms of their respective generic mathematical constructs.

Each phase also has a scaling function \( \mu_t \) that can carry risk factors. This parameter was selected by sensitivity analyses and was not arbitrary. The form of the regression model may be either logit-linear or log-linear (see Box 6-5); they yield nearly identical coefficients and shapes.

All phases of the model are defined from time 0 to infinity. The phases are overlapping and additive across time (see Fig. 6-22, B), but the nature of the shaping functions allows a phase to predominate more at one time than another (see Fig. 6-22, C). This property permits the model to accommodate risk factors not displaying proportional hazard properties across all time (see “Cox Proportional Hazards Regression” later in this section).

A computer software program interfaced to the SAS system\textsuperscript{44} is available at http://my.clevelandclinic.org/professionals/software/hazard/default.aspx.

**Estimating Time-Related Hazard Function**  The first step in developing a model specific to a set of event-time data is to determine the overall hazard function across time (without considering risk factors). This is the step, sometimes a time-consuming one, that differs from the work required in using the Cox model described later in this section. The work is best done in the cumulative hazard domain by taking minus the logarithm of the life-table estimates\textsuperscript{36} (Fig. 6-23). This depiction makes evident the early phase of hazard, the duration of its predominance, and the point at which it levels off (its asymptotic value). Slope of the intermediate phase of risk yields an estimate of the constant hazard scaling parameter. Departures late from the constant hazard slope yield information about the late rising phase of hazard if it is present. Such plots also reveal whether one or two of the three phases may be completely absent, given the duration of follow-up and distribution of observed events.

The method of maximum likelihood is used to estimate values for the parameters of the proposed model, which includes exploring various mathematical forms of the early and late generic shaping equations, defined by the sign of their exponents, and reducing the model to its simplest form (parsimony).\textsuperscript{31} The only input to this process is the sequence of event and censoring intervals. No arbitrary assignment of events to early, constant, or late hazard phase is required. The model simply attempts to best represent the distribution over time of these intervals. An iterative (optimization) procedure is used to estimate the parameter values. Once estimated, these values can be used to solve the resulting equation for

\[ \text{cumulative hazard function, and hazard function (time-related instantaneous risk of event and slope of cumulative hazard).} \]

\[ \text{Box 6-5} \]

\[ \text{Fig. 6-22, } B \]

\[ \text{Relative influence} \]

\[ \text{Fig. 6-23} \]

\[ \text{under most circumstances, the late hazard phase equation is constrained such that hazard increases monotonically (i.e., without decreasing at any point). In reality, the equation is more flexible than this and can conform to late hazards that may at some point diminish. For example, the hazard function for the population of the United States has an early declining hazard phase reflecting infant mortality, a constant hazard phase that over the past century has practically disappeared, and a generally rising late hazard phase. However, this phase is interrupted by a small peaking hazard phase during late teenage and early adulthood years, representing, among other causes, accidental deaths. Furthermore, at the extreme of old age, hazard may not increase to the extent predicted by a Weibull relation, perhaps because these elderly individuals are a highly select robust group.} \]
time-related freedom from the event and the hazard function (Fig. 6-24).

Absence of some phases may be related to duration of follow-up or number of events observed and their intervals, which may make it difficult to identify statistically the existence of a phase. Most commonly, one or two phases are found.

At this juncture, investigation is made of model validity. The calculated (parametric) event-free curves are superimposed on the Kaplan-Meier estimates and examined for lack of correspondence (see Figs. 6-21 and 6-23).

Multivariable Analysis

Feigl and Zelen introduced multivariable analysis of constant hazards using a log-linear model (see Box 6-5). This formalized the method used 300 years earlier by Graunt, but it is inapplicable to data with time-varying hazards that typically characterize risk after interventions.

A number of methods were used in a limited way in demographics and industry, but in 1972 everything changed. That year, D.R. Cox proposed a multivariable method that did not require estimating the hazard function as in Fig. 6-21. A, Nonparametric estimates. B, Superimposed nonparametric and parametric estimates. Note good correspondence between the two sets of estimates. (From Studer and colleagues.)

Figure 6-24  Death after coronary artery bypass grafting (CABG), illustrating survivorship and hazard functions and decomposition of hazard into phases. A, Survival. Solid blue line is survival estimate, and dashed lines enclose confidence limits (CL) equivalent to ±1 standard error. Numbers are percent survival at 30 days, 5, 10, 15, and 20 years after operation. Red line is survival in an age-sex-race–matched population life table. B, Hazard. Solid blue line is hazard estimate, and dashed lines enclose CLs equivalent to ±1 standard error. Red line is hazard in an age-sex-race–matched population life table. C, Components of instantaneous risk of death (hazard). Three are depicted: (1) an early rapidly falling hazard phase, (2) a constant hazard phase, and (3) a late-rising hazard phase. These components sum across time to overall hazard function shown by dotted line. (From Sergeant and colleagues.)
function. Rather, it assumed that an unspecified underlying hazard function of any shape was modulated in a regular way by a set of risk factors. This is called a semiparametric method because the model for risk factors was parametric, but the underlying hazard was unspecified.

Cox Proportional Hazards Regression

The log-linear (see Box 6-5) form of the Cox model of risk factors is:

\[
\ln[\Lambda(t)] = \ln[\Lambda_0(t)] + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_k x_k \tag{6-14}
\]

where \(\Lambda_0(t)\) is the underlying unspecified hazard that is modified by risk factors \((x)\) that are weighted by coefficients \((\beta)\); \(\ln\) is the natural logarithm. The importance of the log-linear form is that the scale of both \(\beta\) and \(x\) can span the entire number line, and still the hazard function will be positive when \(\ln[\Lambda(t)]\) is exponentiated, which must be the case.

Another way to express the Cox model is in the cumulative hazard domain. Let us say there is one dichotomous risk factor, \(x_1\), and coefficient, \(\beta_1\). Then:

\[
\Lambda(t) = \Lambda_0(t)e^{\beta_1 x_1} \tag{6-15}
\]

where \(\Lambda(t)\) is the cumulative hazard function, \(\Lambda_0(t)\) is the underlying cumulative hazard, and \(e\) is the base of the natural logarithms. The ratio of cumulative hazard with the factor present \((x_1 = 1)\) to that with it absent \((x_1 = 0)\) is:

\[
\frac{\Lambda(t, x_1 = 1)}{\Lambda(t, x_1 = 0)} = e^{\beta_1} \tag{6-16}
\]

Taking logarithms and rearranging:

\[
\beta_1 = \ln[\Lambda(t, x_1 = 1)] - \ln[\Lambda(t, x_1 = 0)] \tag{6-17}
\]

Notice that the logarithm of the two cumulative hazard curves is separated across all time by a constant distance \(\beta_1\) (Equation 6-17), and the exponential of \(\beta_1\) (Equation 6-16) represents a constant ratio of cumulative hazards. This idea of a constant distance of separation or constant ratio is known as the proportional hazards assumption of the Cox method. Recall that cumulative hazard is estimated from the survival curve \(S(t)\) by taking minus its logarithm (Equation 6-8). Therefore, if logarithms are taken of cumulative hazard using either Kaplan-Meier or Nelson estimates (or a single logarithm of Nelson cumulative hazard estimates), the proportionality assumption can be checked. If the proportional hazards assumption does not hold, nonproportional hazard methodology must be used.

Often \(\beta\) is expressed in a fashion to reflect relative risk as hazard ratios and their CLs (see Box 6-3). This can be seen from Equation 6-16, where the \(\beta_1\) is exponentiated, showing a ratio of hazards with and without the risk factor. CLs are asymmetric, obtained from the variance of \(\beta\). The hazard ratio makes sense for dichotomous variables, but less sense for continuous ones, particularly if transformation of scale has been necessary.

Parametric Hazard Function Regression

Multivariable analysis of risk factors is no more (or less) difficult in the totally parametric hazard function domain than in the logistic or Cox regression domain (see “Multivariable Analysis” earlier in this section). The only intellectual (not computational) complexity is that risk factors are estimated simultaneously in all phases of hazard. Within each hazard phase, risk factors are assumed to obey a proportional hazards assumption (see “Cox Proportional Hazards Regression” earlier in this section). However, the entire model need not (and generally does not) obey the proportional hazards assumption. It therefore has been classified as a model of nonproportional hazards.

The main additional work in using a multiphase hazard method is obtaining the underlying specified hazard function. Among the diagnostics for such a model is the general depiction of the time frame during which each hazard phase dominates (see Fig. 6-22, C). The data can be examined within these separate time frames for screening and for transformations that may be necessary for continuous and ordinal variables.

After risk factors have been identified in each hazard phase, a final check on which phase a risk factor properly belongs to is performed. Occasionally a risk factor will be found with similar strength in each hazard phase, and such a variable indeed meets the proportional hazards assumption across the entire span of follow-up represented in the data. This suggests that the entire sum in Equation 6-13 could be multiplied by another scaling function consisting of proportional hazards variables.

A complete description of the final equation that emerges from the hazard function multivariable analysis includes a model specification, coefficients for all variables (incremental risk factors) in each phase of the equation (recall that a risk factor can occur in more than one phase), intercept for each phase, shaping parameter estimates, and a variance-covariance matrix. Because the equation is by definition completely parametric, prediction of an event-free curve and its corresponding hazard function, each accompanied by CLs, is possible for any desired combination of values for the risk factors by substituting values for each variable in the equation and solving it for any time interval(s) desired.

Validating the Multivariable Analysis

Validation of the multivariable analysis in a specific study is accomplished by comparing the computed time-related survival of a stratified life-table depiction of the entire study group with that predicted by the multivariable equation (Fig. 6-25). This process can be extended to subgroups to check the adequacy of modeling efforts. The process is similar to that for risk adjustment (see “Risk Stratification” in Section VI) and is accomplished in the following manner. For each patient, the survivorship function is estimated across time \(\hat{S}(t; x_i, \Theta, \beta)\) from each individual’s specific values for the risk factors in the equation. In the above notation, \(t\) is the time interval after time zero, \(\Theta\) is the vector (column of numbers) of shaping parameter estimates, \(\beta\) is the vector of regression coefficient estimates, and \(x_i\) is the corresponding vector of risk factor values for individual \(i\). For clarity, this is abbreviated to notation \(\hat{S}(t; x_i)\). In addition, the upper and lower CLs for \(\hat{S}(t; x_i)\) are calculated using the variance-covariance matrix from the multivariable analysis. The predicted value of time-related survival in a group of \(n\) individuals is then calculated as the average at each point in time of the individual survival estimates:

\[
\hat{S}(t) = \frac{\sum_{i=1}^{n} \hat{S}(t; x_i)}{n} \tag{6-18}
\]

The theoretical justification for this is that the individual \(\hat{S}(t; x_i)\) represents proper cumulative distribution functions.
and these should sum to another proper cumulative distribution function.\textsuperscript{116} On the other hand, specific theory underlying the formulation of CLs for this estimate in a straightforward manner has not been available. A conservative estimate has been made, however, by averaging the upper CLs for each individual to form an upper CL for \( \hat{S}(t) \), and similarly for the lower CL. The error, if present, is that the confidence intervals are too wide. These confidence intervals have been found to be roughly equivalent to those obtained by averaging the variance of the logistic transform of \( \hat{S}(t) \), but they are somewhat more stable.

For the validation, time-related freedoms from the event of stratified groups of the cohort are determined nonparametrically as well and plotted according to the Kaplan-Meier estimator. For example, Fig. 6-26 shows tetralogy data stratified according to presence or absence of a transanular patch. This variable was not identified as a “significant” risk factor in the multivariable analysis. Nonetheless, averaged parametric survival values for the patients in the subset compare well with stratified Kaplan-Meier survival. (This validation study also indicates that difference in prevalence of risk factors in patients with and without transanular patching, not the patching itself, appears to account for the difference in mortality.) Propensity score matching would provide the most reliable support for this inference (see “Propensity Score” in Section I).

In a fashion akin to the logistic model, an overall assessment of validity within each stratum also may be obtained by calculating the number of expected events and comparing that with the number of observed events in the domain of time-related events, conservation of events is attributed to the cumulative hazard function rather than to the probability domain. Thus, for each individual’s specific follow-up interval \( (t) \), the cumulative hazard, \( \Lambda(t; x_i) \), is calculated. These are summed to estimate the expected number of events \( (E) \):

\[
E = \sum_{i=1}^{n} \Lambda(t; x_i)
\]

(6-19)

The expected number of events is compared with the observed number of events by a chi-square goodness-of-fit test.

Expressing Degree of Uncertainty in Time-Related Depictions of Freedom from an Event

There is conflict (or at least difference of opinion) between (1) those who focus on a single overall \( P \) value for the difference between two time-related freedom-from-event depictions (life tables) and (2) those who use time-related depictions as a consideration when recommending therapy for individual patients (see “Time-Related Events” earlier in this section). This stems from their differing needs. Studies involving testing hypotheses, such as clinical trials in which

\begin{table}
\centering
\begin{tabular}{|c|c|c|c|}
\hline
Interval (months) & Life table & Parametric & Life table & Parametric \\
\hline
1 & 97% & 97% & 92% & 93% \\
3 & (97%) & 96% & 90% & 90% \\
6 & (97%) & 95% & 88% & 89% \\
12 & (97%) & 95% & 87% & 89% \\
36 & (97%) & 95% & (87%) & 89% \\
72 & (97%) & 95% & (87%) & 89% \\
\hline
\end{tabular}
\caption{Simple repair (\( n=81 \)) versus transanular patching (TAP) (\( n=92 \)).}
\end{table}
treatment is randomly assigned, usually require a yes/no (true/false) answer to a hypothesis, and a single overall P value may be appropriate. The clinician, on the other hand, lives daily with the reality that for an individual patient, occurrence of an unfavorable outcome event at one point in time (interval after time zero) is often considerably less disadvantageous than occurrence of the same event at another point in time; the clinician also understands that there is considerable variability among patients as to the time of greatest disadvantage.

Mantel recognized in 1966, as no doubt did others, that time-related variability occurs in the relation between survival curves of two different treatments or between groups of patients. He noted that in some cases the difference may be similar throughout time; that in others the relation between the two may be similar at some times but not at others; and that in still others one survival curve may cross another. He also recognized that varying hazard phases are present after surgical procedures, and he understood the variability in the “utility function,” or value, ascribed by different individuals to the same survival curve.

These matters posed difficulties for those seeking a simple yes/no answer to a hypothesis. In response to this, Mantel and others set about to devise tests that would generate a single overall P value. These tests make different assumptions, each attempting to overcome some difficulty posed by the differing patterns of survival. In contrast, clinicians wish to compute, examine, and understand the variability in the time-related comparisons between curves in order to best inform and advise patients. Thus, they wish to know the time-related certainty of differences that may exist.

The scanning method of comparing confidence intervals, as well as methods involving P values, can be applied to develop time-related estimates of the degree of uncertainty in comparing survival and other event-free curves. A depiction of time-related survival is in actuality a series of proportions; the proportions are discrete when determined by the Kaplan-Meier life-table method and are continuously variable when determined by the parametric hazard function regression analysis method. Thus, the overlapping or non-overlapping of confidence intervals around each of two survival curves can be used to scan the possibility, at various specific intervals after time zero, that the difference between the curves is or is not likely to be due to chance alone (Fig. 6-27, A). Also, based on classic statistical principles, the time-related confidence intervals around the difference between the two proportions can be determined and their relation to zero computed and visualized in a continuous, time-related depiction (Fig. 6-27, B). An equivalent expression of absolute difference is absolute risk reduction, the inverse of this difference, often expressed as number to treat to save one life (see Box 6-3). The time-related relation of the difference compared to zero difference can be depicted continuously in terms of the P value (Fig. 6-27, C). The time-related relation of the difference compared to zero difference can be depicted continuously in terms of the hazard function (Fig. 6-27, D). They may also be compared using the CLs around the hazard ratio (Fig. 6-27, E). Alternatively, the area between survival curves—the lifetime function—can be computed (Fig. 6-27, F). We prefer the lifetime function to the alternative statistic, expected lifetime, because the complete hazard function beyond the follow-up information available affects the value of this extrapolated statistic, and its trajectory may not be well characterized.

Repeated Events

Unlike death, morbid events such as thromboembolism or important bleeding after heart valve replacement may recur. Furthermore, the consequences of these events may be variable, from apparently “no functional residual” from a transient ischemic attack to a fatal outcome (Fig. 6-28).

If the hazard function is truly constant, the method of linearized rates, as described earlier in this section under “Parametric Survival Estimation,” may be used. The estimation procedure is simple but rarely appropriate, because most hazard functions are not constant.

When the hazard function is not constant, three general approaches to display and analysis of morbid events have been used: analysis as a terminating event, repeated events analysis, and modulated renewal process analysis.

Terminating Events Approach

The most common method of display and analysis of repeated morbid events is to focus only on the first occurrence, ignoring any further information beyond that point for the patients experiencing the event. It thus becomes a terminating events analysis, with Kaplan-Meier estimation of freedom from occurrence of the event. This is the least informative approach.

Repeated Events Approach

True repeated events analysis can be performed, but generally this requires abandoning the Kaplan-Meier estimator and turning to the Nelson estimator. The Nelson method is formulated in the cumulative hazard domain (see “Fundamentals” under Time-Related Events earlier in this section). Patients continue to be followed after each occurrence of the event until end of follow-up or death or some other appropriate censoring mechanism (see Fig. 6-28). Estimates are made at the time of each occurrence, with the hazard estimated as 1/number at risk, and the cumulative hazard as the sum of all these hazards. Graphical depiction of Nelson estimates is as cumulative hazard across time, with the vertical axis being the number of repetitions of the event expected per patient (Fig. 6-29). Thus:

\[
\Lambda(t) = \sum_{i=1}^{n} \frac{n_{\text{end}}}{n_{\text{start}}} \tag{6-20}
\]

where \( n_{\text{end}} \) is the number experiencing the event (generally 1) at time \( t \), and \( n_{\text{start}} \) is number at risk.

\(^{11}\) Comparison of Kaplan-Meier and Nelson estimators. The Kaplan-Meier estimator for survival at time \( t \), \( S(t) \), is:

\[
S(t) = \prod_{i=1}^{n} \left(1 - \frac{n_i}{n_{\text{start}}}\right)
\]

Transforming \( S(t) \) to cumulative hazard:

\[
\Lambda(t) = -\sum_{i=1}^{n} \ln \left(1 - \frac{n_i}{n_{\text{start}}}\right)
\]

If \( n_{\text{start}} = 100 \) and \( n_{\text{end}} = 1 \), the logarithmic term \( 1 - \frac{n_i}{n_{\text{start}}} \approx 0.99 \) and its logarithm is 0.01005. Compare this with the Nelson estimate of cumulative hazard, \( n_{\text{end}}/n_{\text{start}}, \) which in this case is 1/100 = 0.01. For all practical purposes, the two estimates are equivalent. The advantage of the Nelson estimator is that it can be extracted from the probability domain \( S(t) \) so that repeated and weighted events can be evaluated, neither of which has a probability domain counterpart.
Figure 6-27  Survival estimates for a cachectic diabetic man with unstable angina according to different initial treatment strategy for his ischemic heart disease. This set of graphs depicts the decision-making challenge of intervention versus continued medical therapy (or natural history of a chronic disease) versus one alternative intervention. There are “crossing lines”: an initial higher risk of surgery is traded for a longer-term survival benefit. A patient might prefer to delay surgery or accept an alternative therapy if there are matters of short-term importance that are higher in priority than short-term risk of mortality of medical therapy. Another similar patient may want to undergo immediate high-risk surgery because of importance of long-term goals. Therefore, the decision by patients concerning timing of surgery, if at all, must take into account these crossing lines and their personal short- and long-term goals (preferences). 

A, Survival. Solid lines enclosed within dashed confidence limits (CL) are point estimates for (1) natural history (medical), (2) percutaneous coronary intervention (PCI), and (3) coronary artery bypass grafting (CABG). These predictions are based on patient-specific solutions of the multivariable equations presented in reference. 

Within the first year, procedure mortality results in a survival advantage for medical therapy, but after 2 years, nonoverlapping CLs indicate an advantage for intervention. 

B, Difference in predicted percent survival (solid curve) between CABG and natural history (medical) with dashed 90% CLs. Initially, there is a medical benefit (negative difference), but after 1 year, a CABG benefit. P value for difference in predicted percent survival between CABG and natural history (medical). Difference in benefit shown by overlap and nonoverlap of CLs in B is depicted in terms of P value; note that P value is shown symmetrically above and below 1, reflecting a change in direction of benefit. 

C, Hazard function (solid curves) for death from natural history (medical), PCI, and CABG with dashed 70% CLs. Note that instantaneous risks diverge considerably earlier than survival estimates (A) and lifetime estimates (F), because rates must both change and remain changed sufficiently long to produce a survival or lifetime difference. 

D, Hazard ratio (solid curve) of CABG and natural history (medical) with dashed 90% CLs. Initially, the hazard ratio favors medical therapy, but then CABG. Note that hazards become proportional after about 6 months (flat portion of ratio), but are nonproportional before then. Vertical axis has been arranged to give equal weight to a twofold increase in risk and a 0.5-fold decrease in risk. 

F, Difference in predicted lifetime (solid curve) between CABG and natural history (medical) with dashed 90% CLs. Lifetime difference is the area between the two corresponding survival curves depicted in A.
The Blackstone-Naftel-Turner parametric hazard methodology is designed to analyze repeated morbid events. An interesting but useful technical detail of such an analysis is that each patient’s follow-up history is recorded as a sequence of interevent segments: time zero to first event, first event to second (etc.), last event to censoring mechanism. Each segment has a beginning and ending time. Kalbfleisch and Prentice point out that this approach to the data simplifies what might otherwise appear to be a daunting analytical challenge.\(^1\)

**Modulated Renewal Process Approach**

The hazard function for repeated events such as cardiac rejection episodes may follow a similar pattern after each repeated episode, only modulated to some degree (higher or lower) in its intensity. Such a phenomenon, commonly observed in the industrial setting, is called a modulated renewal process (see Fig. 6-28, D).\(^1\)

The idea behind a modulated renewal process is that the industrial machine (or patient) is restarted at a new time zero each time the event occurs. This permits (1) ordinary Kaplan-Meier methods to be used, (2) the number of occurrences and intervals between each recurrence to be used in multivariable analyses, and (3) change in patient characteristics at each new time zero to be used in analyses. Thus, if the modulated renewal assumption can be shown to be valid, it increases the power and utility of the analysis tremendously. For example, Hickey and colleagues demonstrated that each repeated episode of thromboembolism following mitral valve commissurotomy increased the risk (shortened the interval) of the next\(^2\) (Fig. 6-30). Kubo, Naftel, and colleagues demonstrated that rejection after cardiac transplantation behaved as a modulated renewal process, and among other factors, number of previous rejection episodes was a risk factor for subsequent episodes\(^3\) (Fig. 6-31). Blackstone and colleagues exploited the modulated renewal process methodology for reoperations, periprosthetic leakage, and replacement device endocarditis after valve replacement.\(^4\)

From a data handling perspective, the patient’s follow-up record is segmented just as described earlier in this section for the “Repeated Events Approach,” but the starting time

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Figure 6-28  Repeated morbid events data. Conceptual graph of incomplete data in a group (cohort) of patients followed cross-sectionally after mitral valve replacement (MVR) with a mechanical prosthesis, depicting repeated morbid events. Deaths are depicted by \(D\), and the morbid event (thromboembolism) is depicted by \(E\). Censored patients (alive at follow-up) are indicated by arrows.

**A**  Calendar date is along horizontal axis, and each patient enters on a different date of operation, similar to depictions in Fig. 6-19. Five patients have experienced the morbid event, and two of these have experienced two events; one has experienced three events. However, note that follow-up continues beyond these events.

**B**  Patients are again ordered for analysis by aligning them at time zero.

**C**  From a purely practical point of view, the longitudinal record of each patient is broken into segments, each with a starting and ending time.

**D**  In a modulated renewal process analysis, all segments are moved back to time zero (and for analysis, they would also be reordered from shortest to longest interval, which is not depicted here).
Figure 6-29  Illustration of repeated events data. Repeated bloodstream infections after left ventricular assist device (LVAD) insertion are shown. A, Cumulative number of bloodstream infections, expressed on vertical axis as number per patient (repeating events analysis). Each circle represents an infection, vertical bars represent asymmetric 68% confidence limits (CL), and numbers in parentheses are number of patients remaining at risk. Solid line enclosed by dashed 68% CLs is the parametric estimate of bloodstream infections from which hazard for event was derived. B, Hazard function for bloodstream infections expressed on vertical axis as percent per month (solid line enclosed by 68% CLs). C, Cumulative number of bloodstream infections according to type of LVAD. Open circles represent events experienced by patients receiving implantable pneumatic HeartMate devices (IP); solid circles, vented electric HeartMate devices (VE); and open squares, Novacor devices. (From Navia and colleagues.\textsuperscript{N4})

Figure 6-30  Freedom (risk-adjusted) from a postcommissurotomy thromboembolic event, illustrating analyses of repeated morbid events as a modulated renewal process. Top curve represents freedom from first thromboembolic event, and time zero is time of operation. Middle curve represents freedom from a second thromboembolic event among 33 patients who had a first thromboembolic event after commissurotomy, and time zero for this depiction is time of first thromboembolic event. Lowest curve represents freedom from a third thromboembolic event among patients who already had experienced two, and time zero is time of second episode. (From Hickey and colleagues.\textsuperscript{H20})
of each segment is set to zero and the ending time to duration of the segment.\textsuperscript{31}

**Weighted Events**

When a machine is repaired, there is a cost associated with the repair. Thus, in industrial settings it is important not just to estimate the risk (hazard) of repair but also to weight those risks by the cost of repair.\textsuperscript{37,38} (Fig. 6-32). Mathematically, cost is taken into account by what is termed “weighting” of the hazard estimate. This simply means the hazard is multiplied by the cost.

Medically, there are a number of cost scales that can be used to quantify, or at least grade, severity of an event. The UAB group, for example, used a simple 5-point scale for residual neurologic consequences of a thromboembolic episode, with 0 being no consequences and 4 being death.\textsuperscript{327}

Nonparametric estimation is in the cumulative cost domain, and Nelson’s method is used.\textsuperscript{37,38} The Blackstone-Naftel-Turner parametric hazard function method also accommodates weighted events and complete multivariable analysis.\textsuperscript{844}

**Competing Risks**

Competing risks analysis is a method of time-related data analysis in which multiple mutually exclusive events are considered simultaneously.\textsuperscript{34,317} It is the simplest form of continuous-time Markov process models of transition among states.\textsuperscript{46} In this simplest case, patients make a transition from an initial state (called *event-free survival*) to at most one other state that is considered to be terminating (Fig. 6-33). Thus, there is a single set of intervals from time zero to the earliest occurring of each event for a given patient. Rates of transition from the initial state to one of the events (called an *end state*) are individual independent functions. One way to think about this is that the initial state is represented by a bucket of water (Fig. 6-34). The transition rates are holes in the bucket of varying size. If all but one hole is blocked, the amount of water filling a container beneath the hole is identical to an ordinary survival function turned upside down. In a competing risks analysis, one is interested in discovering the amount of water in each of several containers when all the holes are unblocked simultaneously.

**Motivation**

Analysis of a single time-related event is performed in isolation of any other event. This is ideal for understanding that specific phenomenon. In contrast, competing risks analysis considers multiple outcomes in the context of one another. It is thus an integrative analysis.

Fig. 6-35 shows three events following CABG: death before reintervention, reintervention by percutaneous methods, and operative reintervention. At time zero, all patients are alive and without reintervention. They then migrate at different rates into the above various end states (Fig. 6-35, A). The consequence of these migrations is that the initial state is gradually emptied, and the reintervention states and death state fill (Fig. 6-35, B).

The nature of migration into each of these end states is itself an important phenomenon. Results from the Cardiac Transplant Research Database\textsuperscript{356} and the UAB group\textsuperscript{416} show the provocative difference in the various competing hazard functions for modes of death after transplantation, just as the UAB group had shown for modes of death after valve replacement.\textsuperscript{540}

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**Figure 6-31** Freedom from transplant rejection after 1 year or any rejection episode later than 1 year, stratified according to number of rejection episodes during first year after transplantation. Data illustrate a repeated event analyzed as a modulated renewal process. Vertical bars represent 70% confidence limits. Key: CTRD, Cardiac Transplant Research Database. (Redrawn from Kubo and colleagues.\textsuperscript{5,35})

**Figure 6-32** Weighted repeated events. This compartmental analog shows patients experiencing an initial episode such as a cardiac valve replacement, at time zero. A repeating morbid event is then shown (e.g., thromboembolism). Rate at which these occur is depicted by \( \lambda \)s (which may differ after each event). In addition, medical cost of each episode is depicted by a severity weight (\( W \)). From each compartment (after each event), the patient may die, an eventuality governed by another set of hazard rates not depicted.
Figure 6-33  Competing risks data. Conceptual graph of incomplete data in a group (cohort) of patients followed after coronary artery bypass grafting (CABG) for death (D), redo CABG, or percutaneous coronary intervention (PCI). Depiction is similar to Fig. 6-13. A, Calendar date is along horizontal axis, and patients are operated upon on various dates. They are systematically followed and their status ascertained as of a common closing date, shown by vertical line. Notice that one patient died a while after redo CABG and another after PCI. Four patients experienced no events and are censored. B, Patients are aligned at time zero and rank ordered from shortest to longest follow-up time. First occurring event is shown. Thus, the two patients who died after redo CABG or PCI are depicted only to their intervention (other analyses of events following redo CABG and PCI should also be performed). In this way, each patient falls into exactly one of four mutually exclusive categories: PCI, redo CABG, death before either of these interventions, and event-free survival. Notice that each patient has in this depiction, unlike A, a single follow-up interval. This common follow-up interval to all events is characteristic of this simplest form of competing risks analysis.

Figure 6-34  Competing risks cartoon using a bucket and water analogy. In each case, large bucket is initially filled with water at time zero and represents event-free survival. Each spigot represents a route of exit of water from main bucket to smaller, initially empty, containers. Rate of flow is governed by position of tap. A, In ordinary analysis of single time-related events, there is only one tap. In competing risks analysis, this is analogous to closing all but one tap to permit estimation of its properties (called the hazard function). B, In the simplest competing risks analysis, two taps are opened simultaneously, and each water molecule (representing patients) must flow into only one container through one of the spigots. Level of water across time as each container fills (and main bucket empties) is quantified by the cumulative incidence function. C, A more complex competing risks case with three taps opened. Reintervention is broken down into the two mutually exclusive components of percutaneous coronary intervention (PCI) and repeat coronary artery bypass grafting (CABG).
In the early 18th century, some progress was made in the war against smallpox by inoculating people with small doses of the virus to establish immunity to the full-blown disease. The technique was 10% fatal in otherwise healthy individuals! The search for reliable low-risk protection became intense. Because governments at that time were supported in part by annuities, it was of considerable economic importance to know the consequences a cure of smallpox might bring upon the government’s purse. Daniel Bernoulli tackled this question by classifying deaths into mutually exclusive categories, one of which was death from smallpox. For simplicity, he assumed that modes of death were independent of one another. He then developed kinetic equations for the rate of migration from the state of being alive to any one of several categories of being dead, including from smallpox. It was like hanging a bucket of water with multiple different sizes of holes in the bottom (see Fig. 6-34) and assuming no interactions between the holes. He could then compute how stopping up one large hole, smallpox, would influence both the number of people still alive and the redistribution of deaths into the other categories.

The triumph of the “war on smallpox” came in 1796, just 36 years after his publication.

**What’s in a Name?**

Competing risks analysis has many names, which makes communication among disciplines, as well as assembly of a common body of methodological knowledge, difficult. In vital statistics, competing risks are often called *disease-specific event rates*. In actuarial statistics, they may be called *multiple decrement analyses*. In statistics, they are usually called competing risks, but also *cumulative incidence functions* or *marginal or conditional survival analyses*. In demographics, they may be called *crude vs. net vs. partial crude survival functions*. In medicine, and heart valve procedures specifically, the terms *cumulative events*, *multiple decrement*, *competing risks*, *mode-specific survival*, and *actuarial analysis* (competing risks are called *actual and single-event analyses actuarial*). These methods are contrasted as if they were competing methods, or indeed, as if one were right and the other wrong. We must emphasize that each answers different questions, and assuming independence, the hazard functions are the same. Had one of them not yet been invented, the other surely would have because of the different questions answered. Individual event analyses (actuarial) using the entire patient cohort answer the question, “What is the probability of this event among patients still exposed to risk of the event, and what are its risk factors?” It is an unconditional probability. It is relevant to the investigation of a phenomenon. Such an investigation has to be conducted (as best as possible) free from confounding by occurrence of other outcomes. In contrast, competing risks analyses address the question, “How many patients are expected to experience a certain event before they experience another (specified) event?” Thus, individual event analyses indicate the probability of operative CABG as a function of age; competing risks analyses may indicate that few elderly patients will survive to experience such a reoperation.

We caution against direct display of actual and actuarial estimates on the same graph. In fact, each has a different scale (probability scale for individual events; cumulative incidence

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**Figure 6-35** Illustration of competing risks. Figure depicts time-related competing events after coronary artery bypass grafting. **A**, Risk-unadjusted migration rates (hazard functions) into each of three mutually exclusive event categories: death before reintervention, reoperation by reoperation, and reintervention by percutaneous coronary intervention (PCI). **B**, Competing risks depiction of consequences of the three migration rates shown in **A**. Units along vertical axis are cumulative incidence. Rates shown in **A** deplete proportion (%) of patients “alive, without reintervention” and increase proportion dying before reintervention or experiencing reintervention by reoperation or PCI. At all points in time, percentage of patients in all categories sums to 100%, as shown in percentages at 12 years in right margin of figure. (From Blackstone and Lytle.)

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Because many possible paths of migration exist, it is important for understanding each phenomenon to isolate it from all others, much as one would perform a controlled experiment with all other factors held constant. If one assumes that the rates of migration (hazard functions) are independent of one another, factors influencing those rates (incremental risk factors) can be discovered and their influence explored. So long as it is reasonable to assume independence of events, such analyses are valuable to estimate matters like how often death would occur in the absence of reintervention.

However, individual analyses do not address the question of how often an event might occur in the presence of competing risks of other events. For example, it is valuable to know the influence of age and extent of grafting on reintervention or death. “How often will elderly patients need reoperation given the risk of mortality from old age itself?”
scale for competing risks). Two aspects of scale are noted by Grunkemeier and colleagues.\textsuperscript{328} First, actuarial estimates of multiple different events do not sum to 100%. They should not; this is not a defect but a property of unconditional independent events. Competing risks are conditional, which implies \textit{multiplication} rather than \textit{addition}. Indeed, it is easy to show that multiplication of independent survivorship functions yields event-free survival. Second, they note that the complement of the cumulative incidence function of competing risks is usually a higher number than actuarial estimates. Again, this is guaranteed because competing risks must all sum to 100%, and this number is “adjusted” for occurrence of several competing risks. The more events considered to be competing, the higher the number will be. This “instability” is not a defect of competing risks analysis but rather a fundamental property. In the water bucket analogy, if more holes are punched in the bucket, there are more routes of exit, and each container under each hole will be filled less than when there were fewer holes. Because Grunkemeier and colleagues turn cumulative incidence curves upside down, “less filling” is equivalent to their “higher number.”

Ideally, because competing risks estimates are of the number of patients (or percentage of all patients) in each end state, they should be plotted on the scale of cumulative incidence. In such a plot, the initial state empties (decreases) and all other states fill (increase) (see Fig. 6-35, B).

Limitations and Assumptions

An important assumption of time-related analyses is \textit{noninformative censoring}.\textsuperscript{335} Either systematic anniversary or cross-sectional follow-up methods help with this assumption. However, in analysis of morbid events, death is a censoring mechanism, and it may not be independent of morbidity. In competing risks analysis, all events cause censoring of one another, and the possibility of informative censoring multiplies.

The number of hazard phases resolved in parametric hazard estimation depends on length of follow-up. Therefore, their ability to extrapolate beyond the length of follow-up is limited.

The number of events limits the number of risk factors that can be identified in either Cox proportional hazards analysis or hazard function multivariable analysis (see Box 6-5). If the latter is performed, this limitation is true within each hazard phase.

LONGITUDINAL OUTCOMES

In analysis of time-related events, the event is assumed to be a point process; that is, it is assumed to occur at some specific point in time, and the analysis focuses on the distribution of times until that event occurs. Many phenomena of equal importance to the cardiac surgeon are not point processes but outcomes that evolve across time: longitudinal data. Longitudinal data may be continuous, ordinal, or polytomous (unordered list of possible outcomes).

Specific examples include time-related change in NYHA functional class after a Dor procedure, degree of return of valvar regurgitation and its progression after mitral valve repair, change in ventricular volume after MI, sensitization after left ventricular assist device insertion, pulmonary function after single or double lung transplantation, and atrial fibrillation episodes after a maze procedure. For all these phenomena, information generally is obtained from patients periodically, usually at irregular intervals that differ from patient to patient. These are \textit{longitudinal outcomes}.\textsuperscript{318}

Assessment of longitudinal outcome may be interrupted (censored) permanently by death, temporarily at active cross-sectional follow-up, or by other events that remove patients from risk, just as in time-related events studies (see “\textit{Fundamentals}” under Time-Related Events earlier in this section). One would like to use the data up to the time of censoring. Furthermore, the clinical investigator is interested in factors that affect longitudinal evolution of these phenomena.

Historical Note

Severe technologic barriers to comprehensive analysis of longitudinal data existed before the late 1980s.\textsuperscript{332} Repeated-measures analysis of variance for \textit{continuous} variables had restrictive requirements, including fixed time intervals of assessment and no censored data. \textit{Ordinal} logistic regression for assessment of functional status was useful for assessments made at cross-sectional follow-up,\textsuperscript{11,320} but not for repeated assessment at irregular time intervals with censoring.

In the late 1980s, Zeger and his students and colleagues at Johns Hopkins University incrementally but rapidly evolved the scope, generality, and availability of what they termed “longitudinal data analysis.”\textsuperscript{331} Their methodology accounts for correlation among repeated measurements in individual patients and variables that relate to both the ensemble and the nature of the variability. Because average response and variability are analyzed simultaneously, the technology has been called “mixed modeling.” The technique has been extended to continuous, dichotomous, ordinal, and polytomous outcomes using both linear and nonlinear modeling.

Because of its importance in many fields of investigation, the methodology acquired different names. In 1982, Laird and Ware published a \textit{random effects model} for longitudinal data from a frequentist school of thought.\textsuperscript{14} In 1983, Morris presented his idea on \textit{empirical Bayes} from a Bayesian school of thought.\textsuperscript{325} In the late 1980s, members of Zeger’s department at Johns Hopkins University developed the \textit{generalized estimating equation} (GEE) approach.\textsuperscript{318}

Goldstein’s addition to the Kendall series in 1995 emphasized the hierarchical structure of these models.\textsuperscript{317} His is a particularly apt description. The general idea is that such analyses must account for covariables that are measured or recorded at different hierarchical levels of aggregation. In the simplest cases, time is one level of aggregation, and individual patients with multiple measurements is another. These levels have their corresponding parameters that are estimated, and each may require different assumptions about variability (random vs. fixed-effects distributions).

Except under exceptional circumstances, these techniques have replaced former restrictive varieties of repeated-measures analysis, which we now consider of historical interest except for controlled experiments designed to exactly meet their assumptions.

Concept

One way to think about the concepts underlying longitudinal data analysis is to consider it as a method that summarizes the results of individual regression analyses for each
Individual data points cannot be treated as independent observations. Instead, trends and variability must be analyzed at each successive level of aggregation.

**Implications**

Cardiac surgeons have often collected information on longitudinal outcomes only at the time of last follow-up, such as most recent NYHA functional class, most recent echocardiographic assessment of valve regurgitation after repair, or most recent degree of sensitization at transplant after implanting a permanent left ventricular assist device. Such a strategy cripples establishing time trends, because each patient contributes only one data point, preventing trends from being identified at the individual patient level. Therefore, it is imperative that every observation of longitudinal outcome be gathered and included in the analysis as part of the follow-up process.

A further cautionary note is that one-time survey of patients at follow-up (e.g., a quality-of-life questionnaire) also represents a single observation per patient. Yet often, inferences are desired of a longitudinal nature. It is a huge

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**Figure 6-36** Hypothetical illustration of longitudinal data. Pressure gradient, determined by echocardiography, is shown on vertical axis, and years after operation on horizontal axis. Measurements were obtained at two cross-sectional follow-up studies about 6 months apart in 14 patients. **A**, Scattergram of all measurements. **B**, One hypothetical set of measurements in individual patients, with their two measurements connected by solid lines. In most cases, gradient increased between successive measurements. **C**, Another hypothetical set of measurements in individual patients, connected by solid lines. In most cases, gradient decreased between successive measurements. In both **B** and **C**, data points are identical to those shown in **A**.

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*Note: The diagrams in Figure 6-36 show scattergrams and trends for hypothetical data.*
assumption that ensemble averages based on one point per patient will reflect what multiple longitudinal measurements per patient would tell you (although repeated testing bias must also be considered).

**Assumptions**

Assumptions underlying longitudinal models are important to understand. At one time, mixed models demanded repeated values to be measured at identical times for all subjects. As mathematical and statistical developments progressed, flexibility increased. Thus, today, longitudinal data analyses can be employed for data:

- Observed at haphazard intervals
- With a differing number of observations (including one) per patient
- Encompassing an observation period of variable length
- Containing missing observations in a sequence of observations
- Having sequences interrupted by a censoring mechanism such as death

This flexibility comes at a price. The most important price is the assumption that censoring for any reason is noninformative with respect to the outcome being assessed. Although this assumption is similar to that for time-related events, some aspects of longitudinal data make them even more susceptible to informative bias. If, first, it is not hard to imagine settings in which various factors “deplete” availability of longitudinal outcomes in a systematic fashion. For example, if the outcome is NYHA functional status, death interrupts assessment, and it is likely that the sickest patients with highest NYHA class die; the remaining patients may be more robust, leading to the possible inference that results are improving with time. Immunologic sensitization during permanent left ventricular assist device operation may be interrupted by availability of a donor heart sooner than if patients are doing well, or it may postpone transplant longer than usual; thus, degree of sensitization in remaining patients may skew the ensuing estimates up or down. If patients are being followed longitudinally for rhythm after a maze operation, those with return of atrial fibrillation may be assessed more often than those in sinus rhythm; prevalence of atrial fibrillation may, therefore, appear higher than it actually is. Patients assessed by coronary angiography for recurrent angina often become the basis for assessing longitudinal patency of coronary artery bypass conduits; these patients may not be representative of all patients (estimates are likely to be overly pessimistic). It is questionable whether patients remaining after these mechanisms of censoring are representative of the original group. Biased inferences could result from this informative censoring.

Just as Berkson and Gage in the early 1950s found that one should ignore follow-up intervals beyond the point at which about 10% of the original group was followed, we believe a similar truncation of longitudinal data should be considered. But this does not address an important bias of ascertainment. For example, patients being monitored longitudinally for a disease or because of a recurrent event (e.g., return of atrial fibrillation after ablation, recurrent angina after CABG) may be observed more frequently than patients deemed to be disease or symptom free.

**Modulators**

Factors modulate longitudinal outcomes just as they do any other type of outcome, so multivariable analysis within the longitudinal analysis domain is necessary. Currently the facility for such analyses is limited in available statistical software. However, this may provide an opportunity to use newer algorithmic techniques for risk factor identification, such as random forests. To temporarily overcome these limitations, at present we perform preliminary analyses under the assumption of independence of observations using available multivariable analysis tools. We then construct the longitudinal models “by hand.”

It would also not be surprising if, just as in analysis of time-related events after cardiac surgery, different factors modulate different time frames of longitudinal evolution. However, in most implementations of longitudinal analyses, time is treated no differently from any other variable, so there is little opportunity for variables to meaningfully modulate temporal rates of change. The Cleveland Clinic group is developing a set of novel methods for analysis of longitudinal data that treat time in a special way. One of these is **temporal decomposition**.

**Temporal Decomposition of Longitudinal Data**

Using the same strategy and mathematical formulation that Blackstone, Naftel, and Turner did for time-related events, the temporal occurrence of a binary event, such as presence or absence of atrial fibrillation, is conceived as the addition of a number of temporal components or phases. Each phase is modulated simultaneously by log-linear additive function of risk factors.

For example, Fig. 6-36 illustrates temporal decomposition for return of atrial fibrillation after a surgical ablation procedure in patients with mitral valve disease. Fig. 6-37, A shows decomposition into two phases, early and late. These generate the overall atrial fibrillation pattern of Fig. 6-37, B. Risk factors are identified for both these phases and overall. These are illustrated for extent of lesion set used for ablation (Fig. 6-37, C) and left atrial volume (Fig. 6-37, D).

As of yet, we have not written either robust software for this or a robust method for risk factor identification. However, the method has been extended to ordinal outcomes, such as return of atrophicventricular valve regurgitation after repair, and continuous outcomes, such as regression of left ventricular mass after aortic valve replacement for stenosis and for spirometry values after lung transplantation.

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**Section V Use of Knowledge**

**TRANSFORMING STATISTICAL INFERENCES INTO CLINICAL INFERENCES**

Statistical inferences focus on interpreting magnitude and variability of parameter estimates, reliability of numeric results, summary statistics, behavior of CLs, P values, and many other numeric results. The data truly speak through these results, often revealing what is important and what is not. However, numeric information often does not lead to the kind of mental picture or overview of the data that is needed to generate new knowledge. There must be a view of
analysis on linearizing transformations of scale that may be needed to faithfully depict the relationship (see “Multivariable Analysis” in Section IV). Our experience indicates that most relations of continuous variables with outcome are smooth. They do not show sharp cut-offs (see “Continuity versus Discontinuity in Nature” in Section I), although they may well show evident differences (see Appendix 6B).

Use of Incremental Risk Factors

Multivariable analysis identifies incremental risk factors for outcomes, and this provides one form of new knowledge. The risk factors identified are sometimes proclaimed by cardiac surgeons and others to be “truly independent,” suggesting that such a risk factor is independent of the action of any other risk factor in exerting its influence. Such is not the case, and this idea is not the origin of the adjective “independent.” An independent variable is simply one that may be associated with the dependent (outcome) variable (see Box 6-18). Draper and Smith state, “The words ‘independent variables’ must not be too literally interpreted. In a particular body of data, two or more independent variables may vary together in some definite way.”

In addition to generating specific new knowledge by identifying risk factors for an outcome, multivariable analysis (see Box 6-18) can be used for patient-specific predictions. The wood, not just the trees. Something further is therefore needed to translate statistical inferences into clinical inferences and new knowledge.

One of the most powerful tools to accomplish this is graphics. An important reason for our using and even developing completely parametric models was that they so easily allow graphics to be generated in the form of nomograms, as advocated by the Framingham investigators. For example, if an analysis indicates an association of survival with age, we want to know what the shape of that relationship is. Is it relatively flat for a broad range of age and then rapidly increasing at either extreme of age? Or does risk increase rather linearly with age? Although the answers to these questions are contained within the numbers on computer printouts, these numbers are not easily assimilated by the mind. However, they can be used to demonstrate graphically the shape of the age relation with all other factors held constant (see “Risk Adjustment” in Section VI).

Because graphics are so powerful in the process of generating new knowledge, an important responsibility is placed on the statistician to be sure that relations among variables are correct. Often, variables are examined and statistical inferences made simply to determine whether a continuous variable is a risk factor, without paying particular attention to what the data convey regarding the shape of the relationship to outcome. Instead, the statistician needs to focus during

Figure 6-37 Temporal pattern of atrial fibrillation after surgical ablation. A, Decomposition of pattern into early and late components (phases), each of which will be modulated by risk factors. B, Overall temporal prevalence of atrial fibrillation. C, Effect of lesion set on pattern of atrial fibrillation after ablation. D, Effect of left atrial volume on 1-year prevalence.
Risk-adjusted comparisons can be made of the results of different surgeons, different interventional cardiologists, different methods, and different institutions. Multivariable analysis for these purposes is usually best performed in a parsimonious manner.

Multivariable analysis of clinical experiences can also be used to investigate the nature of cardiac surgery for a specific situation, such as transposition of the great arteries or the post–cardiopulmonary bypass state. For such purposes a series of sequential analyses are often useful, rather than a single analysis performed in a parsimonious manner. In sequential analysis, often the patient-specific potential risk factors are first examined and the multivariable equation for the outcome event generated. Then the procedural variables may be entered, and their effect on the certainty and strength of the patient-specific variables studied. New ideas then generate reanalyses, reevaluation of the correlations between risk factors, and additional new analyses.

Multivariable analysis can also be used to examine and interpret the way one risk factor modulates influence on outcome of another. One such use is to determine if a risk factor, such as age, is neutralized with experience. Another is to determine if treatments modulate some risk factor differently from another (interaction terms). All of this emphasizes the care with which all multivariable analyses must be made. Good, reliable, and valid analyses are not made by computers alone, but by people using computers expertly as just one tool of analysis and synthesis.

**SCIENTIFIC PAPER**

A scientific paper is a formal communication of new knowledge generated by a scientific study. It can be argued that science must be communicated to exist. The importance of communicating clinical research is that evidence-based medicine is literature-based medicine. Thus, medical research can have life-and-death implications, although Day comments, “Good scientific writing is not a matter of life or death... it’s much more serious than that.”

Unlike most other forms of communication, it has all the following elements:

- It is in the public domain and not proprietary.
- It is objective.
- It presents sufficient information to allow verification elsewhere.
- It builds on what has been previously discovered.
- It predicts what should subsequently transpire in an orderly universe.
- It is not written with just authority as its basis, but rather with information, data, and analyses at its core.
- It does not intuit or pass along traditions, but draws inferences and relates these to the context of past investigations.
- It is a formally structured communication.

The structure of a scientific paper is said to have been formalized by Louis Pasteur, who established the “IMRD” format for reporting scientific information: Introduction, Methods, Results, Discussion. This format has been codified into requirements of all scientific journals. It provides a valuable structure for thinking about and clearly expressing the findings of one’s research. However, a scientific paper is not literature to be read from beginning to end. Rather, it is for selective strategic reading.
structure) linear. That is, the paper, written on the basis of what has been discovered from the investigation, likely cannot simply reflect the original study proposal. The best way then to begin writing a scientific paper is to study intently the descriptive statistics, results of the various analyses, tabular results, and graphical depictions from the analyses, allowing “the data to speak for themselves.”

Goals for the paper are then set that establish its message and those purposes of the study that relate directly to supporting this message. These purposes will comprise the last sentences of the introduction. Methods and results likely should follow, then completing the initial portion of the introduction and discussion. We recommend writing the abstract last because it condenses all the text from the introduction through discussion. In the following text, each element of a manuscript is defined and described.

### Title

The title introduces the work. It may be the only thing read and so must entice intended readers. A good title is short but specific, truly represents the content of the paper, is indexable, and avoids jargon, qualifiers, abbreviations, and “filler.”

### Ultra-Mini Abstract (the “Message”)

The ultra-mini abstract is the truest two or three sentences (50 words maximum) that capture the essence of the findings—the message of the paper. It is not a brief summary of results. Rather, it is the inferences that will be supported by the results. It is often identical to the conclusion of an abstract.

Only if one can simply and succinctly understand the findings of the study and articulate what they mean will one be able to convey them clearly to the reader. By experimentation, we found that if the essence can be stated adequately in fewer than 25 words, the paper may have low information content and should be conveyed as a brief communication or letter to the editor. If it cannot be stated in 25 to 50 words, there may be information overload, and the study should be split into more than one manuscript, each focused on a different aspect of the results.

Once the essence is written, the entire manuscript—tables, figures, and text—should be sharply focused on those results that are supportive of the paper’s message. Other information should be either relegated to appendices (for the aficionado—usually electronic only) or eliminated altogether.

### Introduction

An introduction answers four important questions:

- What is the problem addressed?
- Why is it important?
- What is the context?
- What is the specific purpose of the study?

Start by writing a clear statement of the purpose of the study. Although this has been the most important aspect of the original research proposal, it now must be refined and either limited or expanded to include the one, two, or three aspects of the study that led to the essence of the findings.

For example, your original research purpose may have been to discover any possible adverse effect of reoperation for bleeding on hospital outcomes. However, to investigate this properly, you likely would have determined the prevalence of postoperative bleeding and incremental risk factors associated with bleeding, perhaps then using these to develop a propensity score so that apples-to-apples comparison could be made of outcomes in patients who did and did not require reoperation. Thus, for the manuscript, the stated purpose may be to (1) determine the prevalence of postoperative bleeding, (2) identify incremental risk factors for postoperative bleeding, and (3) compare the prevalence of hospital complications between those who experienced bleeding and those who did not. These purposes lay a complete roadmap for every subsequent section of the paper.

These purposes constitute the last part of the introduction, preceded by a paragraph simply setting the problem being addressed, its importance, the context of the study, or the controversy. (A mistake many writers make is to confuse the function of an introduction with that of a discussion or an exhaustive review of the literature.) For a specialty journal, there is no need for the introduction to start with a review of the literature. Rather, within the first two sentences, state the questions your research addresses (the gap in knowledge) and why it is important to answer it.

Given a clear message for the paper (the 50-word essence) and a clear statement of purpose or purposes that will support that essential message, it becomes rather easy to organize subsequent sections of the paper (Patients and Methods, Results, and Discussion) to exactly follow the organization suggested by the purposes (using identical words each time). In this way, the manuscript stays focused, supporting material is highlighted, and triage of extraneous information is facilitated.

### Patients and Methods

This section tells how the study was done. It is rarely read in its entirety, in part because readers assume that the peer-reviewed process has vetted the methods. There are some important elements for a clinical paper that have to be provided about the patients: what was done and where, inclusive dates (time frame), number of patients, inclusion and exclusion criteria, and patient characteristics. End points (outcomes) should be defined and details of follow-up (active and passive) summarized. Data analysis should be organized according to each purpose of the study. Finally, details of the presentation should be provided.

### Results

This section answers the simple question, “For each purpose, what was found?” This is the core—the lasting value—of the paper. Of necessity, it is rarely all the raw data. Rather, it is a selected well-digested summary that relates directly to purposes of the paper. It does not interpret the results of the study; it uses tables and figures to summarize and illustrate the results. It is an unfortunate fact that reviewers of manuscripts suggest elimination of tables and figures as a first priority to shorten a paper. Instead, it is text that should be shortened (including placing detailed methods in electronic appendices).
Discussion

The discussion tells the reader how the authors have interpreted the results. A suggested outline for a discussion is:

- Brief summary of results (controversial)
- Principal findings, organized by purpose that puts results into context of work by others
- Limitations
- Conclusions (inferences, clinical recommendations)

The discussion should be concise and focused. Interpretation should be reasonable (e.g., avoiding causal statements when only associations are established), and quotation of work by others should be accurate. Inferences should be supported by the data and speculations beyond that so identified. There should be no new results introduced. Promissory notes should be avoided.

Submission

Coupled with initial manuscript writing, decision should be made regarding the appropriate audience, and therefore journal, for the paper. As general rules, manuscripts of interest to a broad spectrum of medicine should be targeted to general medical journals; those that should be read by both cardiologists and cardiac surgeons should be targeted to general cardiology journals; those that should be read by cardiac surgeons should be targeted to cardiac surgical journals.

When the manuscript has been completed, one may be tempted to send it immediately to the targeted journal, but the quality of the manuscript can be improved considerably by allowing it to sit on the shelf for a time. After a few weeks, review the manuscript afresh from beginning to end, along with comments that may have been solicited from coauthors. By this time, three things have happened. First, you have distanced yourself just a bit from the manuscript and can see more clearly its possible deficiencies. Second, the passage of time has allowed your unconscious mind to work on the material, and by the time the manuscript is revisited, this process has provided further insights and clarity. Third, you have had the opportunity to present the material intramurally and have received valuable feedback. In other words, the work has matured. (In addition, the manuscript shelf provides the best possible resource for abstracts for upcoming scientific meetings.)

Responding to Reviewers

The next important step is to respond to peer review of the manuscript. Some authors become despondent and never revise and return their paper. Others decide to send the original manuscript to another journal, ignoring the peer review, which is wasteful of reviewers’ time and expertise. Others respond defensively, making little change in the manuscript. Instead, this important phase of generating new knowledge should be viewed as an essential exercise to improve the manuscript. Sometimes it will require performing new analyses or gathering new information. If some point is confusing to a reviewer, and particularly if it is confusing to more than one, or if the reviewers have completely missed the point, simplification and clarity are needed. Rethink the

purposes, structure the paper anew, move overly detailed material from the text to appendices, construct new tables and simplify others, prepare more intuitive graphics, or state things more clearly and logically. The peer review process may delay publication for some days to weeks, but as a whole, it functions superbly to improve the quality of papers.

SCIENTIFIC PRESENTATIONS

Meeting Abstract

The best possible preparation for writing and submitting a meeting abstract and for subsequently presenting the findings is to have completed a well-crafted manuscript. There is no substitute for this. If it is not possible to complete all analyses and to prepare a manuscript, at least enough of this must be done so the essence of the findings is known, the purpose of the study is clear, and the conclusions are supported.

It is common practice to use meeting abstract deadlines either to drive the research process or serve as a triage function for bouncing half-formulated and partially analyzed data off reviewers; if the paper is not accepted, the research is not pursued. This is not serious clinical research. It also represents a lack of understanding of the process whereby papers are accepted for presentations at meetings. For example, if there are two excellent abstracts submitted by two groups on the same subject, one may be taken and the other not; it would be a mistake for the submitter of the rejected abstract to conclude that the work is unworthy! A poor abstract may be the only abstract submitted on a subject that is deemed to be needed for a well-rounded meeting, so it is accepted. An entire category of abstracts may be jettisoned because there is no room for them on the program. Other abstracts, because of the appealing way they are crafted, are accepted, but the work is of less than stellar quality when presented.

A meeting abstract does not serve the same function as the abstract for a scientific paper. Its purpose is to get the work onto a program. Thus, crafting a meeting abstract is an art. The title must be eye-catching. Such a title may not be appropriate for a manuscript, but it is the first thing the graders will see. Second, the purposes and conclusions of the abstract must be clear and must match one to one. The purposes and conclusions may be all that is read before the abstract is discarded! If there is a gripping title, clear and interesting purposes, and new conclusions, the abstract graders will read the methods and results sections. There is no sense in including detailed methods that are well known; instead, focus on those that (1) succinctly define the patient sample, (2) address each purpose, and (3) make the study novel or more valid than other work in the field. Results are usually less detailed than for a manuscript abstract, highlighting just those numeric findings that relate to the purposes. A well-crafted table, or especially a seminal figure, often speaks louder than words and may constitute nearly the entire results section. Importantly, the presentation can be almost entirely crafted from this abstract.

Presentation

Preparation

For a short 5- to 10-minute presentation, you must know the intended audience. Is it a general audience for whom medical jargon and abbreviations will not be understood, or
is it a group of experts in your field who will be distracted by summary of well-known introductory material?

Text
Before writing the text (which we recommend), clearly articulate the message you wish to convey to your audience. For a short talk, this will be two or three main points. Your talk should focus on these points and nothing more. Ideally, it will be divided with clear signposts (orally or visually) for each point.

What is generally not taught to presenters is that the audience will listen serially. No one in the audience can go back to review the material; there is no second chance to determine whether your progression of thought is logical or to study a table or figure in detail. The classic IMRD format for a scientific paper is not conducive to serial aural disclosure!

Elements of a good presentation are more akin to telling a good story than writing a good scientific paper.⁹ At the outset, you must capture the attention of the audience. This can be accomplished, for example, by illustrating the nature of the problem that is the object of the presentation. This may be a clinical example, an echocardiogram, a picture of a pathologic specimen, or a statement of controversy. The purposes of the research can then be presented, followed by a simple depiction of the characteristics of the patients being studied. The temptation will now be to present methods, followed by results and discussion. This should be resisted. Instead, as you present evidence (“let the data speak for themselves”), weave in methodology for obtaining the data and results of analysis if essential. Generally, however, very little presentation of methodology is necessary for clinical studies, and the time restrictions preclude lengthy description. Results should be presented extraordinarily simply with “just in time” listening; that is, introduce nothing before it is needed. Typically, slides (generally computer-generated presentation frames) should contain only one idea each and as few words as possible.

Your presentation delivery should be semi-conversational, with a balance between formal and casual styles. Above all, plainly emphasize the message you want to deliver by connecting with the audience through attitude, energy, and motions. Ways to engage the audience include introducing ideas in threes (I came, I saw, I conquered; the good, the bad, the ugly), contrasting pairs, introducing anticipation, and using occasional pauses and repetition. Although it may seem awkward, you connect best with an audience if your eyes are “up” at the beginning and ending of sentences, and “down” on your text in the middle of sentences.

At the end of the presentation, it is common for speakers to simply summarize the results. But if the presentation has been logical and has focused primarily on results, there is little need for recapitulation. It is better to spend the last portion of the presentation on the clinical inference you have drawn from the study. Leave the audience with the essence of your findings (“the message”) and what it should mean to them and to their patients. End the talk with a simple “thank you” so that the audience knows you are finished.

Finally, never plan to give a presentation without writing the manuscript, preferably prior to submission of the abstract. Presentations are soon forgotten, or are remembered but not retrievable because the presenter has never pushed the study through to publication.

Visuals (“Slides”)
The purpose of visuals accompanying a presentation is to emphasize and illustrate your ideas. They are not for entertainment or to provide supplemental material. They are not the talk.

Although visuals are a matter of taste, a few comments may be helpful for those who have never been taught the art of creating presentation slides, but rather follow the formats and styles generally seen in medical meetings.

Keep the slides plain with no distracting or extraneous material. Avoid textured backgrounds that distract listeners from your talk. Eliminate “cute” transitions from slide to slide. Simple graphs and figures are more effective than complex ones. Package one thought per slide. Avoid complete sentences and paragraphs on slides; references in tiny print cannot be seen.

Use as few “word slides” as possible. Those that are used are most effective if they have single-line titles, three or fewer major heads, and only one subhead level. It is best to set a word slide format and stick to it rather than showing a haphazard mix of left-justified and centered text starting at different spots on the slide. A consistent format reduces the work of the listener so that he or she can listen to you.

Visual order when first seeing a slide is top down, left to right, and clockwise. Thus, text and visuals should follow this order.

We recommend avoiding tables. Generally, only specific pieces of information on a table are useful. There are usually ways to present them as bar graphs or pie charts that are more readily digested.

From a practical standpoint, use a sans serif font of no less than 32-point size so that slides are visible from the back of the auditorium.

Question and Answer Period
The question and answer period is part of your presentation, and you should be prepared for it. Your attitude should be that this is a final opportunity to get your message across. Anticipate what questions the audience should have for you. You don’t have to respond directly to the questions actually asked if they lead you away from your message; rather, rephrase the question to bring it back to your message.

Finally, in many meetings there may be no questions. A well-prepared moderator should have a question for you, but if not, you have been given an opportunity to drive home your message. So if there is silence, you might say, “You may be wondering…” or “A question I have been thinking about….” This in turn may stimulate someone in the audience to ask a question along these lines.

DECISION SUPPORT
Publication is a static medium. However, most analyses generate mathematical models that, at least in theory, can be solved for the characteristics of a specific patient (patient-specific predictions), complete with CLs. Fig. 6-26 illustrates how these equations can be used to predict survival for a specific patient, were they to be initially managed medically, surgically, or by percutaneous intervention. Used in this way, static presentation of “risk factors” becomes a basis for dynamic decision support for individual patients.
The most important impediment to using equations resulting from clinical research data analysis is lack of the CPR (see “Computer-Based Patient Record” in Section II). If such systems were in place to provide values for variables in the course of working up a patient, they could be automatically inserted into appropriate equations, the equations solved, and the solutions displayed. These results could then be used by physicians for making recommendations about the most appropriate course of treatment, and also by patients as a personalized basis for informed consent.

It will be argued that medical and surgical treatment are changing so rapidly that no data from the past are relevant for today’s decision support; at best, general guidelines and judgment are all that is available. However, this gives more credit to new therapy than medical and surgical innovations deserve. Furthermore, a decision must be made, and making it on the basis of past data is likely to be less faulty than using no data at all.

In most places in the world today, the resources available for cardiac operations are insufficient to treat every patient potentially amenable to this kind of intervention. Thus, a process of triage (the sorting process used by military surgeons during combat) is consciously or unconsciously used to allocate resources among the patients most likely to benefit.112 Again, such decisions are best made when potential benefits can be described factually and with knowledge of the degree of uncertainty attached to the conclusions. The special circumstances of each patient and the need for continued probing into the possibility and methods of extending and improving the results of cardiac surgery must also form part of each patient care decision.

To improve surgical outcome, errors (both active and latent) must be reduced and scientific progress made. Errors can be reduced by various mechanisms of decision support, particularly obvious pharmaceutical errors. Error reduction in the operating room may be reduced by the vigilance suggested in “Human Error” in Section I.

Some surgical failures are related to inadequacies in the decision-making process for an individual patient, either as a result of human error or lack of scientific progress. For example, deciding not to operate on a patient whose risks without operation are known to be significantly greater than those with operation is a human error. Deciding to operate on a patient whose risk of an early fatal outcome is probable with considerable certainty is also an error.

Analysis of clinical information, either by use of risk-adjusted information from applying benchmarks (see “Risk Stratification” in Section VI) or by formal analysis of surgical experience, yields risk factors that may be amenable to neutralization (see Appendix 6C).

Decision Making for Individual Patients

When cardiac operation is advised, it is in anticipation of cure or palliation. In either case, operation should be recommended only when life expectancy and functional capacity are predicted to be better with than without operation. Thus, each patient care decision involves a comparison, and the comparison should be made with full knowledge of the degree of uncertainty imposed by the available data and their analysis.836 In fact, one goal of research is providing this information for decision making in as many areas of cardiac surgery as possible and with as high a degree of certainty as possible.

When patients fall into defined categories for which reliable information is available, individual patient care decisions can be made largely on the basis of prior appropriate comparisons of the options. That is, the option can be chosen that has been shown to result in the lowest hospital mortality, the highest long-term survival, and the least incidence of reoperation in similar patients. One of the goals of this book is to present data in sufficient detail to be useful for most individual patient care decisions. However, decision making is not always easy. Indeed, some decisions that may appear easy in fact are not. This is when solution of equations using a patient’s specific characteristics becomes valuable.

When reliable information is unavailable or the options being considered are different from those that have been studied, the same principles can be used, but only anecdotal information, judgments, and general knowledge of the area are available as a basis for the decision. Obviously, the degree of uncertainty is considerably greater. In such situations, a proper clinical study of some type is needed to generate the knowledge desired.

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**Section VI  Special Methods and Controversies**

**RISK STRATIFICATION**

The goal of risk stratification is to account broadly for differences in patient characteristics that affect outcomes of interest. These include cost of healthcare services and outcomes that have been selected to reflect institutional quality822,823 (clinical report cards815,816). Risk stratification can be used for profiling practices or to develop guidelines and indications for procedures.

There are two general approaches to risk stratification: risk scores and risk equations.

Risk Scores

Primarily in the older literature, risk scores were reported that were based partly on data and partly on expert opinion.821,822 These have a common feature: addition of risks. Those that understand probability theory will immediately notice that the logistic equation, by virtue of the exponential function, is a multiplicative function of risk factors (see Fig. 6-1, A and Box 6-5).811 Even today, investigators attempt to develop “modern” additive risk scores, claiming that busy physicians can add but not multiply.811

Unless a score is specifically calibrated to outcome, it is useful merely for risk stratification, not for calculation of absolute risk.

Initial use of risk scores was to broadly classify patient mix according to outcome, usually into a small number of groups with increasing risk (see “Classification Methods” later in this section). Subsequently, however, they have been used as a basis for reimbursement, quality assessment, and institutional comparisons rather than generation of new knowledge. Therefore, they have been simultaneously welcomed and
distrusted. What is likely true is that they perform well for risk-stratifying typical patients, but poorly for patients at the extremes of low and high risk.

Risk Equations

Multivariable analysis is used to develop risk equations, usually by logistic regression. The equation is used to calculate absolute risk of events in a group of patients (e.g., those from an institutional experience), or the calculation may be left in terms of logit units as a type of quantitative score. Patients can then be sorted according to increasing probability score for risk stratification.

Use of multivariable analysis for risk stratification was anticipated by Gordon and Kannel in the Framingham study when they wrote, “In the multivariate case it is possible to make statements for one variable which are invariant whatever the values assumed by the other variables. This makes it possible to estimate the net effect of one variable taking into account the effect of other related variables.”

If equations are used, the distinction between risk stratification (grouping) and risk adjustment (placing patients on a level playing field) becomes blurred.

**RISK ADJUSTMENT**

Risk adjustment has been used in two senses. In both, a formal statistical multivariable model has been generated and then used in a predictive fashion. In the first, predictions are made in which a single variable is explored in relation to outcome while all other variables are held constant. This technique is an essential part of clinical research, and we have termed such depictions *nomograms*.

The second use is part of a process whereby two or more protocols, procedures, surgeons, physicians, or institutions with patient populations that are to some extent heterogeneous are compared with regard to outcome. A multivariable risk factor equation is used to generate hypothetical patient populations that are identical except for the variables being compared (leveling the playing field).

To generate the risk factor equation, a large group of patients representing all the subgroups being compared (e.g., institutions) are pooled, and a multivariable analysis of the pooled data is performed in which the subgroups themselves may or may not be variables. From a statistical point of view, it would seem ideal to assess subgroups as institutions within the context of the analysis. This could include exploration of specific interaction of subgroups with other variables, and other investigations that might yield important insight into institutional variance. This has been done, for example, in the context of the Congenital Heart Surgeons Society.

More commonly, subgroups are ignored completely when generating a generic overall equation that will be applied to them subsequently. This is the strategy behind the EuroSCORE.

In contrast, the Society of Thoracic Surgeons Database adjusts for within-institution variance. 

**Technique of Risk Adjustment**

After the risk factor equation is generated, it is typically used as follows. Characteristics of each patient in a subgroup (institution, country) are inserted into the regression equation, and the equation is solved to yield the absolute predicted risk of the outcome of interest for each patient. These individual probabilities are added to yield expected outcome. Expected outcome is then compared to actual outcome.

The theory behind this technique is this: When estimates of the weights (the βs, coefficients, or parameter estimates; see Box 6-5) are generated by maximum likelihood estimation, events are conserved. Conservation of events is, in statistics, analogous to conservation of mass in biochemistry. Specifically, if for the patients used to generate the equation, the probability of the event is calculated for each patient, the sum of these probabilities is guaranteed to equal the total number of events that actually occurred. If for some subgroup of patients this sum deviates from actual, either unaccounted-for factors have not been included in the risk factor equation, or the subgroup is behaving differently from the average.

**Comparison Statistic**

One statistic that may be used to compare observed (O) and expected (E) number of events in a subgroup of n patients is the chi-square goodness-of-fit test. A value for chi-square (χ²) is obtained from the formula:

$$\chi^2 = \frac{n(O - E)^2}{E(n - E)}$$  \hspace{1cm} (6-21)

A P value is obtained from a chi-square table or computer program equivalent.

DeLong and colleagues have studied eight methods for comparing observed and expected outcomes, focusing particularly on fairness in judging a subgroup to be an “outlier.”

Treasure and colleagues have developed a highly sophisticated method of using risk-adjusted CUSUM charts to continuously monitor deviation of individual institution programs from the norm.

**Illustrations of Risk Assessment**

Risk adjustment by multivariable analysis can be illustrated as follows. Hospital A experienced 18 (8.3%) hospital deaths among 205 patients undergoing mitral valve replacement, while hospital B experienced 16 (2.6%) hospital deaths among 612 patients undergoing the same operation. The *P value* for the difference is <.0001, so the difference is unlikely to be due to chance alone.

Hospital A believes the difference is attributable to a more severe case mix, while hospital B believes it reflects a difference in expertise. Using a risk-adjustment equation that accounts for NYHA functional class, age, left ventricular size, and other factors, a probability of death is computed for each patient by solving the logistic equation, using the patient’s specific values for each of the risk factors. The 205 probabilities for hospital A are summed and found to total 11.07, the number of expected deaths (if divided by 205, this yields 5.4%). The difference between expected deaths (11.07) and observed deaths (18) is unlikely to be due to chance alone, *P = .03*.

This is equivalent to saying that if the patients in hospital A had been operated on in hospital B, their mortality would have been 5.4%, not 8.3%. We could ask for the hospital mortality had B’s patients been operated on at hospital A. We already know that hospital A had a higher actual than expected...
mortality, and that actual divided by expected mortality equals 1.6. This ratio quantifies the difference in what could be called the expertise of the two institutions. This means that had hospital B’s patients been operated on at hospital A, there would have been more deaths, specifically, 1.6 times 16 or 26 deaths; 26 deaths among 612 patients is a mortality of 4.3%. This is what the state of New York has termed risk-adjusted mortality (the state as a whole is analogous to hospital B), an index it uses to rank hospitals.199

Controversies

Naturally, different risk adjustment equations yield different estimates of expected events.565,566 In addition, the variables used in developing the risk equation—administrative, laboratory, or clinical—make a difference.11 Even more important is the number of risk factors in the risk equation (richness, depth).59,74 Probabilities for patients with a large number or unusual combination of risk factors—the very patients for whom we want risk adjustment—are systematically underestimated.59

Residual Risk

A valuable adjunct to risk adjustment methodology is analysis of residual risk. In analysis of residual risk, the risk score for each patient is calculated. For logistic regression, this is the logit of the probability of the event; for Cox proportional hazards modeling, it is the sum of the weighted risk factors; for hazard function regression, it is the sum of the weighted factors in each hazard phase (see Box 6-5). These are forced into the model, and a search is made for risk factors not accounted for by the risk score or for factors in the risk score that are either underweighted or overweighted.59

For example, Sergeant and colleagues studied 3720 patients prospectively, applying a previously published time-related equation to generate a survival curve for each.52,59 The patients were subsequently followed up and comparison made of actual and expected survival (see Fig. 6-2, A). Estimated survival was too optimistic, so an analysis of residual risk was performed. Five residual risk factors were found, falling into three categories:

- Two factors had been suspected in the original analysis, but they occurred so infrequently that reliable parameter estimates could not be computed.
- Two variables were related to preoperative atrial and ventricular rhythm disturbances. These data had been available for the original analysis, but the investigator ignored them because he thought they were unimportant.
- The fifth variable identified a patient subset that had not been represented at all (extended indication) in the original data set.

These residual risk factors accounted for only a small fraction of the new patient group, but a group whose risk was vastly underestimated (see Fig. 6-2, B and Table 6-2).

This experience has driven us to the opinion that clinically rich models, rather than simple ones, are required for accurate risk adjustment. The factors liable to lead to risk underestimation are (1) rare factors, (2) factors that are important but not included in models, and (3) factors related to subgroups for whom indication for operation has been extended beyond that of patients included in developing the models.

META-ANALYSIS

Definition

Meta-analysis combines or integrates the results of multiple independently conducted clinical trials, observational clinical studies, or sets of individual patient data that are deemed combinable with respect to a common research question, then analyzes them statistically.115 Other terms for meta-analysis are quantitative overview, pooling studies, systematic review, and quantitative synthesis. The root of the prefix meta—means “later in time.”

Historical Note

There is a nearly 300-year history of using statistical methods to draw inferences broader than any individual study from a combined analysis of results. In 1722, Cotes used weighted averages to combine measurements of different astronomical observers.226 In 1805, Legendre introduced the now familiar method of least squares, used in linear regression (see Box 6-5), for similar synthesis. In 1904, Pearson averaged five different estimates of correlation because “many of the groups… are far too small to allow any definite opinion being formed.”177 In 1931, Trippett combined P values.15 In 1937 and 1938, Cochran and Yates combined results of agricultural experiments.51,72

Beecher is credited as having performed the first medical meta-analysis in 1955, but the appropriate methodology developed primarily in educational research.810 In 1976, Glass coined the term meta-analysis to mean “the analysis of analyses.”148 Most statistical procedures used today were introduced at that time in the social sciences.

In 1993, clinicians, epidemiologists, statisticians, and other professionals joined together to prepare, maintain, and discriminate comprehensive and systematic reviews of health-related questions. This was called the Cochrane Collaboration, named after epidemiologist Archie Cochrane.821,C6 In 1994, an international group developed the Quality of Reporting of Meta-analyses (QUOROM) guideline document for meta-analysis of randomized clinical trials.823 Subsequently these were updated to checklists and diagrams called Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA).824 A parallel effort was mounted to develop a guidance document for meta-analysis of observational studies, MOOSE.556

Motivation

Motivations for meta-analysis are to:

- Increase sample size and thereby better protect against either (1) misplaced enthusiasm for positive results (type I error) or (2) failure to find a beneficial effect (type II error)
- Detect small effects (or exclude small effects more definitively)
- Detect bias of reporting multiple, possibly underpowered, trials (positive results of trials tend to be reported more frequently than negative ones)
Make better use of studies performed independently by synthesizing the results
Suggest the most promising avenue for future research on a subject and the sample size likely needed to study the question definitively
Formalize the review process of past studies, including independent assessment of study quality by individuals not associated with the original studies
Determine whether “enough is enough” and no further corroborative studies are needed to establish a relation
Corroborate, refute, or modify evidence-based medical guidelines that emanate from expert opinion and literature review rather than from statistical analysis of data

Types
Meta-analyses may be categorized according to (1) type of studies assembled and (2) type of data gathered. The types of analyses assembled may be only randomized clinical trials, only observational clinical studies, or a combination. Just as any clinical study, there is a presumed hierarchy of quality; generally, preference is given to randomized clinical trials.

Type of data used in a meta-analysis may be (1) summary (aggregated) statistics or (2) raw individual patient data from each trial or study, the highest level of quality. The latter is considered to be the most time-consuming and politically most difficult to perform, because investigators are often wary (and rightly so) of relinquishing raw data to a third party.

Conduct
Because the design of a meta-analysis is that of an observational study of accumulated evidence from prior investigations, a rigorous plan for conducting the study must be put into place. Elements of conduct include:

- Formulating the question to be addressed, without which comparability of studies cannot be assessed
- Establishing criteria for studies to be included and excluded
- Identifying all relevant studies
- Assessing the quality of each study
- Establishing a rigorous protocol for data extraction, including calculations necessary for putting all data into a standard format on a uniform scale
- Extracting and verifying data
- Diagnosing bias and sensitivity to inclusion and exclusion criteria to be sure the analysis should proceed further
- Diagnosing heterogeneity among studies that may call into question poolability
- Analyzing the analyses, generally using mixed (hierarchical) models that account for fixed and random effects at various levels of aggregation (see “Longitudinal Outcomes” in Section IV)

In calculating an overall effect from multiple studies, the simple arithmetic average gives misleading results. Specifically, small studies have more scatter by chance alone and should be weighted less than large studies. Proper analyses can be broadly grouped into two approaches that differ only in the way variability among studies is managed: (1) fixed effects models that assume variability is simply random variation and (2) random effects models that assume a different mechanism of variation for each study. Tests of heterogeneity of variation may be used to assess which model may be more applicable. Ideally, features of each study, such as gender ratio, publication date, patient status, and age, are incorporated into the analysis. Such a model has both fixed and random effects. Details of these and other considerations are found in the now abundant literature on the topic.

We enumerate these points of study conduct to emphasize that meta-analysis is a disciplined, rigorous, and often statistically challenging type of observational study. In the cardiac surgical literature, including some publications cited in this book, less rigorous methods have been used to synthesize multiple independent, but related, analyses. Attention to meta-analytic techniques is necessary to raise the quality of such syntheses.

Limitations
Shortly after its introduction, Eysenck declared meta-analysis “mega-silliness.” Similar skepticism or outright disdain has been voiced in medicine. These attitudes are based on such findings as two separate meta-analyses of the same subject coming to diametrically opposite conclusions and the contradiction of meta-analysis results by large randomized trials.

Not often appreciated is that limitations of meta-analyses are similar to those of observational clinical studies. First, they require an extremely focused question, without which it is not possible to assess combinability of studies. It may be found that in fact there are no truly combinable studies for some topics of interest, or that there are too few studies to achieve sufficient statistical power to determine from diagnostic testing whether the studies are combinable (heterogeneity).

Second, it may be difficult to assemble the entire literature on a well-framed question. Medical libraries are generally more successful in doing this than physicians using search engines. References in identified articles must be found. In the process, it is common to uncover either wholly duplicate publications or some overlap that may be challenging to pull apart. Even a thorough search will not correct for confounding from publication bias that favors large studies, positive results, and mainstream topics.

Third, different meta-analyses may produce conflicting results, depending on thoroughness of the search and evaluation of applicability and combinability. These represent forms of selection bias over and above publication bias.

Fourth, there are limitations of data. One would like to adjust the analysis for multiple variables, but often the number of variables in common across studies is small. This is why combining individual data with many variables in common leads to the most robust estimates.

Finally, there are limitations in methodology, variance in professional skill and experience in using the methodology, and potential problems in both data presentation and interpretation.

CLASSIFICATION METHODS
Classification methods encompass a group of machine learning methods that will become of increasing importance in
analysis of clinical experiences. The techniques may be purely logic based, high-order logic and ontology-based (artificial intelligence), or algorithmically based. Classification methods can be used in a number of ways for the following:

- Classification (e.g., stages of disease, associations with outcomes)
- Identification, including nonlinear effects and complex interactions
- Prediction

Classifying Disease

Classification and regression tree (CART) and recursive partitioning analyses have been particularly useful in devising simple classification trees for cancer. Thus, they would seem ideal for risk stratification, not just disease classification. However, single trees grown in this way are unstable. Instability is a consequence of high prediction error that involves a trade-off between bias and variance. Growing a shallow tree (few branches) reduces variance and improves interpretation but introduces bias and inflates prediction error. Growing a richer tree (more branches) reduces bias but can inflate variance. To reduce prediction error, bias, and variance simultaneously, a whole forest of trees is needed. To do this, bootstrap samples are drawn from the original data (drawn randomly with replacement; about a third of observations are not chosen and a third duplicated). Simple trees are grown from each sample, followed by aggregating the results (so-called bagging). Prediction error is assessed by using the observations not selected for a given bootstrap sample (called “out-of-bootstrap” samples). Using a variety of random forest methods, we have constructed a new staging system, for example, for esophageal cancer.

Identifying Risk Factors

Risk factor identification is surely a classification problem: a variable is a risk factor or it is not. Enormous strides have been made in machine learning (see “Multivariable Analysis” in Section IV) for this and other classification problems. Prominent among current researchers in this area are Jerome Friedman and colleagues at Stanford University and the late Leo Brieman at the University of California, Berkeley. Their work addresses the instability of a single multivariable analysis of a single set of data, using resampling and other adaptive methods to arrive at a believable set of variables that can be claimed as risk factors. We have extended this work to survival data.

Two features of analyses are important to emphasize. First, there is no assumption of additivity, a hallmark of most regression models. This permits possible complex nonlinearities to be identified. Second, complex interactions are an intrinsic aspect of the analyses, a property that was of particular importance in developing a cancer staging system. However, because a forest of trees can become a “black forest,” identifying the variables of greatest importance for scientific insight and prediction can be challenging.

Two types of approaches we have explored are (1) a calculation of variable importance, quantified as increase in prediction error when “noise” is substituted for a variable; and (2) tree depth, variables that tend to be initially split near the root of the tree (see Fig. 6-16).

In identifying risk factors using these machine learning methods, we have been exploring criteria other than $P$ values for variable selection. $P$ values are highly dependent on $n$. An alternative is to approach variable selection as a signal-to-noise problem. One can ascertain for each variable its “noise” threshold by “noising-up” the variable (random permutation to generate noise) and examining whether the effect of the variable is outside the noise (signal) or within it. This approach is less dependent on $n$ than are $P$ values.

An important finding of our work with variable importance is that incorporating some variables in random forest analyses actually increases prediction error. It has formerly been thought that the more variables included, the better the prediction. This makes us believe that there may be a quantitative theorem of parsimony hidden in these analyses.

Finally, any machine learning algorithm can be tuned and variably supervised by humans. At present, optimum speed of learning (fast learning, slow learning) is uncertain. Because classification methods are computationally simple and therefore fast, we are exploring the possibility of combining forest-based variable selection with regression modeling, and even with aspects of artificial intelligence–based machine learning.

Predicting Outcome

One motivation for using classification methods to predict outcome is to answer the question, “Who will experience the event (and when)?” Conventional methodology is focused on probabilities, not “who” and “when.” Nevertheless, any method that more accurately identifies patients at risk is valuable. The methods include neural networks, which have largely been replaced by a host of machine learning techniques, multivariable optimal discriminant analysis, and more recent additions to the arsenal, such as logistic analysis of data (LAD), which is a purely mathematical technique. However, to date it is not clear that these methods outperform the standard regression approaches outlined in this chapter.

An interesting hypothesis is that deterministic, logic-based, artificial-intelligence machine learning technology can be coupled with more “black box” technologies, such as random forests, to discover why a particular prediction is being made for a given patient. This may be particularly valuable in genomic analyses of cancers, for example, to identify genes that machine learning technologies have identified that affect rate of cancer recurrence.

Limitations

A limitation of many machine learning techniques is that they either require data in dichotomous format, or split continuous variables into optimal classes rather than treating them as a continuum. This at times produces results that defy continuity in nature and represent local properties of a specific data set and not generalizable information. One advantage of techniques such as random forests is that in aggregating trees over a large forest (e.g., 10,000 trees), the results become essentially continuous.

The most important limitation of the methods at this writing is that they are still young and developing rapidly. Software is beginning to be available, but the user community is still narrow.
Chapter 6 Generating Knowledge from Information, Data, and Analyses

6A Knowledge-Generating Team

Serious clinical research in cardiac surgery can be accomplished, no doubt, by the cardiac surgeon alone. Individual cases can be reported (case reports) with keen insight. Data can be entered and tallied with both simple calculators and user-friendly statistical software such as SPSS (http://www.spss.com).

More commonly, though, a surgeon or full-time clinical investigator will be either the leader of, or the medical expert for, a small to medium-sized research team. With the growing sophistication of data management and analytic tools, it becomes necessary to assemble a research group with varied roles and expertise, all focused on the goals of clinical investigation.

Structure

Regardless of whether the same individuals are involved, clinical research generally includes two fundamentally different activities: (1) continuous registry and database activity (see Box 6-1) and (2) individual clinical studies activity. The registry activity involves gathering and entering data for a prescribed set of core data elements for every case. Until the advent of effective computer-based patient record (CPR) systems in the form of values for variables (rather than narrative) that contain the life history of a patient, at least some portions of a registry or database will have to be abstracted manually from medical records (see “Computer-Based Patient Record” in Section II). Individual clinical studies activity can be categorized roughly into two classes that require different skill sets: (1) clinical trials (either intramurally funded or extramurally sponsored by government or industry) and (2) studies of clinical experience (cohort studies).

Roles

Surgeon-Investigator

The surgeon (clinical) investigator, with collaboration of key individuals in data management, statistics, and study coordination, must develop the clinical question (aims, objectives), define the study group of interest, identify variables and endpoints (outcomes) of interest, review the literature, and develop all elements of a study protocol (see “Technique for Successful Clinical Research” in Section I). He or she must adjudicate data quality, often gather values for variables in addition to the core data elements, help interpret the analyses performed, putting them into clinical context, present the findings to colleagues, and write manuscripts.

Data Manager

There is no more key support person than the data manager. He or she is at the interface between data gathering and data analysis. Assembly of data for meaningful analysis is often complex, requiring information to be retrieved from a variety of electronic sources. Data managers usually need formal training in computer science and specifically in database construction and management. They must master an effective data query language.

Their most valuable skill, however, perhaps inborn rather than developed, is attention to the smallest detail of the data. Surgeons are usually not of the temperament for this kind of work, and statisticians by training are “big-picture” oriented; if surgeons see the forest, data managers must see the trees. Thus, data management is not simply skill in formulating databases, writing and executing query logic, and documenting these in detail (although these are important); rather, it is skill in examining the actual data, finding errors in them, finding inconsistencies and deviation from the norm that should be verified, verifying what appear as outliers, and assessing quality of data for every variable.

The surgeon and data manager then together organize the variables in a way that is meaningful for analysis. If time-related or longitudinal outcomes are being assessed, we recommend that the data manager become expert in forming intervals and assessing time-related data (time zero, events, intervals), two of the most demanding and essential tasks for such analyses.

For larger clinical quality and research organizations, a member of the data management team is the statistical programmer, who must convert data from database format into analysis data sets that make sense to the statistician (see “Data Conversion for Analysis” under Technique for Successful Clinical Research in Section I).

Data Gatherers

Persons skilled in data gathering for data entry fall into a hierarchy of individuals. For gathering some variables, expert medical domain knowledge as possessed by the surgeon or a knowledgeable research nurse is essential. Other data elements can be extracted by individuals with little formal training other than medical terminology. Essential ingredients are accuracy and integrity. Accuracy may be inborn and is indispensable; it can be assessed prospectively by testing and maintained by quality management and education.

Education/Quality

If large quantities of data are maintained, one or more individuals must assess the quality of the data and from these findings educate the data gatherers. Such individuals must have expert medical domain knowledge; for example, the surgeon or a research and education nurse. In large organizations, this role includes maintaining clinical documentation of the database, keeping current with new surgical trends, and pruning variables that no longer are of value or are of questionable quality.

Statistician

Most serious clinical research efforts require equally serious collaboration with one or more statisticians. The applied
Nonoverlapping Confidence Limits

To find the point at which the effect of a variable is evident using nonoverlapping CLs, consider a simple linear relationship between effect $x$ and outcome $z$:

$$z = \beta_0 + \beta_1 x_1$$  \hspace{1cm} (6B-1)

where coefficients $\beta_0$, the intercept, and $\beta_1$, the slope, are determined from a regression analysis (see Box 6-5). The first requisite is to select a reference value of $x_1$ call it $x_1$. The object is to find a different $x_2$, call it $x_2$, at and beyond which the effect is evident—that is, different from that at $x_1$.

The CLs for $z$ at $x_1$, calculated from the variance of $z$, $\text{Var}[z(x_1)]$, and a confidence coefficient transformed to an appropriate $t$ (e.g., $t = 1$ for 68.3% CL), are calculated as follows:

$$\text{Var}[z(x_1)] = V_0 + V_1 x_1^2 + 2\text{Cov}_{0,1}x_1$$  \hspace{1cm} (6B-2)

and

$$\text{CL}[z(x_1)] = z(x_1) \pm t \sqrt{\text{Var}[z(x_1)]}$$  \hspace{1cm} (6B-3)

where $V_0$ and $V_1$ are the variances of $\beta_0$ and $\beta_1$ (variance being the square of the standard deviation, SD) and $\text{Cov}_{0,1}$ is the covariance term between $\beta_0$ and $\beta_1$ ($\text{Cov}_{0,1}$ is related to the correlation $r$ between $\beta_0$ and $\beta_1$ by the expression $SD_{\beta_0}SD_{\beta_1}r$). The CLs of the unknown $x_2$ are given by Appendix Equations 6B-2 and 6B-3, with $x_2$ substituted for $x_1$.

Because CLs of $z(x_2)$ must exactly equal either the upper or lower CLs of $z(x_1)$, we can write, using Equations 6B-2 and 6B-3:

$$\text{CL}[z(x_1)] = \text{CL}[z(x_2)] = z(x_2) \pm t \sqrt{\text{Var}[z(x_2)]}$$  \hspace{1cm} (6B-4)

or

$$\text{CL}[z(x_1)] = \beta_0 + \beta_1 x_2 \pm t \sqrt{V_0 + V_1 x_2^2 + 2\text{Cov}_{0,1}x_2}$$  \hspace{1cm} (6B-5)

The only unknown in Equation 6B-5 is $x_2$, which, in this case, can be found using the general solution for roots of a quadratic equation. For uncomplicated situations that reduce to Equation 6B-5, the four roots (two each for the ± expression) can be calculated using a handheld calculator program. Two of the roots will simply yield $x_1$. Which of the other two roots is the desired $x_2$ is easily selected by inspection. For more complex multivariable cases, the equation must be solved for explicit values of all variables except $x_2$; thus, even a complex set of coefficients often can be reduced to the form of Equation 6B-5. However, if higher-order terms in $x$ (higher powers) are involved, it is probably easier to solve the

6B

Equations for Calculating Evident Differences

**Nonoverlapping Confidence Limits**

To find the point at which the effect of a variable is evident using nonoverlapping CLs, consider a simple linear relationship between effect $x$ and outcome $z$:

$$z = \beta_0 + \beta_1 x_1$$  \hspace{1cm} (6B-1)

where coefficients $\beta_0$, the intercept, and $\beta_1$, the slope, are determined from a regression analysis (see Box 6-5). The first requisite is to select a reference value of $x_1$ call it $x_1$. The object is to find a different $x_2$, call it $x_2$, at and beyond which the effect is evident—that is, different from that at $x_1$.

The CLs for $z$ at $x_1$, calculated from the variance of $z$, $\text{Var}[z(x_1)]$, and a confidence coefficient transformed to an appropriate $t$ (e.g., $t = 1$ for 68.3% CL), are calculated as follows:

$$\text{Var}[z(x_1)] = V_0 + V_1 x_1^2 + 2\text{Cov}_{0,1}x_1$$  \hspace{1cm} (6B-2)

and

$$\text{CL}[z(x_1)] = z(x_1) \pm t \sqrt{\text{Var}[z(x_1)]}$$  \hspace{1cm} (6B-3)

where $V_0$ and $V_1$ are the variances of $\beta_0$ and $\beta_1$ (variance being the square of the standard deviation, SD) and $\text{Cov}_{0,1}$ is the covariance term between $\beta_0$ and $\beta_1$ ($\text{Cov}_{0,1}$ is related to the correlation $r$ between $\beta_0$ and $\beta_1$ by the expression $SD_{\beta_0}SD_{\beta_1}r$). The CLs of the unknown $x_2$ are given by Appendix Equations 6B-2 and 6B-3, with $x_2$ substituted for $x_1$.

Because CLs of $z(x_2)$ must exactly equal either the upper or lower CLs of $z(x_1)$, we can write, using Equations 6B-2 and 6B-3:

$$\text{CL}[z(x_1)] = \text{CL}[z(x_2)] = z(x_2) \pm t \sqrt{\text{Var}[z(x_2)]}$$  \hspace{1cm} (6B-4)

or

$$\text{CL}[z(x_1)] = \beta_0 + \beta_1 x_2 \pm t \sqrt{V_0 + V_1 x_2^2 + 2\text{Cov}_{0,1}x_2}$$  \hspace{1cm} (6B-5)

The only unknown in Equation 6B-5 is $x_2$, which, in this case, can be found using the general solution for roots of a quadratic equation. For uncomplicated situations that reduce to Equation 6B-5, the four roots (two each for the ± expression) can be calculated using a handheld calculator program. Two of the roots will simply yield $x_1$. Which of the other two roots is the desired $x_2$ is easily selected by inspection. For more complex multivariable cases, the equation must be solved for explicit values of all variables except $x_2$; thus, even a complex set of coefficients often can be reduced to the form of Equation 6B-5. However, if higher-order terms in $x$ (higher powers) are involved, it is probably easier to solve the
equation using an iterative method for solving nonlinear equations.

\[ P \text{ Values} \]

If, instead of (or in addition to) determining an evident difference using nonoverlapping CLs, one wishes to detect an evident difference at some level of significance (\( P \text{ value} \)), then Equations 6B-1 and 6B-2 are used to define \( z(x_1), z(x_2), \) \( \text{Var}[z(x_1)],\) and \( \text{Var}[z(x_2)] \). Then the general equation for a test of significance is used:

\[
t = \frac{z(x_1) - z(x_2)}{\sqrt{\text{Var}[z(x_1)] + \text{Var}[z(x_2)]}} \quad (6B-6)
\]

where \( t \) is the number of standard deviations represented by the selected significance level (\( P \text{ value} \)). Expanding Equation 6B-6:

\[
t = \frac{z(x_1) - (\beta_0 + \beta_1 x_1)}{\sqrt{\text{Var}[z(x_1)] + \text{Var}[z(x_2)]}}
\]

\[
\text{Equation 6B-7}\]

yields an equation with only one unknown, \( x_2 \). In the simplest cases, Equation 6B-7 can be solved using a solution for roots of a quadratic equation. Higher-order terms of \( x \) require use of iterative methods.

Note that if Equation 6B-2 represents a logistic equation, solving for evident differences is performed in the logit domain, not the probability domain. Similarly, if time-related evident differences are desired, calculations are performed in the domain in which estimation of the parameters is performed.

**REFERENCES**


Multivariable analysis (see Box 6-18) can be used to discover if an incremental risk factor has been neutralized with experience (see “Incremental Risk Factor Concept” in Section IV). Date of operation (expressed on a “continuous” scale from, for example, the beginning of a program or beginning of a calendar year) is multiplied by the risk factor to form a new variable, called an interaction term, and the risk factor, date of operation (both called main effects), and interaction term are forced into the multivariable model. If a risk factor has been completely neutralized, the magnitude of the interaction term should have a sign opposite that of the main effect and be of equal magnitude.

Besides complete neutralization of a risk factor, risk factors may be partially neutralized. This may be documented by observing over time, for example, a decreasing strength of a risk factor. Risk factors may also be neutralized effectively by an overall change in risk, recognized by a decrease in the intercept without change in magnitude of risk factors.

**Interaction**

A note on interaction terms and their interpretation in general is in order. Interaction can be found between factors \( x_1 \) and \( x_2 \) in the following ways, particularly if one (say \( x_2 \)) is dichotomous:

- \( x_1, x_2, x_1 \cdot x_2 \)
- \( x_1, x_1 \cdot x_2, x_1 \cdot (1 - x_2) \)
- \( x_1, 1 - x_2, x_1 \cdot (1 - x_2) \)

Note that the interaction term is the one that multiplies one \( x \) by another. Depending on the signs and magnitude of these factors, they provide equivalent model fit but different insights. Specifically, they may identify possible neutralization of an effect. In another setting, they examine the relation when a factor is present, and the same relation when it is not. Finally, the increment of risk from interaction can be quantified. Thus, simply multiplying two factors should not be done blindly but in several ways to explore each aspect of interaction.

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7
Stenotic Arteriosclerotic Coronary Artery Disease

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Results
Stenotic atherosclerotic coronary artery disease (CAD) is narrowing of the coronary arteries caused by thickening and loss of elasticity of their walls (atherosclerosis) that, when sufficiently severe, limits blood flow to the myocardium. Initially, the disease limits only coronary flow reserve (increase in flow that normally accompanies increased myocardial oxygen demands), but when sufficiently advanced, CAD reduces blood flow through the affected artery even at rest. In its most severe form, atherosclerotic CAD occludes the coronary artery.

HISTORICAL NOTE

Development of coronary cineangiography by Sones and Shirey at the Cleveland Clinic during the early 1960s made possible direct identification of stenotic and occlusive atherosclerotic lesions in the coronary arteries during life and laid the foundation for coronary artery surgery. Sporadic surgical attempts to improve coronary blood flow had previously been made, but these efforts were ineffective because of lack of precise anatomic diagnosis. In 1951 in Montreal, Vineberg attempted to improve coronary blood flow had previously been made, but these efforts were ineffective because of lack of precise anatomic diagnosis. In 1951 in Montreal, Vineberg and Miller reported direct implantation of an internal thoracic artery (ITA), also known as the internal mammary artery (IMA), into the myocardium. More than a decade later, the Cleveland Clinic group demonstrated that this procedure brought new blood to the left ventricular (LV) myocardium, but the new blood flow was too limited in quantity and distribution to be effective. In 1954, Murray and colleagues were considering a direct surgical approach to CAD and reported experimental studies of anastomosing the ITA to a coronary artery. Shortly thereafter, Longmire and colleagues at the University of California in Los Angeles reported a series of patients in whom direct-vision coronary endarterectomy was performed without cardiopulmonary bypass (CPB). Subsequently, CPB was used to facilitate the operation, and Senning reported patch grafting of a stenotic coronary artery in 1961. At about this time, Effler and colleagues at the Cleveland Clinic began their pioneering efforts to achieve myocardial revascularization by a direct surgical attack on stenotic coronary lesions, as demonstrated by Sones using coronary angiography.

DEFINITION

Largely overlooked is the first operation for CAD by Kolesov in Leningrad in 1964, in which the ITA was anastomosed to the left anterior descending coronary artery (LAD), probably without knowledge of this contribution, in May 1967, Favaloro and Effler at the Cleveland Clinic began performing reversed saphenous vein bypass grafting, and by January 1971, this group had performed 741 such operations. Even earlier, Garrett, at that time working with DeBakey in Houston, successfully performed a reversed saphenous vein coronary artery bypass graft to the LAD in...
an unplanned way, at restudy 7 years later, the vein graft was patent.

Progress was rapid after this early era. In 1968 in New York, Green and colleagues re-reported anastomosing the distal end of the left ITA to the LAD using a dissecting microscope, and Edwards and colleagues began using this procedure at UAB in 1969. In Milwaukee in 1971, Flemma, Johnson, and Lepley described the technique and advantages of sequential grafting, in which one vein was used for several distal anastomoses. Advantages of this technique were further amplified by the reports of Bartley, Bigelow, and Page in 1972 and Sewell in 1974. Bilateral ITA grafting was performed at least by 1972 and probably as early as 1968. Thus, within a very short time, the foundations were laid for rapid worldwide adoption of coronary artery bypass grafting (CABG).

MORPHOLOGY

Development of Coronary Artery Stenosis

Atherosclerosis, the most common form of arteriosclerosis, is a process that occurs in coronary arteries, as in other blood vessels, consists of focal intimal accumulations of lipids, complex carbohydrates, blood and blood products, fibrous tissue, and calcium deposits, as well as associated changes in the media. Lipoid foci are associated with or converted into plaques of fibrous or hyaline connective tissue, although at least some atherosclerotic plaques may result from organization of thrombi.

Fibrolipoid plaques may become thick enough to encroach on the lumen of the artery, producing a stenotic lesion. Probably episodically and at times over a period of years, new material is deposited on the luminal side of the plaque, resulting in further narrowing and sometimes complete coronary occlusion. Small blood vessels form around and within the plaque. Gradual regression of plaque enlargement, seen clinically as regression of stenoses in a few patients, and development of collateral coronary blood flow can result in at least partial spontaneous restoration of antegrade regional myocardial blood flow.

Hemorrhage may occur suddenly within a plaque (see “Atherosclerotic Plaque Rupture and Thrombosis” later in chapter); occasionally this may suddenly increase the degree of coronary stenosis and precipitate acute myocardial infarction (MI) or unstable angina pectoris. Thrombosis occasionally complicates the coronary atherosclerotic process, generally when there is luminal narrowing. Sudden complete obstruction may result, and it is generally agreed that acute thrombotic occlusion is the genesis of acute MI in most patients. Rapid recanalization frequently follows this process. Platelet aggregation within the lumen of an already narrowed coronary artery may induce thrombosis or suddenly narrow the lumen and provoke an acute MI or unstable angina, and it may play a role in development of the atherosclerotic plaque itself. Platelet aggregation releases thromboxane A2, an extremely potent vasoconstrictor. Thus, interrelationships among atherosclerotic narrowing, platelet aggregation, and coronary spasm are important.

The atherosclerotic process usually affects multiple coronary arteries. In 1975, Gensini reported that 40% of patients with CAD sufficient to lead to cineangiographic study had important stenoses in all three major coronary arteries, and in 30% two vessels were involved. Ninety-five percent of patients with complete occlusion of one artery had important stenoses in at least one of the other two arteries.

Atherosclerotic CAD usually involves the proximal portion of the larger coronary arteries, particularly at or just beyond sites of branching. Thus, stenoses in the main trunks of the LAD, circumflex (Cx) coronary artery, and right coronary artery (RCA) often involve the first of the secondary branches (first diagonal branch of LAD, obtuse marginal branch of Cx artery, and posterior descending branch of RCA). When CAD is more extensive in the main trunks, origins and first portions of secondary branches may be involved. Diffuse distal disease severe enough to render the patient unsuitable for CABG is uncommon. In 10% to 20% of patients with atherosclerotic CAD, the left main coronary artery is importantly stenotic.

Occasionally, a major coronary artery may lie beneath a muscle bridge. This is most common in the middle third of the LAD, but sometimes one or all of the obtuse marginal branches of the Cx artery are buried in muscle throughout their course. These portions of artery are typically free of severe atherosclerotic changes.

Myocardial Infarction and Morphologic Sequelae

When myocardial blood flow is sufficiently impaired in relation to myocardial oxygen demands, myocardial necrosis occurs. The resultant infarction may be subendocardial—that is, not involving the entire thickness of the ventricular wall, but only the inner third. In its most extreme form, subendocardial infarction may be diffuse and result from multiple-system disease. More often, however, subendocardial infarcts are regional and result primarily from a stenotic lesion in one or two systems. These infarcts are generally less extensive than so-called transmural infarcts, but still have serious implications. A transmural MI involves the entire thickness of the ventricular wall. Transmural infarction usually results from a sudden increase in luminal narrowing or complete obstruction of the artery supplying that area, or a sudden generalized increase in myocardial oxygen demand in the presence of a severely stenotic coronary artery. Although categorization of acute infarctions as subendocardial or transmural is convenient, most transmural MIs are not homogeneous but contain islands of viable muscle of varying number and size.

The process of infarction is complex. Animal studies indicate that some myocardial cells die after 20 minutes of complete coronary artery occlusion, and that extensive myocardial cell death occurs after 60 minutes. Although these time frames may vary, some reperfusion generally occurs within the ischemic area of myocardium within minutes of onset of acute ischemia, particularly in the zone between ischemic and nonischemic myocardium (border zone). If this spontaneous reperfusion occurs within 3 to 4 hours, the amount of necrosis is limited, at times substantially, and mortality is decreased. The process is complex because, in addition to these beneficial effects, spontaneous reperfusion can result in hemorrhage, edema, and ventricular electrical instability.

Healing of the acute MI leaves a scarred area of myocardium. In most cases, this area is a mixture of fibrous tissue and viable myocardial cells in varying proportions. Such scarring is evident from (1) intraoperative inspection of areas of
previous infarction at the time of CABG and (2) change from akinia or dyskinesia to hypokinesia or normal wall motion in some LV wall segments when patients go from a symptomatic to an asymptomatic state after percutaneous coronary intervention (PCI) or CABG. When the scar is almost all fibrous tissue, it is usually large, and the LV wall may become akinetic or aneurysmal (see Chapter 8).

These morphologic changes may be self-aggravating because of their effect on circulation to the subendocardial layer. Repeated infarctions may occur and add still more scarring. In the aggregate, myocardial scarring leads to LV systolic and diastolic dysfunction and, ultimately, if the patient survives long enough, to the syndrome of chronic heart failure with elevated right atrial and jugular venous pressure, hepatomegaly, and fluid retention. More often, however, patients with severe ischemic LV dysfunction die of another infarction or ventricular fibrillation.

Atherosclerotic Plaque Rupture and Thrombosis

Several studies have emphasized the dynamic nature of coronary atherosclerotic plaque as a fundamental feature of CAD.\textsuperscript{106,128} Rupturing, or rupture, of atherosclerotic plaques is probably the genesis of the acute coronary syndromes termed unstable angina and acute MI. When this occurs, mural or occlusive coronary thrombosis often coexist and contribute further to development of the unstable states.\textsuperscript{220}

Coronary stenoses that produce less than 50% reduction in lumen diameter are often the site of the atherosclerotic plaque rupture that precipitates unstable angina or acute MI.\textsuperscript{11,17,128} More severe stenoses also undergo plaque rupture, and total vessel occlusion may occur. However, an acute ischemic episode does not always develop, possibly because severely stenotic lesions are long-standing and have stimulated development of a protective collateral circulation.

Certain atherosclerotic plaques appear to have a higher risk of rupture than others. These plaques are characterized by relative softness, a high concentration of cholesterol and cholesterol esters, and a lipid pool that tends to be situated eccentrically.\textsuperscript{128} Rupture is through the cap of the plaque, and areas in which the cap lacks underlying collagen support seem particularly vulnerable.\textsuperscript{11,111}

**Clinical Features and Diagnostic Criteria**

**Routine Methods**

CAD is usually first suspected with development of the symptom complex of angina pectoris or an acute MI, occasionally because of electrocardiographic (ECG) evidence of a silent acute MI, a positive ECG response to a graded exercise test, or sudden death with resuscitation. Occasionally, CAD is first suspected because of cardiomegaly and symptoms of chronic heart failure without any other obvious cause.

The precise nature, location, duration, and severity of any chest pain are determined by carefully questioning the patient. Precipitating causes and maneuvers that relieve the pain are noted, as are any recent changes in pain pattern. Findings on physical examination are usually nonspecific.

Many noninvasive tests, beginning with a chest radiograph and ECG at rest and during exercise and then proceeding to more complex studies, are currently used to identify and quantify CAD and its sequelae. However, such tests cannot yet define extent or distribution of anatomic coronary disease with great accuracy. From a surgical standpoint, therefore, properly performed coronary angiography remains the definitive diagnostic procedure (see “Coronary Angiography” in text that follows). Contrast-enhanced computed tomographic coronary angiography (CTCA) is emerging as a promising technique for detecting coronary artery disease (see “Computed Tomographic Angiography” later in this section) and may, with increased spatial and temporal resolution, be suitable as an accurate and noninvasive method to select candidates for CABG.\textsuperscript{115,11,10,111,546,153} Methods of evaluating LV function are also necessary. These may be based in part on historical data, physical findings, and chest radiography. Noninvasive and invasive special study methods may be used. Even when complex study methods are employed, results must be interpreted with knowledge of the simple but reliable clinical data. An ejection fraction (EF) of 35% has a different implication when accompanied by minimal LV enlargement seen on a chest radiograph than when enlargement is marked. An EF of 30% is much more ominous when accompanied by important elevation of jugular and right atrial pressure with hepatomegaly and fluid retention than when these pressures are normal. Exercise capacity may be variable in patients with similar EFs, and the variations are prognostically important. It should be emphasized, however, that heart size can be deceptive because it can remain normal in the presence of severe LV dysfunction.

Important associated conditions such as hyperlipidemia, arterial hypertension, and diabetes, and a history of MI, smoking, or a particularly stressful occupation or lifestyle should be noted. Because arteriosclerosis is the cause of CAD, its presence elsewhere in the circulatory system should be sought. A history suggesting transient cerebral ischemic attacks or stroke, particularly when carotid bruits are present, must be carefully pursued. A history of intermittent claudication and presence of diminished femoral, popliteal, or pedal pulses are indicative of peripheral arterial occlusive disease. The thoracic and abdominal aorta are examined for possible aneurysm or occlusive disease. Renal and pulmonary function should also be evaluated.

**Coronary Angiography**

Coronary angiograms provide important information. Their quality must be sufficient to permit detailed assessment from several angles of both coronary ostia and all major and minor branches of the left and right coronary arterial systems. However, angiography remains an imperfect method. Severity of a visualized stenotic lesion may be underestimated, and diameter of vessels distal to a stenosis is often underestimated.

Assessment of coronary arteries at operation by external palpation or probing of the open vessel cannot substitute for coronary angiography. When the arteries cannot be adequately filled by contrast media, however, or the available study is incomplete and cannot be repeated (this should be uncommon), intraoperative observations can be used to supplement angiographic findings. The surgeon should assess all coronary arterial branches carefully at the time of operation, rather than assume the coronary angiogram is a totally accurate diagnostic tool.
Recording and Reporting Data

Whatever the techniques used for coronary angiography, methods of recording and analyzing the data are crucial. A 75% cross-sectional area loss (50% diameter) is considered an important but moderate stenosis, and a 90% cross-sectional area loss (67% diameter) is considered severe (Fig. 7-1). Some groups consider only those lesions with 70% or more diameter loss (90% or more cross-sectional area loss) as important; an appropriately documented basis for this has not been established.

Extent of important coronary artery stenoses has conventionally been summarized as “single-vessel,” “double-vessel,” or “triple-vessel” disease, usually with left main coronary artery disease as a separate category. This chapter uses the terms single-system, two-system, and three-system disease, because each coronary system (LAD, Cx, and RCA) consists of several vessels. Use of the term system is therefore more accurate than vessel.

These classifications have been criticized because they give no indication of the amount of LV myocardium rendered ischemic by the lesions. For example, a stenosis in the LAD system has a different significance when it lies at the origin of a large first diagonal artery than when it involves the middle third of the LAD beyond its major septal and diagonal branches, or only the first portion of a large first diagonal branch. A single stenosis in the proximal portion of the Cx artery varies in significance depending on whether this artery is dominant. Single-system disease involving the proximal RCA has a different implication from that involving only the posterior descending branch of the RCA. Many other examples can be given of the inadequacies of these classifications.

A few classification systems have been described to circumvent these limitations. These include Gensini’s old and rather complex scheme that takes into account severity of the stenoses, the various segments of the coronary artery tree involved, and the area of myocardium usually perfused by them; a simple scheme from Massachusetts General Hospital; and the method of the Coronary Artery Surgery Study (CASS) of the U.S. National Heart, Lung, and Blood Institute (NHLBI), dividing the coronary arteries into a total of 27 specified segments. Some myocardial jeopardy scores have attempted to provide similar information but are limited by the assumption that akinetic areas cannot be revascularized.

Whatever the recording and reporting methods, they are not a substitute for the surgeon critically reviewing cineangiograms before deciding for or against operation, and again immediately before operation.

Computed Tomographic Angiography

Although conventional coronary angiography remains the gold standard to determine extent and severity of CAD and indications for CABG, CTCA using 64-slice multidetector CT scanners (MDCT) has been evaluated as an alternative method to select patients for CABG (Fig. 7-2).

Initial studies suggest that this technique is a suitable alternative to conventional coronary angiography in selected patients. However, concerns regarding exposure to excessive radiation and the small but defined increased risk of cancer in later life associated with exposure to radiation may limit its widespread application.

Coronary Intravascular Ultrasound

Intravascular ultrasound (IVUS) uses a high-frequency miniaturized ultrasound transducer positioned on the tip of a coronary artery catheter to provide detailed cross-sectional images of the coronary vessel wall (Fig. 7-3, A). Unlike coronary angiography, which details only luminal encroachment, IVUS provides images of the atherosclerotic plaque, characterizes its composition, and assesses severity of stenosis (Fig. 7-3, B). When compared with formalin-fixed and fresh histologic specimens of coronary arteries, it correlates significantly ($P < .0001$) with coronary artery cross-sectional area ($r = 0.94$), residual lumen cross-sectional area ($r = 0.85$), and percent cross-sectional area ($r = 0.84$). It is useful in determining the need for CABG in situations when the severity of coronary artery stenosis cannot be precisely determined by angiography, particularly for left main and LAD disease (Fig. 7-3, C).

Coronary Artery Pressure and Fractional Flow Reserve

Fractional flow reserve (FFR) is a simple, reliable, and reproducible physiologic index of lesion severity in patients with intermediate stenosis, and is another method to determine the need for CABG and PCI in equivocal situations, particularly stenosis of the left main coronary artery. The concept of FFR is illustrated in Fig. 7-4. Pressure measured distal to the stenotic coronary lesion during maximum hyperemia (Pd) divided by mean aortic pressure (Pa) correlates with maximum myocardial blood flow in the presence of a stenosis $Q^f$ divided by the normal maximum myocardial blood flow $Q^m$. FFR 0.75 to 0.80 or less is generally an indication for intervention.

Left Ventricular Function Testing

Resting and Exercise Tests

Because resting LV function is presumed to depend on the amount of myocardium that is free of scar, severity of LV dysfunction may be a surrogate for amount of myocardial scar. This may not be entirely accurate in patients with ischemic heart disease, because ischemia may result in myocardial stunning or hibernation and reversible depression of at least systolic LV function (see “Myocardial Cell stunning” in Chapter 3). CABG and PCI do not favorably affect myocardial scarring.

<table>
<thead>
<tr>
<th>Average diameter loss</th>
<th>Cross-sectional area loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/3 = 67%</td>
<td>90%</td>
</tr>
<tr>
<td>1/2 = 50%</td>
<td>75%</td>
</tr>
<tr>
<td>1/3 = 33%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Figure 7-1 Diagrammatic representation of relationship between two methods of estimating severity of coronary artery stenosis. (From Brandt and colleagues.)

Resting and Exercise Tests

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Figure 7-2  A-C. Multidetector computed tomographic volume rendering images show significant stenoses of major coronary arteries (arrows), suggestive of three-system disease. These coronary lesions (arrows) were confirmed on conventional coronary arteriography (D-E), and patient underwent coronary artery bypass grafting. Key: LAD, Left anterior descending coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery. (From Lee and colleagues.26)
Global and Segmental Function

Exercise LV function in patients with ischemic heart disease is characteristically depressed; this reflects loss of coronary flow reserve imposed by the distribution and severity of CAD. Amount of decrease in EF or other measures of the heart’s response to stress is a surrogate for the distribution and severity of coronary arterial stenoses.

Systolic and Diastolic Function

LV function can be expressed as systolic or diastolic function. Systolic function is determined by contractility of the ventricle (see “Cardiac Output and Its Determinants” in Section I of Chapter 5). Diastolic function describes compliance, or extensibility, of the ventricle, which is related to preload.

Global LV function is usually described by an index of overall ventricular systolic function, most often EF. EF is not independent of preload or afterload and therefore is not an ideal index, but it is the one most frequently used and is reasonably satisfactory. EF is obtained commonly and least accurately by visual estimation from a cineangiographically recorded left ventriculogram, more accurately (and originally) by quantitative angiography, and also by noninvasive methods such as radioisotopic imaging and echocardiography.

The CASS score was developed by CASS investigators as a measure of global LV function and actually is a summation of five segmental wall scores based on wall motion observed in the right anterior oblique (RAO) projection of the
Atherosclerotic Plaque Rupture and Thrombosis

B21,H15,J5,R9

is a risk factor because plaque rupture is frequently the inciting incident leading to progression in severity of coronary artery stenosis. Eccentric positioning of the lipid pool within the plaque appears to predispose to rupture and thus progression in severity of stenosis. 

Stenotic Coronary Artery Disease

The natural history of patients with a given severity and distribution of CAD depends in part on the rate of progression of both. As an added complexity, regression of some lesions also occurs. In general, however, both severity and distribution of CAD tend to increase with time, although the rate of increase is highly variable and difficult to predict. In general, over a 2-year period in patients with already important stenoses, 20% of the stenoses increase in severity, and about half of patients develop important new lesions. The mechanism of increase in severity is variable, but atherosclerotic plaque rupture and thrombosis play important roles in some cases (see “Atherosclerotic Plaque Rupture and Thrombosis” earlier in this chapter).

Of the usually accepted risk factors for presence of stenotic CAD, not all have been helpful in predicting its rate of progression. Aggressiveness of the atherosclerotic process seems to be a risk factor for progression; surrogates for it include young age at presentation with symptomatic CAD, peripheral arterial disease, diabetes, and hyperlipidemia. Nature of the atherosclerotic plaque is a risk factor because plaque rupture is frequently the inciting incident leading to progression in severity of coronary artery stenosis. Eccentric positioning of the lipid pool within the plaque appears to predispose to rupture and thus progression in severity of stenosis. Rheologic factors play a role; the more severe the stenosis, the more rapid the progression toward total occlusion.

Table 7-1 General Interrelations Among Modifiers Describing Left Ventricular Dysfunction, Ejection Fraction, and Coronary Artery Surgery Study Score

<table>
<thead>
<tr>
<th>LV Dysfunction</th>
<th>EF</th>
<th>CASS Score (Normal = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>.60</td>
<td>≤ 5</td>
</tr>
<tr>
<td>Mild</td>
<td>.50</td>
<td>≤ 9</td>
</tr>
<tr>
<td>Moderate</td>
<td>.35</td>
<td>≤ 15</td>
</tr>
<tr>
<td>Severe</td>
<td>.35</td>
<td>≤ 15</td>
</tr>
</tbody>
</table>

Key: CASS, Coronary Artery Surgery Study; EF, ejection fraction; LV, left ventricular.

cineangiogram. Table 7-1 shows the relationship between EF and CASS scores. Other scoring systems have also been developed.

Segmental wall function refers to function, usually systolic, of segments of the LV wall. Methods usually depend on observation of wall motion or wall thickening throughout the cardiac cycle. Analysis of segmental wall motion is particularly informative in patients who have previously sustained MIs.

Load-Independent Function

High LV afterload tends to depress LV systolic function and therefore cardiac output, and high LV preload generally increases cardiac output (see “Cardiac Output and Its Determinants” in Section I of Chapter 5). Methods previously discussed generally do not reflect load-independent LV function and are therefore suboptimal.

NATURAL HISTORY

Gaps exist in knowledge of the natural history of atherosclerotic CAD. Many of these gaps will be permanent because withholding treatment is no longer justifiable. The closest approach to natural history comes from data gathered in patients seen and treated medically before about 1970. Unfortunately, many studies from that era have the disadvantage that patients were not categorized according to anatomic extent of their disease and LV function.

A further complexity is that in nearly all studies since 1970, patients initially undergoing no treatment or medical treatment have properly been allowed thereafter to cross over to interventional treatment (PCI or CABG). This has made it even more difficult to generate accurate information about the natural history of CAD.

Stenotic Coronary Artery Disease

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Of the usually accepted risk factors for presence of stenotic CAD, not all have been helpful in predicting its rate of progression. Aggressiveness of the atherosclerotic process seems to be a risk factor for progression; surrogates for it include young age at presentation with symptomatic CAD, peripheral arterial disease, diabetes, and hyperlipidemia. Nature of the atherosclerotic plaque is a risk factor because plaque rupture is frequently the inciting incident leading to progression in severity of coronary artery stenosis. Eccentric positioning of the lipid pool within the plaque appears to predispose to rupture and thus progression in severity of stenosis. Rheologic factors play a role; the more severe the stenosis, the more rapid the progression toward total occlusion.

Left Ventricular Dysfunction

Stress-Induced Dysfunction

First indications of LV dysfunction in patients with ischemic heart disease are localized abnormalities of regional wall motion (LV systolic function) during exercise or other forms of stress. These abnormalities are the result of transient myocardial ischemia, which can be demonstrated as myocardial perfusion defects during exercise. Global LV systolic function improves during exercise in normal persons, except in old age. By contrast, when initially localized areas of myocardial ischemia become sufficiently extensive, global LV systolic function declines during exercise. Exercise-induced ECG changes also reflect these reversible myocardial perfusion abnormalities, which may be so severe as to cause hypotension during exercise testing. Related to this exercise-induced decrease in function in some patients, LV end-diastolic volume responds abnormally to exercise by increasing, often to more than 50% above resting value. These reversible abnormalities of regional myocardial perfusion and wall motion occasionally occur at rest, most often in patients with unstable angina.
Abnormalities of LV diastolic function during stress can be demonstrated in most patients with extensive CAD. These abnormalities take the form of reduced peak LV filling rate and increased time to peak filling rate. These phenomena are the clinical reflection of the laboratory demonstration that ischemia impairs rate of diastolic relaxation of papillary muscle, related to the fact that myocardial relaxation during early diastole is an active, energy-dependent process. Abnormalities of diastolic function in patients with coronary artery stenoses may also reflect lack of an increase in early diastolic coronary blood flow.

In the aggregate, these purely ischemic abnormalities of LV systolic and diastolic function may be severe enough during stress to result in a considerable increase in LV end-diastolic pressure. This may produce dyspnea and even transient paroxysmal nocturnal dyspnea and pulmonary edema, as well as angina, during severe ischemic episodes. Further evidence that these abnormalities of LV systolic and diastolic function can result from myocardial ischemia alone is provided by their reversal after successful PCI or CABG.

**Dysfunction at Rest**
LV dysfunction with the patient at rest and under no stress has been considered the result of myocardial scar. Therefore, it can be expected that it will not improve after neutralization of the coronary arterial stenoses by CABG or PCI. However, there is evidence that myocardial stunning or hibernation, or both, may be responsible at times for considerable LV dysfunction, and that this element of resting LV dysfunction can be relieved by revascularization.

Myocardial scars from previous MIs also result in abnormalities of LV diastolic function. Both clinical and experimental studies indicate that increase in LV end-diastolic volume, which results from both diastolic and systolic abnormalities of function, is directly related to the amount of scar in the ventricle.

Patients whose LV function is depressed from myocardial scarring exhibit morphologic, physiologic, and functional variability. Some have moderately increased LV end-diastolic pressure at rest and a considerably reduced exercise capacity but only a mildly increased cardiac size on chest radiography. These patients have moderate scarring and marked ischemic dysfunction in scarred or non-scarred parts of the ventricles that can often be improved by revascularization. Some have chronic symptoms of pulmonary venous hypertension and may still be helped by revascularization. A few have moderate or severe cardiomegaly, reduced cardiac output, importantly elevated right atrial and jugular venous pressure, hepatomegaly, and fluid retention. Patients in the latter group have advanced LV dysfunction from extensive myocardial scarring, and it generally cannot be improved by operation unless the scar is discrete, is full thickness (aneurysmal or akinetic), and can be resected (see Chapter 8).

**Unfavorable Outcome Events**

**Stable Angina**
Development of chest discomfort or pain on exertion is common in patients with coronary artery stenosis, but chest discomfort is not an inevitable accompaniment of even important CAD. Severity of angina is typically categorized by the Canadian class system, which differs from the New York Heart Association (NYHA) classification for heart failure. 

- **Class I:** angina occurring only with strenuous or prolonged exertion at work or recreation and not with ordinary physical activity (thus, Class 0 means no angina under any circumstance).
- **Class II:** angina occurring with walking rapidly on level ground or a grade and with rapidly walking up stairs. Ordinary walking for fewer than two blocks on level ground or climbing one flight of stairs does not cause angina except during the first few hours after awakening, after meals, under emotional stress, in the wind, or in cold weather. This implies slight limitation of ordinary activity.
- **Class III:** angina occurring when walking fewer than two blocks on level ground at a normal pace, under normal conditions, or when climbing one flight of stairs. This implies marked limitation of ordinary physical activity.
- **Class IV:** angina occurring with even mild activity. It may occur at rest but must be brief (<15 minutes) in duration. (If the angina is of longer duration, it is called *unstable angina*.) This implies inability to carry out even mild physical activity.

Angina generally results from reduction in coronary flow reserve in a portion of the myocardium; the more severe the reduction, the greater the severity of angina. However, severity of angina also depends on amount of stress or exercise, which increases myocardial oxygen demand in proportion to the intensity of the activity. Standardization of demand gives graded exercise testing its advantage in quantifying to some extent the amount of “reversible ischemia” (more properly, the amount of reduction of coronary flow reserve). Absence of angina does not eliminate the possibility that the patient has “reversible ischemia.” Although angina tends to become more severe as time passes, a number of patients do not experience this trend.

**Unstable Angina**
Unstable angina undoubtedly signifies a prognostically important change in the coronary circulation, but the syndrome takes so many different forms that its precise definition has been difficult. Not surprisingly, different practitioners and even different randomized trials have used different definitions. In 1989, Braunwald devised a classification system to ensure uniformity of categorization and provide diagnostic and prognostic information.

Although “unstable angina” implies several syndromes, no differences in outcome have been identified among its subgroups. The term applies to patients with severe and persisting angina on presentation to the physician or hospital, with ECG evidence of ischemia and only minor enzymatic evidence (available only later) of MI. The syndrome is considered more ominous if it occurs in the absence of stimuli that increase total body oxygen consumption or catecholamine release (e.g., unusual emotional stress, fever, infection, hypotension or uncontrolled hypertension, tachyarrhythmia, hypoxemia). Unstable angina also applies to patients who have onset of severe angina (Canadian class IV) within 2 months of presentation or who have recurring or prolonged (>15 minutes) severe angina within 10 days of presentation, whether or not it is of new onset. The term is also appropriate for patients who develop (or continue to have) severe angina in the first 2 weeks after an acute MI. All subsets usually demonstrate ECG evidence of myocardial ischemia during...
severe pain, and no enzymatic evidence of more than minimal myocardial necrosis.

The cause of unstable angina is now considered to be an acute change in coronary circulation with or without changes in related neurohumoral responses. Unstable arteriosclerotic plaque, which may fissure and rupture, is the genesis of unstable angina in many patients (see “Arteriosclerotic Plaque Rupture and Thrombosis” earlier in this chapter).\textsuperscript{225} However, superimposed thrombosis and platelet aggregation complicate local situations,\textsuperscript{225,226} and the clinical state largely depends on activity of the patient’s thrombolytic state and mechanisms for reversing platelet aggregation. The process is reversible but tends to recur either as another episode of unstable angina or as an acute MI.

**Acute Myocardial Infarction**

Prevalence of acute MIs in patients with coronary artery stenoses is not known precisely, but it is surely affected by prevalence of risk factors. For example, patients with severe proximal LAD lesions have a particular tendency to develop acute and often fatal MI.\textsuperscript{215} Among patients who are sufficiently symptomatic and undergo coronary angiography, at least 10% have an acute MI within 1 year, 30% within 5 years, 40% within 10 years, and 50% within 15 years, as determined from patients assigned to initial medical treatment in the Veterans Administration (VA) randomized trial of stable angina.\textsuperscript{229}

Acute MI is usually caused by acute subtotal or total occlusion of the vessel supplying the infarcted region, and the vessel usually does not have well-formed collateral arteries. This fact has been suspected for many years and gave rise to the early phrase “coronary thrombosis.” However, thrombosis was first convincingly demonstrated by DeWood and colleagues in Spokane, Washington, in a series of patients undergoing emergency CABG for acute infarction.\textsuperscript{214} Often the acutely occluded vessel has not previously had a severe stenosis, which is consistent with the concept that the myocardium supplied by the diseased vessel is usually devoid of important collateral vessels. Current information suggests that rupture of an unstable arteriosclerotic plaque is the genesis of the acute reduction in luminal diameter, often accompanied by thrombosis and platelet aggregation (see “Arteriosclerotic Plaque Rupture and Thrombosis” earlier in this chapter).\textsuperscript{225,213}

The greater the number of MIs, the greater the likelihood the patient will have another one, which may indicate that some people generate more unstable plaques than others. Also, the more coronary artery systems (LAD, Cx, RCA) that contain important stenoses, the greater the probability of an acute MI.\textsuperscript{229} This may simply be due to the increased number of coronary arteriosclerotic plaques available to rupture.

Early (3-month) mortality after acute MI is difficult to define for the current era. Hospital mortality is usually described, but the early phase of the hazard function continues for about 3 months. In the past, hospital mortality in a heterogeneous group of patients admitted with acute MI was 10% to 50%, depending on prevalence of risk factors. Death was usually in acute or subacute cardiac failure, or suddenly with ventricular fibrillation.\textsuperscript{242} Size of the infarct was an important risk factor; hospital mortality was 5% for patients with small infarcts vs. 50% for those with large infarcts (involving 40% or more of LV mass).\textsuperscript{226,21} Reserve in the adjacent “nonischemic” myocardium appeared also to relate to probability of surviving an acute MI, indicating the importance of metabolically supporting this area and revascularizing it even if the stenoses are not severe.\textsuperscript{224} Overall probability of death was higher after the second infarction and still higher after the third, related to scarring imposed by previous infarctions. Development of pulmonary edema soon after acute MI increased risk of death, but 1-year mortality was as low as 10% when other risk factors were favorable.\textsuperscript{221}

Currently, therapy is directed toward use of inhibitors of platelet aggregation, thrombolytic agents, heparin, and PCI as soon as possible after onset of infarction. Although the optimal protocol may be arguable, effectiveness of this therapy is not. Hospital mortality has been reduced to about 7% to 10% by these measures. When cardiogenic shock develops, emergency PCI or CABG with maximal measures for myocardial management can salvage many patients (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).\textsuperscript{A13,A15,G17,H19,H20,L5}

**Death**

Approximately 70% to 80% of a heterogeneous group of patients with CAD of sufficient severity to cause them to seek medical advice ultimately die a cardiae death. The remaining 20% to 30% die of unrelated causes. Overall survival for a heterogeneous group of patients with clinically evident CAD is 75% at 5 years after initiation of medical treatment, 60% at 10 years, and 45% at 15 years.\textsuperscript{229} However, time-related probability of death in a group of CAD patients is so related to prevalence of risk factors that overall estimates are of little value.

Most often, death occurs with acute or subacute cardiac failure, often within a few months of an acute MI and sometimes precipitated by a ventricular arrhythmia.\textsuperscript{229} Infrequently, death is attributable to chronic heart failure, either late after one or more infarctions or without any identifiable earlier episode of infarction. This mode of death is generally characterized by a slow downhill course, eventually leading to hepatomegaly, ascites, and ultimately death. Death in this mode is usually the direct result of myocardial scarring.

About 20% of patients with important CAD who have had no interventional therapy die suddenly.\textsuperscript{229} Acute MI is not the only cause of sudden death. Presumably, sudden cardiac death in patients with ischemic heart disease can result from acute, severe myocardial ischemia, resulting in ventricular fibrillation, asystole, or acute severe depression of ventricular function.\textsuperscript{B18}

**Incremental Risk Factors for Unfavorable Outcome Events**

Understanding the benefit of interventional therapy, whether CABG or PCI, demands a knowledge of the incremental risk factors for unfavorable outcome events in patients treated medically for CAD.

Multivariable analysis is used to generate incremental risk factors for various unfavorable events after CABG, PCI, or medical treatment. However, those identified are often surrogates for more basic risk factors, and at times several surrogates for the same basic risk factors appear. Box 7-1 presents the basic risk factors as currently perceived. In the future, these factors themselves may become more clearly identifiable.
Chapter 7  Stenotic Arteriosclerotic Coronary Artery Disease

Box 7-1  Incremental Risk Factors for Death and Other Unfavorable Outcome Events in Patients with Stenotic Atherosclerotic Coronary Artery Disease

<table>
<thead>
<tr>
<th>Severity of Reduction in Regional Coronary Flow Reserve</th>
<th>Rate of Progression of Coronary Arterial Stenoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina severity (Canadian class I to IV)</td>
<td>Amount and Distribution of Myocardial Scar</td>
</tr>
<tr>
<td>Degree of positive response to stress testing</td>
<td>Number of previous acute myocardial infarctions</td>
</tr>
<tr>
<td>Severity and number of stenoses</td>
<td>Left ventricular ejection fraction</td>
</tr>
<tr>
<td>Number of Myocardial Regions with Reduced Coronary Flow Reserve</td>
<td>Left ventricular Coronary Artery Surgery Study (CASS) score</td>
</tr>
<tr>
<td>Left main stenosis and severity</td>
<td>Left ventricular end-diastolic pressure</td>
</tr>
<tr>
<td>Distribution and severity of coronary stenoses</td>
<td>Defects identified by exercise or resting thallium-201 scintigraphy (delayed or after reinjection)</td>
</tr>
<tr>
<td>Myocardial score</td>
<td></td>
</tr>
<tr>
<td>Nature of Coronary Arteriosclerotic Plaque</td>
<td>Secondary Conditions</td>
</tr>
<tr>
<td>Number of previous myocardial infarctions</td>
<td>Hemodynamic instability</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>Cardiogenic shock</td>
</tr>
<tr>
<td>Distribution of coronary stenoses</td>
<td>Ischemic instability (unstable angina)</td>
</tr>
<tr>
<td>Internal Milieu (Thrombotic or Fibrinolytic)</td>
<td>Ventricular electrical instability</td>
</tr>
<tr>
<td>Number of previous myocardial infarctions</td>
<td></td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td></td>
</tr>
<tr>
<td>Distribution of coronary stenoses</td>
<td></td>
</tr>
<tr>
<td>Aggressiveness of Atherosclerotic Process</td>
<td>Coexisting Conditions (Comorbidity)</td>
</tr>
<tr>
<td>Diffusely narrowed coronary arteries</td>
<td>Older and younger age</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>Larger and smaller body size</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>Ethnicity</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Hyperlipidemia</td>
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<tr>
<td>Hypertension</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Chronic pulmonary disease</td>
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<tr>
<td>Younger age at intervention</td>
<td>Chronic renal disease</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
</tr>
<tr>
<td></td>
<td>Previous stroke</td>
</tr>
</tbody>
</table>

Factors/events listed are not the result of a formal multivariable analysis, but rather a composite of many such analyses. These categories constitute reversible ischemia.

Reduced Regional Coronary Flow Reserve
Reduced regional flow reserve results from severity of the coronary arterial stenoses and number of coronary arterial systems with important stenoses. The left main coronary artery is an additional “system.”

Time-related survival for a heterogeneous group of patients with single-system stenosis is high, approximately 90% to 95% at 5 years (Fig. 7-5, A). At 15 years, survival is about 50%. Additional risk factors relating to reduction in regional coronary flow reserve include (1) specific vessel(s) diseased, (2) location of stenosis within the vessel, and (3) severity of stenosis. Because time-related mortality from single-system disease is relatively low, the differences attributable to further refinements in this category will be small and therefore difficult to identify. Also, inferences from the analyses are only as good as reliability of the cineangiogram.

In any event, single-system disease with stenosis in the RCA appears to confer better survival than can be expected with LAD disease, at least for 5 years (RCA 96%, LAD 92%). When single-system stenosis is in the LAD, a very proximal location (proximal to the large septal branch) imposes less favorable survival than more distal lesions (proximal 90% at 5 years, distal 98%). Although not conclusively demonstrated, more severe stenoses (>90%), especially those proximal in the artery, probably impose higher time-related mortality than less severe stenoses.

Patients with two-system disease as a heterogeneous group have lower survival than those with single-system stenoses, with 5-year survival of about 88% (Fig. 7-5, B). At 15 years, survival is about 56%. When the LAD is one of the two systems, the same effects of location and severity as mentioned for single-system disease pertain. Differences in outcome between single- and two-system disease are not as great as those between two- and three-system disease.

As a heterogeneous group, patients with three-system disease have a 5-year survival without interventional treatment of about 70% (Fig. 7-5, C) and a 10- and 15-year survival of about 60% and 40%, respectively. Factors affecting survival in patients with important single-system disease involving the LAD also affect survival in patients with three-system disease. Also, the greater the number of systems with important proximal stenoses, the lower the time-related survival: at 5 years, survival with no, one, two, and three systems with proximal stenoses is 71%, 64%, 51%, and 45%, respectively. Important left main coronary artery disease imposes an even lower survival: 40% to 60% at 5 years (Fig. 7-5, D). Survival falls to about 10% to 26% by 15 years (Fig. 7-6).

Severity of angina is a surrogate for the basic risk factor of severity of reduction in coronary blood flow reserve (Fig. 7-7). Also, graded exercise testing (GXT) is a surrogate for the basic risk factor of severity of reduced coronary blood flow reserve and is related to outcome events in CAD patients. For example, in the heterogeneous group of patients randomly assigned to initial medical treatment in the European Coronary Surgery Study Group randomized trial, 1-, 5-, and
Figure 7-5  Survival of medically treated men with coronary artery disease, stable angina of at least 6 months’ duration, and less than severe left ventricular dysfunction enrolled in the U.S. Veterans Administration (VA) Cooperative Study (solid squares). 83 For comparison, survival is shown of a population matched for age and gender from the 1976 U.S. life tables (solid line). Data for other groups of medically treated patients published earlier by Burggraf, 86 Oberman, 87 and Webster and their colleagues are also shown. Lower survival in the last three groups may have been the result of less restrictive selection of patients than for the VA group and better medical treatment in the more recent VA group. Data from the Coronary Artery Surgery Study (CASS), in which important stenosis meant a 70% diameter reduction, are also presented. 88 These data include patients treated medically in the current era with all types of ventricular function. Left main coronary artery data from CASS refer to left main coronary artery plus triple-system disease.

Figure 7-6  Nomograms of specific solutions of multivariable risk factor equations illustrating effect of number of coronary artery systems with important stenoses on time-related freedom from cardiac death in patients randomly assigned to initial medical treatment in Veterans Administration randomized trial of chronic stable angina. For this depiction, patients were censored if they crossed over to coronary artery bypass grafting. Values for each risk factor in the specific solutions of the multivariable equation represented by these nomograms are provided in the American College of Cardiology/American Heart Association Joint Task Force Subcommittee on Coronary Artery Bypass Graft Surgery. 41 A, Patients with normal left ventricular (LV) function. B, Patients with importantly impaired LV function. Key: ACC, American College of Cardiology; AHA, American Heart Association; CABG, coronary artery bypass grafting; LM, left main coronary artery disease; SD, systems diseased.
10-year survival was 94%, 83%, and 71% in patients with a mildly positive GXT but 92%, 77%, and 62% in those with a strongly positive GXT. Similarly, in a study from the CASS Registry, survival at 12 years after medical treatment was substantially lower among patients with a strongly positive GXT (55% for men, 62% for women) than among those with a mildly positive test (75% for men, 82% for women).

Progression of Coronary Arteriosclerosis
Rate of progression of coronary arteriosclerosis, which could also be termed aggressiveness of the arteriosclerotic process, cannot as yet be examined directly in multivariable risk factor analyses. Its surrogates have appeared in a number of such analyses. The surrogates may be a substitute not solely for one basic risk factor but at times for several factors. Among them are young age at presentation, diabetes, hypertension, and hyperlipidemia.

An important advance has been the demonstration that progression of arteriosclerotic CAD can be slowed, and that regression of some lesions in some circumstances can be initiated by intensive lipid-lowering therapy.

Coronary Arteriosclerotic Plaques
Number of previous episodes of acute MI may be a surrogate for coronary arteriosclerotic plaques as well as for total area (or number) of arteriosclerotic plaques within the coronary arterial tree. Presence of unstable angina and number of recent episodes may likewise be surrogates. In this regard, however, status of the patient’s fibrinolytic and disaggregating systems also plays a role. During very active periods, these systems may neutralize the effects of plaque rupture and minimize severity and frequency of unstable angina and acute MI.

Myocardial Scar
To the extent that resting LV dysfunction in patients with CAD is related directly to amount of scar in the myocardium, surrogates for presence and extent of this basic risk factor include number of prior episodes of acute MI, resting LV systolic and diastolic dysfunction (presence and severity) determined by any of several methods, and a history of chronic heart failure.

Reversible ischemia is capable of producing resting LV dysfunction. Myocardial stunning may persist after reversible ischemia has disappeared and result in LV dysfunction. Unfortunately, methods for distinguishing between scar and reversible ischemia, although useful, are neither entirely accurate nor precise. The frequent finding of only a 0.05 to 0.10 increase in preoperatively depressed EF in many patients after CABG suggests that the proportion of LV dysfunction not attributable to myocardial scarring is small.

In CAD patients treated noninterventionally, mild resting LV dysfunction (EF 35%-50%) minimally affects survival, but severe dysfunction (EF < 35%) substantially reduces it. Thus, other factors being equal, 1- and 5-year survival in patients with mild LV dysfunction is about 95% and 80%, respectively, whereas with severe dysfunction it is about 70% and 40%. Good LV function is found more frequently in patients with single-system disease than those with three-system disease (Table 7-2).

Secondary Conditions
Certain conditions develop secondary to ischemic heart disease and are additional incremental risk factors for death and other unfavorable events.

Hemodynamic Instability Grade 1 hemodynamic instability is mild and responds to catecholamine infusion. Grade 2 is more severe and responds only when intraaortic balloon pumping is added. Grade 3 is unresponsive even to addition of intraaortic balloon pumping and requires cardiopulmonary support (cardiopulmonary bypass, extracorporeal membrane oxygenation) or a ventricular assist device (see Section 1 in Chapter 5). Because hemodynamic instability in patients with ischemic heart disease typically reflects acute myocardial ischemia or necrosis and produces secondary deleterious effects throughout the body, it adversely affects outcome.

Ischemic Instability Ischemic instability is a state of unstable angina and implies acute myocardial ischemia. It carries the risk that severe myocardial stunning and necrosis or ischemic ventricular electrical instability can develop acutely.

Ventricular Electrical Instability Either ischemic or secondary to phenomena associated with myocardial scarring,
ventricular electrical instability is a risk factor incremental to that of the basic milieu that gives rise to it.

Coexisting Conditions

Older Age Older age at presentation is a risk factor for death in patients with ischemic heart disease, and probably acts as a coexisting condition rather than directly affecting CAD.

Diabetes Diabetes is a strong risk factor for death in CAD patients because of its effect as a coexisting condition and its accelerating effect on the arteriosclerotic process. Fig. 7-8 illustrates the powerful effect of diabetes in elderly patients who have undergone PCI.

Hypertension The strong effect of hypertension as a risk factor for death in CAD patients is related to kidney damage, intracranial complications, LV hypertrophy, and acceleration of the arteriosclerotic process (Fig. 7-9).

Gender Although overall mortality is lower in women with angina than men, for patients older than 65, relative risks are similar (2.7 vs. 2.4, respectively).

Other Comorbidity Any serious coexisting disease adversely affects survival in patients with CAD. Of particular importance, because of their prevalence in this group of patients, are chronic obstructive pulmonary disease and chronic renal disease. Smoking can be considered an important coexisting condition.

TECHNIQUE OF OPERATION

Most patients undergoing CABG have extensive three-system disease, often with important stenoses in four, five, or six arteries. Many have substantial impairment of LV function. This discussion focuses on operation under these circumstances and tactics for accomplishing optimal revascularization and optimal intraoperative management of the myocardium.

Surgical management of arteriosclerotic CAD has evolved from treatment primarily of patients with stable coronary syndromes undergoing elective operation, to treatment of more heterogeneous groups of patients with various clinical syndromes who are older and have more comorbid conditions, including patients who require urgent or emergency operation. Economic and other external pressures often result in CABG being performed within hours after diagnostic coronary angiography or PCI.
At present, CABG with use of total CPB through a full sternotomy remains the most widely used surgical technique. Because of extensive experience, this approach is the technique to which all others must be compared. Other techniques currently in use include CABG through a full sternotomy but without use of CPB, and operations through smaller sternal, parasternal, or thoracotomy incisions with or without use of CPB (see Fig. 2-23).

Here, the conventional operation with CPB, as well as the off-pump procedure, are presented. Other procedures are discussed under Special Situations and Controversies later in this chapter.

Preoperative Preparation

Many patients come to CABG taking β-adrenergic receptor or calcium channel blocking agents, angiotensin-converting enzyme (ACE) inhibitors, digitalis preparations, antiarrhythmic agents, and platelet antiaggregating drugs. Some are receiving intravenous heparin and nitroglycerin. It is advisable in most circumstances to continue β-adrenergic receptor and calcium channel blockers, as well as ACE inhibitors, up to the time of operation (see “Management of Preoperative Medications” in Section I of Chapter 4). Several studies have shown a tendency toward development of acute MI in patients in whom β-adrenergic receptor agents are discontinued. Boudoulas and colleagues demonstrated an important increase in adrenergic tone in most patients the day before operation that could be reduced by propranolol. Propranolol has also been shown to lessen prevalence of intraoperative ventricular arrhythmias without compromising LV function in low or moderate dosages. Patients receiving preoperative β-adrenergic receptor agents, amiodarone, or sotalol are less likely to develop atrial fibrillation postoperatively. Digitalis preparations can be discontinued preoperatively unless atrial fibrillation is present (see Chapter 4). They can be administered intraoperatively and postoperatively for control of heart rate if atrial fibrillation or other atrial arrhythmias are present.

Platelet antiaggregating drugs such as abciximab, eptifibatide, tirofiban, clopidogrel, prasugrel, and ticagrelor bind to the glycoprotein IIb/IIIa platelet receptors. When feasible, these drugs as well as aspirin should be discontinued at the appropriate time interval before operation (each has a different half-life) if the patient has a stable coronary syndrome, because their use is associated with increased postoperative bleeding and need for transfusion of blood products.

Patients who have received plasminogen-activating (fibrinolytic) agents such as streptokinase, alteplase, and reteplase are less likely to develop atrial fibrillation postoperatively. Digitalis preparations can be discontinued preoperatively unless atrial fibrillation is present (see Chapter 4). They can be administered intraoperatively and postoperatively for control of heart rate if atrial fibrillation or other atrial arrhythmias are present.

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Operating Room Preparation

Anesthetic methods for CABG are described in Chapter 4. After inserting an endotracheal tube and appropriate monitoring devices (see Chapter 2), the skin is prepared over the chest, abdomen, groin, one or both arms if indicated, and the complete circumference of both legs, including the feet. Draping includes isolating the feet, genitalia, and pubis and placing sterile waterproof drapes beneath the legs.

Surgical Strategy

The prime objective of CABG is to obtain complete revascularization by bypassing all severe stenoses (at least 50% diameter reduction) in all coronary arterial trunks and branches having a diameter of about 1 mm or more. Because five or more individual conduits cannot be conveniently used in most patients, at least some of the grafts may require sequential (side-to-side) anastomoses. To increase the likelihood that the entire graft will remain patent, the distal end-to-side anastomosis of a sequential graft should be made, whenever possible, to a relatively large artery with a substantial proximal stenosis and good runoff. Although it is not clearly established whether grafts with more than one distal anastomosis have the same, higher, or lower patency rates than those with only a single distal anastomosis, several studies suggest that sequential grafts are associated with higher mean flows and graft patency. As a general principle, conservation of conduit by employing sequential grafting is prudent because of the likelihood of subsequent CAGB or peripheral arterial procedures that may require use of saphenous vein grafts.

A widely used strategy involves routine use of the left ITA to the LAD and segments of saphenous vein to the remaining coronary arteries requiring revascularization. The right ITA, one or both radial arteries, and the right gastroepiploic artery can also be used in combination with the left ITA. Sequential anastomoses with the ITA and radial artery can be performed with satisfactory results. Figs. 7-10 and 7-11 show the most widely used combinations and configurations of bypass grafts. Details of graft placement are often individualized according to location and severity of arteriosclerotic disease, surgeon preference, availability of suitable conduit, and knowledge of the long-term function of various conduits.

The cineangiogram provides key information for planning CABG, but based on either the cineangiogram or observations made at operation, the surgeon may elect to open vessels suspected of having important stenosis. A few errors will inevitably be made regarding which vessels should be grafted. The surgeon must decide which error is more acceptable: opening and grafting an artery that does not need it or failing to open and graft a vessel with an important stenosis. The latter is generally considered a more serious error.

Coronary Artery Bypass Grafting

With Cardiopulmonary Bypass

A median sternotomy is made, and at the same time a segment of greater saphenous vein (or radial artery or other conduit) is removed. Before the pericardium is opened, the left ITA (and the right if indicated) is completely mobilized. Heparin is administered as dissection of the ITA is being completed. The ITA is then divided. A bulldog clamp or clip is placed on the artery near the open end, and the distal segment of the artery on the chest wall is ligated or clipped. The pericardium is opened, and pericardial stay sutures are placed. Purse-string sutures are placed at the sites for cannulation and also in the ascending aorta and right atrial wall for controlled aortic root perfusion and delivery of cardioplegia into the coronary sinus (see Fig. 2.22). Because arteriosclerosis is frequently present in the ascending aorta and proximal aortic arch in patients with CAD, particularly elderly patients, epi-aortic ultrasonographic scanning of the aorta is advisable.
Figure 7-10 Combinations and configurations of saphenous vein bypass grafts. **A**, Vein graft is anastomosed side to side to a diagonal branch of left anterior descending coronary artery (LAD) and end to side to LAD. **B**, In circumflex system, vein graft is anastomosed side to side to one or more proximal marginal branches and end to side to most distal marginal branch. **C**, Sequential grafts to circumflex system (Cx) can be extended to include branches of right coronary artery (RCA). **D**, In RCA system, vein graft can be anastomosed side to side to posterior descending coronary artery and end to side to one or more left ventricular branches of RCA. **E**, Sequential grafts to RCA system can be extended to include branches of Cx artery. Direction of a sequential graft to RCA and Cx artery systems (configuration **C** or **E**) is chosen so that the largest coronary artery branch is placed at end of sequence.
before aortic cannulation to obtain information that can lead
to safe positioning of cannulae and aortic clamps (see “Epi-
aortic Ultrasonography” in Chapter 26).510,542,523,67,92

CPB is established using a single venous cannula. Cata-
ters for administering cardioplegic solution are placed into
the ascending aorta and coronary sinus through the previ-
ously placed purse-string sutures and secured with tourni-
quets. The aorta is clamped and cardioplegic solution infused
(see “Cold Cardioplegia, Controlled Aortic Root Reperfu-
sion, and [When Needed] Warm Cardioplegic Induction” in
Chapter 3). The heart can be covered with cold saline during
administration of cold cardioplegia to facilitate cooling.

With the heart retracted out of the pericardial cavity and
toward the head of the patient by an assistant standing to the
surgeon’s left or by traction sutures placed on the acute
margin of the heart, the first anastomosis of the conduit that
has been selected is made to the distal RCA or to the poste-
rior descending artery (PDA) (see Fig. 7-10, D). (See “Distal
Anastomosis” later in this chapter.) Sequential anastomoses
of the conduit can be performed to more distal branches of
the RCA or to the marginal branches of the Cx coronary
artery (see Fig. 7-10, E). The graft is then distended gently
with cardioplegic solution, positioned along the right atrium
up to the right side of the ascending aorta, and transected at
the point that will permit a smooth course of the conduit
without kinking or tension. The free end of the graft is
spatulated.

The heart is then retracted to the right by the assistant. A
separate conduit is anastomosed to one or more of the mar-
ginal branches of the Cx artery (see Fig. 7-10, B). The graft
is properly oriented to avoid twisting, and the heart is repo-
sitioned in the pericardial cavity. The graft is disended gently
Right gastroepiploic artery or splenic artery may be used to bypass branches of right and circumflex coronary arteries in combination with ITA or other grafts to LAD circulation.

Figure 7-11, cont’d  

**E**, Right ITA can be brought across midline and used to bypass LAD, and if indicated, left ITA can be anastomosed to one or more marginal branches of left circumflex coronary artery. **F**, When extensive revascularization of posterior wall of left ventricle (LV) is required, a posteriorly positioned sequential vein graft (or radial artery) in combination with a left ITA graft to the LAD is typically used. **G**, Radial artery graft may be used as a sequential graft to bypass arteries on lateral and posterior surfaces of LV. Radial artery can be anastomosed proximally to left ITA, which is used to bypass the LAD. Alternatively, radial artery can be anastomosed directly to ascending aorta. **H**, Right gastroepiploic artery or splenic artery may be used to bypass branches of right and circumflex coronary arteries in combination with ITA or other grafts to LAD circulation.

with cardioplegic solution, cut to the appropriate length, and spatulated. This graft can be positioned anterior to the pulmonary artery or passed through the transverse sinus for anastomosis to the right side of the aorta. A third segment of conduit can be anastomosed to one or more diagonal branches of the LAD. This segment can be brought anterior to the pulmonary artery or through the transverse sinus.

The ITA is cut to the appropriate length, and a bulldog clamp is placed on the proximal portion. If the operation has been performed using hypothermia, rewarming is begun at this time. The pericardium is incised widely to permit proper alignment of the ITA with the LAD and its diagonal branches, taking care to avoid injury to the left phrenic nerve. A pad is placed beneath the LV, and the LAD is isolated and incised. The distal end of the ITA is spatulated and sutured to the LAD and sequentially to a diagonal branch of the LAD if indicated (see Fig. 7-11, A and B).

The aortic clamp is removed, a partially occluding clamp is placed on the ascending aorta, and two or three openings are made with a punch in the isolated aortic segment. The grafts are sutured to the aorta so that they are free of kinking or tension. If grafts have been passed through the transverse sinus, they are anastomosed to openings made on the right lateral surface of the ascending aorta. Because of increasing evidence implicating the arteriosclerotic ascending aorta as an important source of emboli to the brain and other organs, it
may be preferable to avoid placing the partially occluding clamp on it and to perform the proximal anastomoses during a single period of aortic clamping with the heart arrested. A25

The partially occluding clamp (or the aortic clamp if a partially occluding clamp has not been used) is then removed. Air is evacuated from the ascending aorta, and controlled aortic reperfusion, if indicated, is begun. Once rewarming has been completed and the heart is beating well, CPB is discontinued and cannulae are removed. Temporary atrial and ventricular pacing wires and chest drainage tubes are placed. Remainder of operation is completed in the standard manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Without Cardiopulmonary Bypass

Perfection of techniques and equipment for stabilizing the beating heart has resulted in an increased number of CAGB procedures performed without use of CPB (OPCAB). Procedures involving placement of grafts to more than one of the three major coronary arteries are generally performed through a median sternotomy. With development of stabilization devices that permit adequate and safe exposure of all surfaces of the LV, OPCAB can be safely performed in patients with three-system disease and with left main coronary artery disease. C43,K36,P20,Y1

In contrast to CAGB performed with CPB, methodology for OPCAB continues to evolve, and many issues relating to preoperative selection and preparation of patients, their anesthetic management, and conduct of the operation remain incompletely defined and unresolved. The following discussion presents a generalized representation of OPCAB, with schematic illustrations of the techniques and equipment for exposing and stabilizing surfaces of the LV.

Anesthetic management of patients undergoing CAGB without CPB is discussed in Section I of Chapter 4. Close communication between the surgeon and anesthesiologist is essential during OPCAB. The surgeon must inform the anesthesiologist when and how the heart is being displaced, when a coronary artery is occluded, and when a shunt or other perfusion device is used. The anesthesiologist must keep the surgeon informed of ischemic changes detected by the ECG, occurrence of arrhythmias, and the patient’s overall hemodynamic status. When the heart is displaced, amplitude of the ECG signal may be greatly decreased, and thus severity of ST-segment changes indicative of ischemia may be underestimated. Transesophageal echocardiography is used to monitor regional wall motion and right and left ventricular volumes.

A median sternotomy is made, and at the same time a segment of the greater saphenous vein (or a radial artery or other conduit) is removed (see “Vein Graft” in text that follows). Before the pericardium is opened, the left ITA and right ITA (if indicated) are completely mobilized (see “Internal Thoracic Artery” later in this chapter). Heparin is administered as dissection of the ITA is being completed. The ITA is then divided. A bulldog clamp is placed on the artery near the open end, and the distal segment of the artery on the chest wall is ligated or clipped. The pericardium is opened and pericardial stay sutures placed. Epiaortic ultrasonographic scanning of the ascending aorta to detect severe atherosclerosis that may affect the conduct of the operation is advisable in older patients (see Chapter 26). R10,C42,F23,G7,W2

Heparin dose, optimal activated clotting time (ACT), and protocol for administering protamine vary from institution to institution. Heparin dose varies from a minimum of 5000 units to full heparization (3 mg · kg⁻¹). Protocols to reverse heparin activity with protamine range from no administration to partial or full doses.

Hypothermia should be avoided. Normothermia can be maintained by use of warm intravenous and irrigating fluids or a heated mattress or blanket, by humidification of the airway, and by maintaining a warm temperature in the operating room.

Hemodynamic stability during manipulation of the heart can be preserved by several maneuvers. These include placing the patient in the head-down (Trendelenburg) position, which increases preload by redistributing blood volume; rotating the operating table; and opening the right pleural space by incising the pericardium vertically. The latter two maneuvers minimize the manipulation required to create optimal exposure of the lateral wall of the LV. Placing and using temporary ventricular pacing wires will prevent prolonged periods of bradycardia. Preoperative insertion of an intraaortic balloon pump in high-risk patients may increase tolerance of the heart to manipulation.

Exposure of the LV surfaces containing the arteries to be bypassed is achieved by different combinations of elevation (apex of heart toward ceiling) and lateral displacement (apex of heart to right or left). To facilitate these maneuvers, a heavy suture (size 0 silk or polyester) is placed in the posterior pericardium opposite the oblique sinus and midway between the right and left inferior pulmonary veins (Fig. 7-12, A), the most dependent portion of the pericardial cavity. R10 This should be done quickly to avoid prolonged hypotension. The suture should not be placed too deeply because this may result in injury to the descending aorta or esophagus. The suture is passed through a wide strip of cloth tape (Fig. 7-12, B), and a snare is placed over both ends of the suture and tightened (Fig. 7-12, C). By adjusting orientation of the snare and tape sling and the traction placed on them, adequate exposure of the coronary arteries requiring bypass grafting can be accomplished in nearly all patients. R10 Circumferential pressure on the heart should be avoided.

Next, the artery to be grafted is stabilized with a device that depresses the myocardium to expose the segment to be grafted (Fig. 7-13, A). Alternatively, a device that elevates the myocardium on both sides of the segment of artery to be grafted (typically a suction device) can be used (Fig. 7-13, B).

Exposure of the posterior descending branch of the RCA is achieved by marked elevation of the apex of the heart with minimal lateral displacement. This is facilitated by applying traction on the ends of the cloth tape upward toward the head and to the left (avoiding compression of the heart) and using downward traction on the snare (Fig. 7-14, A). A stabilizing device is then applied.

Exposure of the distal RCA is obtained by leftward traction on the ends of the cloth tape, downward traction on the snare, rotation of the table to the left, and use of Trendelenburg position.

The LAD is exposed by traction on the ends of the cloth tape to the left and upward toward the head and gentle downward traction on the snare. A stabilizing device is then applied (Fig. 7-14, B). These maneuvers are applied more
Figure 7-12 Maneuvers to facilitate exposure of surfaces of left ventricle. A, Heavy suture (size 0 silk or polyester) is placed in posterior pericardium opposite oblique sinus and midway between right and left inferior pulmonary veins. B, Suture is placed through a wide strip of cloth tape. C, Snare is placed over both ends of suture and tightened.

Figure 7-13 Stabilization devices to facilitate exposure of segment of artery to be grafted. A, Generic device that depresses myocardium on both sides of artery. B, Generic device that elevates myocardium on both sides of artery, using suction.
After exposing the appropriate wall of the LV, the artery to be grafted is encircled proximal to the site of the arteriotomy with a fine suture, an elastic vessel loop, or a tourniquet. Encircling the artery distal to the arteriotomy site is not always necessary and should be avoided when possible. After the stabilization device is applied, the artery is incised, and anastomosis to the appropriate conduit is performed using techniques described later in this chapter (see “Distal Anastomoses”). Performing the anastomosis can be facilitated by use of a blowing device that disperses humidified carbon dioxide over the anastomotic site to remove blood. This device should be directed at the anastomotic site only during actual placement of sutures to minimize injury to the endothelium of the coronary artery. An intracoronary shunt may also facilitate performing the anastomosis, although it also may result in injury to the endothelium (Fig. 7-15). When the anastomosis is performed on a distal RCA that is not critically narrowed or occluded proximally, a shunt may be particularly valuable because bradycardia and hypotension may occur when the artery is temporarily occluded. A shunt may also provide sufficient distal flow to an arterial segment that may be an important source of collateral blood flow to other segments of the LV that have not been bypassed, thus preventing hypotension and cardiac decompensation.

Proximal anastomoses of vein grafts, radial arteries, or free ITA grafts to the ascending aorta are performed after placing a partially occluding clamp on the aorta (see “Proximal Anastomoses” later in this chapter). These can be performed before or after the distal anastomoses. Temporary atrial and ventricular pacing wires (if not already in place) and chest drainage tubes are placed. Remainder of the operation is completed in the standard manner (see Chapter 2).

When OPCAB is used in patients with multisystem disease, sequence of performing the distal anastomoses becomes important. As a general rule, it is advisable to first graft the artery or arteries that have evidence for collateral blood supply to the distal arterial bed. If an ITA graft is used, the clamp on the ITA pedicle is released as soon as the distal anastomosis to the coronary artery is completed. If a vein graft or another conduit is used, the proximal anastomosis of this conduit to the aorta is performed before the distal anastomosis. Flow is thus established to the distal arterial bed as soon as the distal anastomosis is completed. Vessels without demonstrable collateral blood supply are then grafted. With this approach, important collateral flow is not interrupted before flow through the grafts is established.

The common practice of performing the left ITA to LAD anastomosis first is based on the principle of restoring flow to the anterior wall and septum of the LV before substantial manipulation of the heart is performed to expose the Cx arterial branches. This approach may be valid in many patients, but it is not advised if the LAD provides substantial collateral flow to the remainder of the LV.

Vein Graft

After preoperative examination of both legs with the patient erect, and with ultrasonic imaging when indicated, the right or left greater saphenous vein is chosen for removal. Presence of superficial varicosities does not indicate an unusable saphenous vein. However, wound healing may be poor in such extremities. If possible, a leg without varicosities is chosen; multiple large varicosities in the saphenous vein render it

Figure 7-14  Exposure of posterior and anterior descending coronary arteries. A, Posterior descending coronary artery. Heart is elevated with minimal lateral displacement by upward traction toward the head on ends of tape and downward traction on the snare. Stabilizing device is then applied. B, Anterior descending coronary artery. Ends of tape are pulled upward and slightly to patient’s left, and downward traction in opposite direction is exerted on snare. Stabilization device is then applied.
unsuitable. If vein from one leg is too short or too abnormal for use, an additional segment of appropriate length is removed from the other leg. Occasionally, particularly during reoperations, suitable segments of greater saphenous vein cannot be found, and the lesser saphenous vein can be used if it is of adequate diameter. If suitable segments of vein cannot be found in the legs by any method, use of alternative conduits becomes necessary. These include the right ITA, one or both radial arteries, right gastroepiploic artery, inferior epigastric artery, and, in rare circumstances, the splenic or ulnar artery. The cephalic vein can be taken from wrist to shoulder, but its walls are usually thinner than those of leg veins, and its late patency is less. In critical situations in which sufficient autologous conduit is not available, suitable prepared allograft veins may be used, recognizing their reduced long-term patency.

For removal of the greater saphenous vein, the leg is abducted and the knee flexed about 45 degrees and supported (Fig. 7-16, A). If the vein from the lower leg is to be used, the initial skin incision is made just anterior to the medial malleolus. If the upper portion of the vein will be used, the initial skin incision is made in the groin. The desired plane is accessed by blunt dissection with scissors down to the level of the vein. Skin and subcutaneous fat are undermined with the scissors, staying just superficial to the saphenous vein and spreading the tips of the scissors over the vein. A continuous incision or multiple small incisions over the length of the vein may be used (Fig. 7-16, B and C). Creation of flaps is avoided. Care is taken to preserve the saphenous nerve. The vein may divide just above the knee, becoming confluent again just below the knee. Either of the two branches may be the larger vessel, which is preserved. The saphenous vein usually becomes too large and unsuitable for bypass purposes just before it penetrates the fascia lata and joins the femoral vein. Therefore, dissection is usually not performed in this area.

Whenever possible, a single long segment (usually 50-65 cm) of the greater saphenous vein is removed. About 12 to 15 cm may be needed for diagonal branches of the LAD, about 20 to 24 cm for marginal Cx branches, and about 18 to 22 cm for the RCA and its branches. So long as the external diameter of the vein is greater than about 3.0 to 3.5 mm, vein width is probably not an important consideration. Large veins generally reduce in size with time after insertion, and thus adaptation to function can occur. Veins of overall poor quality should be avoided whenever possible; experience in peripheral vascular surgery indicates they are prone to failure.

When the usable vein has been exposed and its length measured, the proximal (femoral) end is isolated and divided between ligatures. A vascular clamp is placed on the vein to mark what will become the distal end of the graft. The vein is then removed, retracting it upward so that just enough tension exists to expose but not tear the branches. Branches may be ligated with fine sutures and divided, or divided between hemostatic clips (Fig. 7-17, A). The saphenous vein must not be narrowed by ligating or clipping the branches too close to it (Fig. 7-17, A [upper inset]). Branches should be ligated or clipped flush with the saphenous vein to avoid creating diverticula, which can be the nidus for thrombus formation (Fig. 7-17, A [lower inset]). After division of all branches and removal from its bed, the vein is divided between ligatures at its peripheral end (proximal end of the graft) and removed.

Alternatively, the greater saphenous vein can be removed endoscopically. Using small transverse or vertical incisions, a lighted dissector is introduced into the wounds (Fig. 7-18, A). A plane of dissection anterior to the vein is established with a balloon-tipped dilator or other device (Fig. 7-18, B) and the dissector used to isolate the vein and its branches (Fig. 7-18, C). The branches are clipped and divided with a cautery, and after ligating its proximal and distal ends, the vein is removed. Time required to remove veins with this technique is somewhat longer than with the conventional method, but a lower prevalence of leg wound complications and leg discomfort have been observed.

If the lesser saphenous vein is to be used, it can be removed with the patient in the prone or supine position with the leg...
Figure 7-16  Removing greater saphenous vein. A, Location of greater saphenous vein and line of incision. B, Continuous incision over entire length of saphenous vein. C, Multiple small incisions over saphenous vein.

Figure 7-17  Division of side branches of saphenous vein using fine ligatures or hemostatic clips. A, Venous branches should be secured just flush with saphenous vein to avoid narrowing (upper inset) or creating diverticula (lower inset), which can be a nidus for thrombus formation. B, Avulsed branches are secured with a double-loop 7-0 polypropylene suture.
Endoscopic removal of greater saphenous vein.

- Vasodilating drugs (nitroprusside, papaverine) can be added to reduce vasospasm. The vein is gently
  been added. Vasodilating drugs (nitroprusside, papaverine)
  to which a small amount of heparinized blood (30 mL) has
  temperature, heparinized, balanced salt solution (500 mL)
  end of the graft is removed. The vein is flushed with a room-
  with a ligature. The previously placed clamp on the central
  adaptor is inserted into the open peripheral end and secured
  administered.

- It is generally agreed that details of removing and storing saphenous veins until their insertion are important in mini-
  minimizing damage, which may include intimal disruption, depo-
  sition of platelets and leukocytes on the intimal surface,
  damage to smooth muscle, and disruption of the extracellular
  matrix. Despite this general agreement, opinions differ as to which maneuvers or interventions result
  in the least injury. Overdistention of the vein \[ \text{H}^{3} \] and venous spasm \[ \text{H}^{18} \] are surely disadvantageous. No consensus exists as
  to the optimal temperature to maintain the graft or the optimal solution to flush and distend the graft before
  its insertion.

### Arterial Grafts

#### Internal Thoracic Artery

The ITA is usually mobilized immediately after dividing the sternum, and before incising the pericardium and administ-
ering heparin. A standard sternal retractor can be used to widely
separate the divided sternal edges, tilting the retractor to
elevate the left half of the sternum and expose the ITA.
Alternatively, an externally positioned retractor, such as that
developed by Favaloro, can be used. With either type of
retractor, the operating table is elevated and rotated to opti-
lessly expose the undersurface of the left sternal segment and
left ITA. The ITA can be skeletonized or removed as a pedicle
with the internal thoracic veins, fat, muscle, and pleura. Skel-
etonization better preserves blood supply of the sternum and
may be preferable in situations in which risk of sternal infec-
tion may be increased (e.g., obese patients, diabetic patients,
use of both ITAs).

Fig. 7-19 shows the technique for removing the ITA with
a pedicle. An incision using the electrocautery at low power
is made in the parietal pleura and muscle on the medial side
of the ITA, several millimeters from the accompanying inter-
nal thoracic vein (Fig. 7-17, A). The incision is extended
along most of the length of the vessel down to the sixth intercostal space. A parallel incision lateral to the ITA and the
accompanying lateral internal thoracic vein (if present) is
made. Dissection is begun in the sixth intercostal space,
where there are usually no branches. Using the tip of the
electrocautery blade without current, the pedicle is freed
from the sixth costal cartilage. With the pedicle gently
retracted downward and with gentle blunt dissection, the
intercostal arteries are identified and either occluded with
small metal clips and divided, or simply divided with the
electrocautery (Fig. 7-19, B). The ITA should not be grasped
with instruments.

The pedicle is dissected up to the level of the second or
first rib (Fig. 7-19, C), and the left phrenic nerve is identified
and protected. If there is sufficient length, the internal tho-
racic vein is preserved at its junction with the brachiocephalic
vein; if not, the vein is ligated or clipped and divided. It is
not necessary to routinely divide the proximal branches of
the ITA, although it is recognized that such branches, if not

![Figure 7-18](image)

**Figure 7-18** Endoscopic removal of greater saphenous vein.

A, Insertion of lighted dissector into incision over saphenous vein.

B, Plane of dissection immediately above saphenous vein is estab-

Dashed lines show the technique for removing the ITA with

A, insertion of lighted dissector. B, Plane of dissection immedi-
ately above saphenous vein. C, Isolation of saphenous vein

and branches with lighted dissector. *Inset*, Endoscopic view.

either straightened (prone position) and elevated or flexed at
the knee and rotated medially (supine position). If the prone
position is used, the patient is subsequently repositioned and
redraped in the supine position. Initial skin incision is made
posterior to the lateral malleolus and extended superiorly
toward the popliteal fossa. The vein is divided at the level
where it penetrates the deep fascia to join the greater saphe-
nous vein. The sural nerve lies parallel to the vein and is
preserved. Branches of the vein are secured and divided as
described for the greater saphenous vein.

Leg incisions are closed with continuous absorbable suture
in the subcutaneous layers. A small drainage catheter is placed
beneath these layers in the thigh, and the skin is closed with
a continuous subcuticular suture or with metal clips. This can
be done immediately after the vein is removed or deferred
until after CPB has been discontinued and protamine
administered.

The vein is removed to a preparation table, and a small
adaptor is inserted into the open peripheral end and secured
with a ligature. The previously placed clamp on the central
end of the graft is removed. The vein is flushed with a room-
temperature, heparinized, balanced salt solution (500 mL)
to which a small amount of heparinized blood (30 mL) has
been added. Vasodilating drugs (nitroprusside, papaverine)
can be added to reduce vasospasm. The vein is gently

distended (<150 mmHg) with the solution. Any remaining
unsecured branches are ligated or clipped and any constrict-
ing adventitial bands removed. Branches that have been
avulsed are secured with 7-0 polypropylene sutures (see Fig.
7-17, B). The vein is then gently distended and clamped at
the end, and a thin straight line is drawn along its length
with an indelible surgical pencil. The vein is placed in the
heparinized solution at room temperature until used.

![Image](image)
Figure 7-19  Preparation of internal thoracic artery (ITA) pedicle. A, Using electrocautery, pleura and muscle are incised on either side of ITA and its accompanying veins. B, Branches of ITA and accompanying veins are divided between clips or with electrocautery. C, Dissection is continued to level of second or first rib. D, ITA pedicle is divided at level of sixth or seventh intercostal space. E, End of ITA is freed from adherent fascia, muscle, and veins.

divided, can result in “steal” of blood from the LAD in some situations.510

After proximal dissection is completed, heparin is administered and the ITA divided in the sixth or seventh intercostal space (Fig. 7-19, D). The proximal end is controlled with a small bulldog clamp or clip and the distal end ligated or clipped. The ITA is wrapped in a sponge saturated either with a balanced salt solution containing papaverine (20 mg) dissolved in 20 mL of saline solution, or with 500 mL of lactated Ringer solution to which 50 mg of sodium nitroprusside and 30 mL of heparinized blood have been added. If the ITA bleeds freely, even though not briskly, the graft is generally considered satisfactory for use. The ITA is not probed or injected with fluid unless there is no flow; probing or
PART II Ischemic Heart Disease

Figure 7-19, cont’d  F, ITA is incised to appropriate length. G, For a side-to-side anastomosis using the ITA, pleura is incised over artery at site of anastomosis. H, Anastomosis is completed using a continuous 7-0 or 8-0 polypropylene suture.

injecting may produce endothelial damage and dysfunction.\textsuperscript{16} If the right ITA is to be used, it is prepared in the same manner. The internal thoracic vein leaves the chest wall to enter the brachiocephalic vein at a lower level on the right than on the left, and it is usually divided. Care is taken to avoid injuring the phrenic nerve.

The left ITA pedicle is brought into the surgical field after the LAD has been opened, usually through a wide incision in the pericardium. The ITA is cut obliquely at the site for anastomosis and freed from adjacent tissue for a short distance (Fig. 7-19, E). It is then incised at the bottom of the bevel for the appropriate distance to correspond to the size of the opening in the artery (Fig. 7-19, F). It is anastomosed to the artery with a continuous 7-0 or 8-0 polypropylene suture. The ITA is not dilated or otherwise manipulated, and only the adventitia is grasped with forceps. After anastomosis is completed, the pedicle is tacked to the epicardium with a fine suture on both sides of the artery.

If the ITA is to be anastomosed to a diagonal branch of the LAD as well as to the LAD itself, anastomosis to the diagonal artery is performed first. The pleura is incised over the ITA at the site of the anastomosis (Fig. 7-19, G). The anastomosis is completed with a 7-0 or 8-0 polypropylene suture (Fig. 7-19, H). Anastomosis to the LAD is then performed.

When the left ITA does not reach the LAD but is patent, it can be used as a free graft. The proximal end of the ITA can be anastomosed directly to the aorta, to the right ITA, or to a segment of vein that has been used to bypass other coronary arteries. Patency of free ITA grafts is almost as good as that of in situ ITA grafts.\textsuperscript{12} If the ITA has been used as a pedicle graft and is under tension after CPB is discontinued,
it can be lengthened by completely dividing the tissues of the pedicle at several sites.

**Radial Artery**

Before operation, an Allen test is performed on the nondominant hand. The radial and ulnar arteries are compressed at the wrist while the patient opens and closes the fist vigorously (5-10 times) to produce blanching of the skin on the palm of the hand. Pressure on the ulnar artery is then released while the radial artery remains compressed. Skin of the palm of the hand should immediately become flushed as flow is restored to the palmar arch from the ulnar artery. If the test is equivocal, ultrasonic imaging may be necessary to establish the safety of removing the radial artery.

The arm is positioned on an arm board at the side of the patient. An incision is made in the forearm beginning over the radial pulse at the wrist (Fig. 7-20, A). It is then extended proximally over the belly of the brachioradialis muscle. The lateral antebrachial cutaneous nerve is located lateral to the incision and retracted. The deep fascia is opened at the wrist, exposing the radial vascular pedicle. Incision in the fascia is extended proximally, exposing the muscles of the forearm (Fig. 7-20, B). The superficial radial nerve is also lateral to the incision and should be preserved.

The vascular pedicle containing the radial artery and accompanying veins is mobilized in the middle of the forearm, then encircled in this area with an elastic vessel loop for retraction (Fig. 7-20, C). Dissection proceeds proximally up to the origin of the recurrent radial artery and distally to the tendons at the wrist. Branches of the artery and accompanying veins are controlled with small hemostatic clips or with cautery and are divided lateral to the accompanying veins. Proximal and distal ends of the artery are ligated, and the artery is removed. Alternatively, the artery can be removed using an endoscopic technique.

After removal, a small olive-tipped catheter is inserted into the distal end of the artery. The artery is gently irrigated and dilated with heparinized whole blood or a solution of lactated Ringer solution (500 mL) to which 50 mg of sodium nitroprusside and 30 mL of heparinized blood have been added. The graft is then immersed in this solution until it is used. The incision in the arm is closed with two continuous absorbable sutures in the subcutaneous and subcuticular layers. A compression dressing is applied, and the arm is repositioned for proper orientation.

**Right Gastroepiploic Artery**

To expose the right gastroepiploic artery, the midline incision over the sternum is extended over the upper abdomen, and the linea alba is divided halfway from the tip of the xiphoid to the umbilicus (Fig. 7-21, A [inset]). With the sternum divided, excellent exposure of the upper abdomen can be obtained. The triangular ligament of the liver is divided, and the liver is retracted superiorly and to the right. Branches of the right gastroepiploic artery to the stomach and omentum are ligated or clipped and divided, creating a pedicle (Fig. 7-21, A). Dissection extends from the pylorus along the greater curvature of the stomach until sufficient length is achieved. After the distal end is divided, the arterial pedicle is wrapped in a sponge saturated with a solution containing 50 mg of sodium nitroprusside and 30 mL of heparinized blood dissolved in 500 mL of lactated Ringer solution.

The prepared pedicle can be positioned either anterior or posterior to the duodenum and stomach, depending on anatomic conditions (Fig. 7-21, B). The pedicle should be positioned where there is the least amount of tension and distortion. A circular opening is made in the diaphragm medial to the inferior vena cava, and the pedicle is passed through this opening into the pericardial cavity.

The right gastroepiploic artery can be used to bypass most coronary arteries, but it is usually anastomosed to the distal RCA or PDA (see Fig. 7-11, H) because these arteries are closer to the proximal portion of the gastroepiploic artery than other vessels. This approach allows creation of an anastomosis with a relatively large diameter. Anastomoses can be performed to the LAD or its diagonal branches by bringing the pedicle anteriorly over the acute margin of the heart. The pedicle can also be positioned adjacent to the atrioventricular groove posteriorly and anastomosed to a marginal branch of the Cx coronary artery (see Fig. 7-11, H).

**Inferior Epigastric Artery**

The inferior epigastric artery (IEA) originates from the medial side of the external iliac artery posterior to the inguinal ligament. The IEA pursues a course along the medial edge of the deep inguinal ring, encircling the vas deferens in men and the round ligament in women. It then ascends obliquely toward the umbilicus. In an angiographic study of 100 right IEAs by Schroeder and colleagues, 96 were considered suitable as conduits for CABG. The mean length in situ from the origin to the distal bifurcation was 13 ± 1.3 cm, and the mean diameter measured 5 cm from its origin was 2.4 ± 0.40 mm.

The IEA is removed through a paramedian incision beginning at the umbilicus. Incision follows the external edge of the rectus muscle and ends 2 to 3 cm above the inguinal ligament. The anterior sheath of the rectus muscle is divided and the muscle retracted medially. The artery is mobilized with accompanying veins, and branches of the IEA and accompanying veins are clipped and divided. The pedicle containing the artery is divided at or near its origin and at the level of the first major bifurcation. The IEA is removed and wrapped in a gauze sponge soaked with a solution containing papaverine or sodium nitroprusside and immersed in this solution until it is used (see “Radial Artery” earlier in this chapter). The abdominal wound is packed with a gauze sponge and closed in two layers with absorbable suture after discontinuing CPB.

**Splenic Artery**

When no other conduit is available, the splenic artery can be used. It is exposed through a midline extension of the median sternotomy. The lesser peritoneal sac is opened to gain access to the splenic artery, which courses along the superior margin of the pancreas. Branches of the artery to the pancreas are ligated or clipped and divided, and the artery is then mobilized in the hilum of the spleen, where it is ligated and divided. It is not necessary to remove the spleen because it is also supplied with blood from short gastric branches of the
Figure 7-20  Removing radial artery.  **A**, Location of radial artery and line of incision.  **B**, Deep fascia is divided over vascular pedicle, which contains radial artery and accompanying veins.  **C**, Elastic vessel loop is passed around pedicle and branches of radial artery and accompanying veins are doubly clipped and divided.
The epicardium is incised over the area of the coronary artery that has been selected for anastomosis using a scalpel blade with a rounded end or small scissors. The anterior surface of the artery can be cleared by gentle brushing with the scalpel blade. Even when crystalloid cardioplegic solution has been infused, careful inspection of the artery usually reveals a thin central line that is red or translucent, indicating location of the lumen. The anterior wall of the artery is opened longitudinally in this area with a pointed scalpel blade to avoid injury to the posterior wall (Fig. 7-22, A). The blade must enter the artery obliquely to avoid this injury. The incision is enlarged with fine angled scissors to a length of 4 to 6 mm (Fig. 7-22, B and C). The incision in the epicardium must extend beyond each end of the arteriotomy to facilitate the anastomosis. The artery is sized by passing calibrated probes into it, and patency of the proximal and distal segments is assessed.

When the end of the vein (or other conduit) is being prepared for the most distal anastomosis, it is beveled so that the circumference of the opening is slightly larger than the opening of the artery. The incision is made about 10% to 20% longer than that in the artery, and sutures in the vein are placed slightly farther apart than those in the artery to create the desired “cobra head” configuration. If the vein is small, a larger vertical incision provides a larger hood over the distal anastomosis.

The technique of anastomosis uses one double-armed 6-0 or 7-0 polypropylene suture placed as a continuous stitch (Fig. 7-23, A). Stitches in the coronary artery generally are placed from intima to adventitia (inside to outside). The stitch pierces the intima near the vessel edge, but often emerges through periarterial tissue several millimeters away from the edge. Stitches in the vein are passed from outside to inside. The stitches are generally placed separately through the artery and the vein unless it is convenient to place them with one pass of the needle holder. Even then, the vein and artery should be held apart so that the needle can be visualized after it has pierced the vein and before it pierces the artery (Fig. 7-23, A). This maneuver ensures that the stitch is placed accurately and no extraneous tissue has been incorporated.

The sequence of stitching varies from one location on the heart to another and may vary in the same location because of special conditions of exposure or arterial pathology. For anastomoses to the left coronary system, the suture is passed first through the vein (outside to inside) near the midpoint of the arterial wall opposite the surgeon for the LAD system (see Fig. 7-23, A) and to the surgeon’s right for branches of the Cx system. The suture is then passed through the artery (inside to outside) and continued to the heel of the anastomosis. The vein is approximated to the artery by tension on the suture, and the stitch is placed accurately and no extraneous tissue has been incorporated.

The sequence of stitching varies from one location on the heart to another and may vary in the same location because of special conditions of exposure or arterial pathology. For anastomoses to the left coronary system, the suture is passed first through the vein (outside to inside) near the midpoint of the arterial wall opposite the surgeon for the LAD system (see Fig. 7-23, A) and to the surgeon’s right for branches of the Cx system. The suture is then passed through the artery (inside to outside) and continued to the heel of the anastomosis. The vein is approximated to the artery by tension on both ends of the suture (Fig. 7-23, B). The suture line is then continued around the toe of the anastomosis, and the two ends of the suture are tied (Fig. 7-23, C).

For anastomoses to the right coronary system, the suture is passed first through the vein (outside to inside) near the midpoint of the wall of the artery opposite the surgeon (Fig. 7-24, A). It is then passed through the artery (inside to outside) and continued to the toe of the anastomosis. The vein is approximated to the artery, and the suture line is completed around the heel of the anastomosis and remaining far wall of the artery (Fig. 7-24, B). The two ends of the suture are then tied (Fig. 7-24, C).

Distal Anastomoses

The technique for anastomosing the ITA to the LAD and its diagonal branches is described earlier (see Fig. 7-19, E to H). Here, techniques for anastomosis of a segment of vein are described. Although the description is explicitly for vein grafts, the techniques are applicable to anastomosis of ITA, radial artery, and other conduits to a coronary artery.
Figure 7-22  Distal anastomosis in coronary artery bypass grafting.  
A, Anterior wall of coronary artery is opened with a scalpel.  
B and C, Incision is enlarged to the appropriate length with angled scissors.

Figure 7-23  Technique of anastomosis for left coronary system grafts.  
A, Suture is passed through artery and continued to heel of anastomosis.  
Inset, Direction of suture placement.  
B, Vein is approximated to artery.  
C, Suture line is continued around toe of anastomosis and ends of suture tied.
Figure 7-24  Technique of anastomosis for right coronary system grafts. A, Suture line begins near midpoint of arterial wall and is continued to toe of anastomosis. Inset, Direction of suture placement. B, Vein is approximated to artery, and suture line is continued around heel of anastomosis. C, Suture ends are tied.

For sequential anastomoses in which the vein or other conduit will lie perpendicular to the arterial branches, the conduit can be opened perpendicular to its long axis for the side-to-side anastomosis if it is of sufficient diameter (Fig. 7-25, A). The incision should not exceed one third of the circumference of the conduit. The anastomosis is begun at the midpoint of the arteriotomy on the right side. The suture is passed inside to outside on the artery and then through the vein at the midpoint of the incision on its right side (Fig. 7-25, B). The suture is continued across the heel of the anastomosis, along the left side, across the toe of the anastomosis, and completed at the midpoint on the right side. If the vein is small or if the radial artery or ITA is used, the conduit is incised parallel to its long axis (Fig. 7-25, C), the diamond anastomosis. The anastomosis is begun close to the midpoint of the arteriotomy on the right side, and the suture is passed through the graft close to the right end of the longitudinal incision (Fig. 7-25, D). The suture line is continued leftward across the heel of the anastomosis and completed as already described.

For terminal end-to-side anastomosis, the conduit is beveled and the suture line begun at the midpoint of the arteriotomy on the left side (Fig. 7-25, E). The suture line is continued to the right across the proximal end of the arteriotomy and along the right side of the artery to its midportion. Using the other end of the suture, the anastomosis is completed by continuing the suture line across the distal end of the arteriotomy and completing it at the midpoint on the right side.

If the conduit and artery are parallel rather than perpendicular, a side-to-side anastomosis is performed as shown in Fig. 7-25, F and G. The technique is identical to that for side-to-side anastomosis of the ITA to the LAD (see Fig. 7-19, G-H). After each sequential anastomosis is completed, the conduit is gently distended by injection of cardioplegic solution or a balanced salt solution to avoid excessive length or tension between sequential anastomoses.

Coronary Artery Endarterectomy

Endarterectomy is most often performed on the distal RCA and its major branches and only infrequently on branches of the Cx artery and LAD. If the distal RCA and its branches are diffusely diseased or occluded, endarterectomy is an alternative to bypass of the branches.

A common procedure involves incising the distal RCA just proximal to the origin of the PDA (Fig. 7-26, A). An endarterectomy plane in the outer third of the medial layer of the artery is developed with a dissector (Fig. 7-26, B). A small curved clamp is placed beneath the isolated atheromatous core, which is divided (Fig. 7-26, C). Using the dissector, the core is freed distally from the arterial wall (Fig. 7-26, D). The core is then teased from the PDA and distal RCA using a clamp and exerting pressure on the core in the opposite direction from the clamp (Fig. 7-26, E). The core usually separates cleanly from the distal vessels and is then removed from the proximal RCA using the same technique (Fig. 7-26,
Figure 7-25  Technique of sequential grafting. **A**, Vein graft is opened perpendicular to its long axis. **B**, Anastomosis is begun at midpoint of arteriotomy on its right side. **C**, Alternatively, vein is incised parallel to its long axis. **D**, In alternative approach (diamond anastomosis with longitudinal incision in graft), suture is passed through graft close to right end of incision and continued across heel of anastomosis. **E**, End-to-side anastomosis. *Inset*, Direction of suture placement for side-to-side and end-to-side anastomoses. **F** and **G**, Side-to-side anastomosis. Technique is identical to that in Fig. 7-16, **G** and **H**. Key: **A**, Coronary artery; **G**, graft.

A saphenous vein or other conduit is then sewn to the edges of the artery with 6-0 or 7-0 polypropylene suture (Fig. 7-26, **G**).

Proximal Anastomoses

After completing the last distal anastomosis, and when the procedure is being performed with CPB, the proximal anastomoses are performed. The aortic clamp can be removed, and a partially occluding, side-biting clamp placed on the ascending aorta. This permits reperfusion of the heart and resumption of cardiac contractions as rewarming is completed. However, the side-biting clamp is not necessary, and is not used when there is important arteriosclerosis of the ascending aorta (see “Surgical Strategy” earlier in this chapter) or if it is of insufficient length. In these situations, the aortic clamp is left in place and the heart remains arrested.

Using a punch, openings are made in the ascending aorta. Vein grafts or other conduits are positioned so that they will be free of kinking or tension when the heart is filled with blood. They are aligned properly using the mark previously placed on the conduit to avoid twisting. The vein is cut obliquely and incised to create a circumference that is 10% to 20% larger than that of the circular opening in the aorta, resulting in a “cobra head.” A double-armed 5-0 or 6-0 polypropylene suture line is begun in the middle of the right
Endarterectomy of right coronary artery (RCA). A, RCA is incised just proximal to origin of posterior descending coronary artery (PDA). B, Endarterectomy plane is developed with a dissector. C, Atheromatous core is divided over a clamp. D, Core is freed distally from arterial wall. E, Core is teased from posterior descending coronary artery and distal RCA. F, Core is removed from proximal RCA. G, Vein graft is sewn to edges of artery (see Fig. 7-24).

Edge of the vein graft, passing the suture from outside to inside on the vein and then inside to outside on the aorta (Fig. 7-27, A). This suture line is continued leftward across the heel of the anastomosis. The vein is approximated to the aorta by exerting tension on both ends of the suture. The suture line is continued across the toe of the anastomosis (Fig. 7-27, B), and the ends of the suture are tied on the right side of the anastomosis (Fig. 7-27, C).

When CPB is not used, these proximal anastomoses are generally performed before the distal anastomoses using a partially occlusive, side-biting clamp (see “Without Cardiopulmonary Bypass” under Coronary Artery Bypass Grafting earlier in this chapter). When CPB is used, proximal anastomoses can be performed before or after CPB is established, but before the aorta is occluded and cardioplegic solution is administered. Use of CPB facilitates performing proximal anastomoses because of lower pressure in the ascending aorta.

Several devices are available to attach vein grafts to the aorta without use of sutures. Other devices permit suture of grafts to the aorta without need for aortic clamping.

Emergency Operation for Cardiogenic Shock

If the patient is hemodynamically unstable at the time of operation, an intraaortic balloon pump is inserted if one is not already in place. Appropriate monitoring devices are inserted, the sternum quickly opened, and CPB expeditiously established. The left ITA can be mobilized after CPB is established, with the heart decompressed but still beating. Saphenous vein is removed from one or both legs as needed.
Reoperation

**Secondary Median Sternotomy**

The technique of most (but not all) CABG reoperations is similar to that of the original operation, with a few important differences. Sternotomy is most often made with an oscillating saw (see Section III of Chapter 2 for technique). Vein grafts are obtained from the leg, and one or both ITAs can be mobilized if they were not used at the initial operation. The radial artery can also be used. If difficulties are anticipated with mobilizing the heart, ascending aorta, or previously inserted vein grafts (i.e., they are adherent to the undersurface of the sternum), provisions are made for peripheral cannulation, such as through the femoral or axillary artery and femoral vein (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2). CPB can be established before dividing the sternum, then temporarily discontinued until the heart has been mobilized, or it can be established and maintained until the operation is completed.

After the sternum is divided, and if peripheral cannulation is not used, the right atrium and ascending aorta are mobilized to permit placing cannulae and clamps. Mobilization of the ventricles (the left in particular) is begun only after CPB is initiated. The heart is completely mobilized. If the left or right ITA was used at the initial operation and is patent, the pedicle is sufficiently mobilized to permit placing a small clamp across it. Manipulation of previously placed vein grafts is minimized to avoid dislodging atheromatous debris into the distal coronary circulation.

The heart is completely mobilized. If the left or right ITA was used at the initial operation and is patent, the pedicle is sufficiently mobilized to permit placing a small clamp across it. Manipulation of previously placed vein grafts is minimized to avoid dislodging atheromatous debris into the distal coronary circulation.

After CPB is established and cardioplegic solution is administered into the aortic root. Subsequent infusions are given into the aortic root or retrogradely into the coronary sinus (see “Technique of Retrograde Infusion” in Chapter 3). Severely narrowed or diffusely atherosclerotic vein grafts are divided and ligated immediately after the first dose of antegrade cardioplegia. If there is concern about possible dislodgement of atheromatous debris into the distal coronary circulation as a result of manipulating a diseased graft, it is divided and ligated proximally, and retrograde cardioplegia is then administered. This may permit washout of debris from the opened graft. The distal end of the divided graft is then ligated.

Managing vein grafts that have no or minimal evidence of atherosclerosis (as determined by angiography) and that are soft and relatively normal in appearance is controversial. Some centers favor complete removal of grafts that have been in place for more than 5 or 6 years; other centers leave such grafts in place. If a diseased graft is to be removed and there is no important obstruction in the coronary artery distal to the site of attachment, it is possible in some circumstances to leave a small cuff of this graft adjacent to the artery, which can then be anastomosed to the new graft. If there is important occlusive disease in the coronary artery distal to the site of the previous anastomosis, a new vein graft should be anastomosed directly to the artery beyond the obstruction. If an ITA is to be attached to the LAD previously bypassed by a vein graft that is not occluded or critically stenotic, the vein graft should not be ligated, because the ITA may not initially provide sufficient flow to prevent serious myocardial ischemia.

A diligent search should be made for all graftable vessels. After completing the distal anastomoses, proximal anastomoses to the ascending aorta are completed. In general,
it is preferable to perform these anastomoses with the aortic clamp in place, thus avoiding need for placing a partially occluding clamp on the aorta. After completing the proximal anastomoses, the aortic clamp is removed and the operation completed as previously described.

Reoperations can be performed without use of CPB, employing the OPCAB technique described previously in this chapter.\textsuperscript{S16,S55}

**Left Thoracotomy**

An alternative approach through a left thoracotomy is a convenient and safe method for reoperation\textsuperscript{K20,S71,S81,K1,1} and is frequently chosen when branches of the Cx artery and diagonal branches of the LAD are to be revascularized. Occasionally, branches of the posterolateral segment of the RCA are accessible through this approach. It is particularly useful in the presence of a patent and functioning ITA graft to the LAD. It may also have value when the ascending aorta is heavily calcified and therefore hazardous to manipulate.

It is sometimes necessary to remove the needed segment of saphenous vein with the patient supine. After rotating the patient to a near right lateral decubitus position, a left thoracotomy is made through the bed of the resected or nonresected fifth rib. The left femoral artery and vein are simultaneously exposed through a vertical or oblique groin incision after rotating the patient’s hips back toward the surgeon. The femoral artery and vein are cannulated, making certain the 28F, 30F, or 32F long venous cannula passes over the promontory of the sacrum and into the inferior vena cava (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2). CPB is established in the usual manner, and the patient’s body temperature is reduced to about 22°C with perfusate. If an additional route of venous return is necessary, the pulmonary artery is cannulated with an angled cannula (28F, 30F, or 32F) positioned across the pulmonary valve into the right ventricle. Usually the heart spontaneously fibrillates, but if not, it is electrically fibrillated. Once the patient’s nasopharyngeal temperature is below about 25°C, CPB flow can be reduced to about 1.0 to 1.5 L · min\(^{-1}\) · m\(^{-2}\). A left-sided heart vent may be needed and can be inserted into the left atrial appendage or through the left inferior pulmonary vein. Distal anastomoses are made as usual, using fine sutures or elastic tourniquets around the coronary artery.

When these maneuvers have been completed, rewarming is begun, and the heart usually spontaneously defibrillates. Proximal anastomoses, performed with a side-biting clamp, are made to the proximal descending thoracic aorta, curving the bypass graft superiorly over the hilum of the lung or inferiorly around the hilum, attaching the vein to the lower descending thoracic aorta. The left subclavian artery can also be used as a site for attaching grafts. Remainder of operation is completed in the usual manner.

Reoperations using the left thoracotomy approach can also be performed without CPB.\textsuperscript{K71,S54}

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

**Early Postoperative Care**

Most patients are extubated either in the operating room or a few hours postoperatively and discharged from the intensive care unit the following day. Discharge from the hospital to outpatient supervision may occur on the third or fourth postoperative day. Thus, postoperative care is simple in most patients (see Chapter 5).

Occasionally, 8 to 12 hours after operation, arterial blood pressure falls to levels 10% to 20% below normal, whereas pedal pulses remain full and cardiac index is greater than 2.0. No treatment or a low-dose (2.5 μg · kg\(^{-1}\) · min\(^{-1}\)) infusion of dopamine is indicated.

Oral β-adrenergic receptor blocking agents may be given beginning 4 to 6 hours postoperatively. This regimen is continued until discharge as prophylaxis against supraventricular tachyarrhythmias.\textsuperscript{K23,W16} Alternatively, no prophylactic medication is given, although a case can be made for prophylaxis in elderly patients, who are more susceptible to postoperative atrial fibrillation.\textsuperscript{K22,H11} Digitalis is not routinely used prophylactically because it may produce atrial and ventricular arrhythmias and is less effective than other drugs.\textsuperscript{K52} Other drugs or combinations of drugs are recommended by some authors.\textsuperscript{K21,K3,K12,K4,K82} Biatrial pacing may reduce the prevalence of postoperative atrial fibrillation.\textsuperscript{S53,S4,S27,S14}

Warfarin is not routinely administered. A modification of the aspirin-dipyridamole protocol evolved by Chesebro and colleagues is used to enhance graft patency because of its antiplatelet effect.\textsuperscript{S27,S28} In this modified protocol, aspirin (325 mg) is administered through a nasogastric tube 1 hour after operation. Another 325 mg is given by nasogastric tube 7 hours postoperatively and is continued by mouth once daily thereafter.\textsuperscript{G19,G20} Although perioperative bleeding may be increased with this protocol, major complications are not encountered. The patient is advised to continue this protocol for at least 1 year.\textsuperscript{F14} Aspirin in a dose of 80 mg daily may be sufficient for maintenance, except in large patients. In patients with a history of aspirin intolerance, clopidogrel, ticlopidine, or prasugrel may be substituted. Heparin (5000-7500 units every 8 to 12 hours) can be administered subcutaneously as prophylaxis against deep venous thrombosis and pulmonary embolism in the first 48 to 72 hours postoperatively.

Occasionally, intraaortic balloon pumping is required for a few hours to a few days after operation (see Chapter 5). The indication is usually low cardiac output with high left atrial pressure or occasionally occurrence of intractable ventricular arrhythmias intraoperatively or early postoperatively. If this is not effective, placing temporary left and right ventricular assist devices may be necessary (see “Temporary Ventricular Assistance” in Section I of Chapter 5).

**Late Postoperative Care**

In contrast to many surgical procedures, CABG is simply one facet of treatment of patients with arteriosclerotic CAD. Late postoperative care relative to the basic disease—arteriosclerosis—is as important as late postoperative care relative to the bypassing conduits. This has been discussed in considerable detail in reports by the American College of Cardiology/American Heart Association (ACC/AHA) Joint Task Force Subcommittee on Coronary Artery Bypass Graft Surgery.\textsuperscript{A5,E2}

**Facilitation of Complete Recovery**

Facilitation of Complete Recovery

During the first 6 to 8 weeks of convalescence from CABG, patients often have a poor appetite, insomnia, emotional depression, loss of sexual ability, lack of desire to return to
work, and visual, memory, or intellectual deficits and other potentially disabling manifestations of the postoperative state. Studies have documented the transient nature of most of these phenomena. The responsible physician and staff should reassure the patient in this regard and help him or her return to usual activities as rapidly as possible. During this period, excessive medications may predispose the patient to symptoms, and their minimization is frequently beneficial.

A program of daily exercise should be started as soon as the patient leaves the hospital, with emphasis on regular walking for progressively longer periods. This program should be individualized, based primarily on knowledge of completeness of the operation and LV function, and on preoperative physical status of the patient. Formal programs of rehabilitation can be helpful in guiding some patients through the resumption of physical activity. Ultimately, and unless specifically contraindicated, patients should be encouraged to obtain some form of regular physical activity daily and to increase this over the months after operation. Patients who were active and gainfully employed before surgery are urged to return to full activity and employment as soon as possible and, except in unusual circumstances, no later than 2 to 3 months postoperatively.

Promotion of Graft Patency

Aspirin (325 mg · day⁻¹) should be administered immediately after operation and continued for at least 1 year postoperatively. Efficacy of this regimen has been well established, particularly when anastomoses have been made to smaller coronary arteries (Table 7-3). However, more recent studies indicate that a lower dose of 80 to 100 mg daily appears to be as effective as 325 mg. Ticlopidine, clopidogrel, or prasugrel can be used in patients who are allergic to or intolerant of aspirin.

Control of Risk factors for arteriosclerosis probably retards, and may even reverse to some extent, development of atherosclerosis in vein grafts. This is an added reason for recommendations in the text that follows.

Control of Risk Factors for Arteriosclerosis

A well-developed body of knowledge exists concerning risk factors for arteriosclerosis. The general consensus is that this knowledge should be focused on patients who have established CAD and who undergo CABG. Smoking must be stopped, and cessation must be emphasized to the patient even before operation. An appropriate body weight should be maintained, even if special dieting is required. Hypertension and saturated fats in the diet must be controlled, and serum lipids should be kept within proper levels through dietary measures and administration of specific medication if required.

RESULTS

Because CABG is probably the most completely studied operation in history, an enormous amount of information is available about outcomes. There is minimal value in presenting outcome simply as “survival” or “freedom from some unfavorable event” of a heterogeneous group of patients. Only risk-adjusted depictions are truly informative, as emphasized early by DeRouen, Detre, Green, Kouchoukos, and their colleagues.

This section makes no comparisons of outcomes after medical treatment or PCI. Instead, this information is presented later in this chapter under Indications for Operation, because such comparisons are the basis for these indications. Where appropriate, comparisons between CABG performed with and without CPB are presented.

Early (Hospital) Death

Risk of early (hospital) death has been extensively studied. Risk stratification models have been created to provide accurate prediction of operative risk for groups of patients

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**Table 7-3** Association of Late (1-Year) Graft Patency after Coronary Artery Bypass Grafting with Regimen of Pre/Postoperative Dipyridamole/Aspirin and with Coronary Artery Size

<table>
<thead>
<tr>
<th>Coronary Artery Internal Diameter</th>
<th>Dipyridamole and Aspirin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 2 mm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>1.5</td>
<td>1.5</td>
<td>128</td>
</tr>
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<td>2.0</td>
<td></td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>14</td>
</tr>
</tbody>
</table>

P[<sup>2</sup>χ] = .04

Key: CL, 70% confidence limits.

Modified from Chesebro and colleagues.
undergoing CABG (see “Risk Stratification” in Section VI of Chapter 6). Large databases have been established in single institutions and in multicenter studies, and analyses of these data have established the predictive power of certain preoperative variables. In an analysis of seven large datasets representing more than 172,000 patients, Jones and colleagues identified seven variables most predictive of early mortality:

- Older age (Fig. 7-28)
- Female gender
- Previous CABG
- Urgency of operation
- Increasing LV dysfunction
- Left main disease
- Increasing extent of coronary artery disease

The relative mortality risks of these variables are shown in Table 7-4 for six of the data sets.

Older age has consistently predicted operative risk after CABG (see Fig. 7-28). Female gender is also independently associated with increased operative risk. Previous CABG and emergency operation are associated with substantial increases in relative risk (2.0 or greater). Other variables associated with increased early mortality are recent (<30 days) Q-wave myocardial infarction and comorbidities (e.g., diabetes, metabolic syndrome, end-stage renal disease, valvular heart disease, chronic obstructive pulmonary disease, severe peripheral arterial disease, anemia, atrial fibrillation), and perhaps lack of use of the ITA.

In randomized clinical trials comparing on-pump and off-pump procedures, no difference in early mortality was observed, although Tarakji and colleagues have raised the possibility of decreased intermediate-term survival in their meta-analysis of randomized trials.

### Time-Related Survival

In general, after isolated CABG, approximately 98% of heterogeneous groups of patients survive at least 1 month, and 97%, 92%, 81%, and 66% survive 1, 5, 10, and 15 years or more, respectively (Fig. 7-29, A).

The hazard function for death has an early and rapidly declining phase that merges with a constant hazard phase at about 6 months, and this gives way to a gradually rising phase of hazard at about 1 year (Fig. 7-29, B). This rising phase probably results from closure of grafts, progression of native arterial disease, but mostly from comorbidities. This phase of hazard is particularly favorably affected by use of ITA grafts.

### Morbidity

Common postoperative complications that result in substantial morbidity and their management are discussed in Chapter 5. Several of these morbidities deserve special emphasis.

### Adverse Cerebral Outcomes

Postoperative neurologic deficits are an important cause of postoperative morbidity and mortality after CABG. Important neurologic injury occurs in up to 5% to 6% of patients who undergo CABG with CPB. In several randomized trials, a lower prevalence of neurologic injury was not observed among patients undergoing OPCAB procedures.

A multicenter study by Roach and colleagues of 2108 patients undergoing CABG with CPB documented adverse cerebral outcomes in 129 patients (6.1%). Type 1 deficits (major focal deficits, stupor, and coma) occurred in 3.1%, and type 2 deficits (deterioration in intellectual function or memory) in 3.0% of the patients. In addition to increased early mortality in these groups (21% for type 1 and 10% for type 2 deficits), hospital length of stay and likelihood of discharge to a nursing home were substantially increased compared with the remaining patients. Predictors of type 1 deficits included presence of proximal aortic arteriosclerosis, history of prior neurologic disease, use of intraaortic balloon pump, diabetes, hypertension, unstable angina, and older age.

Tarakji and colleagues differentiated intraoperative strokes from those occurring after awakening, finding that either operative or off-pump techniques that avoided manipulation of the arteriosclerotic aorta were associated with fewer intraoperative strokes.

### Mediastinitis

Deep sternal wound infection occurs in 1% to 4% of patients after CABG with CPB and is associated with increased mortality. Obesity is a risk factor for mediastinitis. Other factors associated with an increased prevalence of deep wound infection include diabetes, previous CABG, use of both ITAs, and duration of operation. Randomized trials have shown that off-pump CABG is not associated with a lower prevalence of sternal wound infection.

### Renal Dysfunction

In a multicenter study of renal dysfunction after CABG with CPB in 2222 patients, “dysfunction” was defined as a postoperative serum creatinine level of 2.0 mg · dL−1 or greater, or an increase of 0.7 mg · dL−1 or more from preoperative level. Renal dysfunction occurred in 171 (7.7%) patients.
Table 7-4  Relative Risks for Early Mortality after Coronary Artery Bypass Grafting in Six Large Data Sets

<table>
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<th></th>
<th>NNE (1)</th>
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<th>STS (3)</th>
<th>NYS (4)</th>
<th>CC (5)</th>
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<td>Vol nat</td>
<td>Man state</td>
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<td>SI</td>
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</tr>
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<td>Female gender</td>
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<td>1.52</td>
<td>1.63</td>
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<td>Prior heart operation</td>
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<td>3.1</td>
<td>3.73</td>
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<td>Left main disease (≥70%)</td>
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<td><strong>Urgency of Operation</strong></td>
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<td>Per 0.1-unit decrease</td>
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<td>2.89 (&lt;30%)</td>
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<td>NA</td>
<td>NA</td>
<td>4.06</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

Data from Eagle and colleagues.52

1Relative risk coefficient for age indicates additional mortality risk per year of age > 50 years.
2Age 60 vs. 50 years, 1.36; age 70 vs. 50 years, 2.53; age 80 vs. 50 years, 4.70.
3Among females: BSA 1.6 vs. 2.0, 1.26; BSA 1.8 vs. 2.0, 1.02; BSA 2.2 vs. 2.0, 1.20. Among males: BSA 1.6 vs. 2.0, 1.75; BSA 1.8 vs. 2.0, 1.20; BSA 2.2 vs. 2.0, 1.01. Female vs. male at BSA 1.8, 1.31.
4Three- vs. two-system disease.
5Urgent indicates that patients are required to stay in hospital but may be scheduled and operated on within a normal scheduling routine; emergency, ongoing cardiopulmonary resuscitation en route to operating room.

Key: AGH, Allegheny General Hospital; CC, Cleveland Clinic; Man, mandatory; multi reops, multiple reoperations; NA, not available; nat, national; NNE, Northern New England Cardiovascular Disease Study Group; NS, not significant; NYS, New York State's Cardiac Surgery Reporting System; reg, regional; SI, single institution; state, single state; STS, Society of Thoracic Surgeons National Cardiac Surgery Database; VA, Veterans Affairs Cardiac Surgery Database; Vol, voluntary.

and 30 (1.4%) required dialysis. Early mortality was 0.9% among patients who did not develop renal dysfunction, 19% in those with renal dysfunction who did not require dialysis, and 65% among those who required dialysis. Preoperative risk factors for renal dysfunction included advanced age, moderate to severe cardiac failure, previous CABG, diabetes, and preexisting renal disease.55 In two randomized trials, prevalence of postoperative renal failure was similar in on-pump and off-pump groups.66,52

**Modes of Death**

Most deaths early and late after CABG are from cardiac failure, which could be termed cardiac death (Table 7-5). A smaller proportion of deaths (about 15%) are sudden, considerably less than in the natural history of patients with CAD. Although it is difficult to be certain, about 25% of all deaths early and late after CABG are unrelated to the ischemic heart disease or the operation.

**Incremental Risk Factors for Premature Death**

Many patient-specific risk factors for death in patients with arteriosclerotic heart disease pertain to patients who have undergone CABG (see Box 7-1). In addition, procedural and institutional incremental risk factors affect outcome (Table 7-6).
Figure 7-29  Survival after coronary artery bypass grafting (CABG). A, Time-related survival in a heterogeneous group of patients. *Circles,* individual deaths, positioned along horizontal axis at time of death and along vertical axis according to Kaplan-Meier estimator; *vertical bars,* 70% confidence limits; *parentheses,* number of patients still being traced; *solid line* (not visible in some areas because of density of circles), nomogram of separately determined parametric survival; *dashed lines* enclose 70% confidence limits; *dot-dash-dot line,* survival of age-gender-ethnicity–matched general population. B, Hazard function for death in same group of patients. Note (1) early, rapidly declining phase; (2) constant phase, which elevates entire hazard function above baseline; and (3) slowly rising third phase. (Modified from Sergeant and colleagues. 124)

Table 7-5  Modes of Death after Coronary Artery Bypass Grafting

<table>
<thead>
<tr>
<th>Mode</th>
<th>No.</th>
<th>Percent of 545</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac</td>
<td>298</td>
<td>55</td>
</tr>
<tr>
<td>Failure*</td>
<td>216</td>
<td>40</td>
</tr>
<tr>
<td>Acute</td>
<td>145</td>
<td>27</td>
</tr>
<tr>
<td>Subacute</td>
<td>35</td>
<td>6</td>
</tr>
<tr>
<td>Chronic</td>
<td>36</td>
<td>7</td>
</tr>
<tr>
<td>Sudden</td>
<td>78</td>
<td>14</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>4</td>
<td>0.7</td>
</tr>
<tr>
<td>Cancer</td>
<td>90</td>
<td>17</td>
</tr>
<tr>
<td>Neurologic</td>
<td>53</td>
<td>10</td>
</tr>
<tr>
<td>Trauma</td>
<td>27</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary failure</td>
<td>19</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>thromboembolism</td>
<td>10</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Acute intraabdominal catastrophe</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Infection</td>
<td>5</td>
<td>0.9</td>
</tr>
<tr>
<td>Renal failure</td>
<td>3</td>
<td>0.6</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>Uncertain</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>545</td>
<td>100.7</td>
</tr>
</tbody>
</table>

Data from Sergeant and colleagues.229

*Cardiac failure, which could be termed cardiac death, is considered acute when it occurs within 3 days of an operation or a new myocardial infarction; subacute when it occurs between 3 days and 6 weeks of such events; and chronic when it occurs more than 6 weeks after an event that appears responsible for it, or when death is in the syndrome of chronic heart failure but is not preceded by an identified proximal previous event.

Table 7-6  Procedural Risk Factors for Death after Coronary Artery Bypass Grafting

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incomplete revascularization</td>
</tr>
<tr>
<td>Nonuse of internal thoracic artery to left anterior descending artery</td>
</tr>
<tr>
<td>( Longer) Global myocardial ischemic time interacting with method of myocardial management</td>
</tr>
<tr>
<td>( Longer) Cardiopulmonary bypass time</td>
</tr>
<tr>
<td>( Earlier) Date of operation</td>
</tr>
</tbody>
</table>

Institution where procedure is performed may also be a risk factor.

The Califf-Harrell nomogram and its conceptual bases are fundamental to understanding risk factors and outcome after interventional therapy21 (Fig. 7-30). Only patient risk factors summarized as “reversible ischemia” (see Box 7-1) can be neutralized by CABG (or PCI), and when neutralized, outcome is determined in large part by other risk factors. “Vessel stenoses neutralized” (see Fig. 7-30) depicts potential for improvement (“comparative benefit”) by interventional therapy because this possibility is determined by number of systems (vessels) stenosed. Actual improvement, or “comparative benefit,” is determined by the actual number of systems with important stenoses that are in fact neutralized by interventional therapy.

The depiction emphasizes that the greater the number and severity of patient-specific risk factors, the greater the comparative benefit (in terms of survival) of interventional therapy. At the same time, 5- or 10-year survival is less when patient risk factors are numerous. It also illustrates that the favorable effect of interventional therapy is difficult to demonstrate, even though present on conceptual grounds, in most patients with good LV function and few unfavorable risk factors.

A classic parsimoniously derived multivariable risk factor equation for death after CABG has been derived by
Use of CABG for primary reperfusion during Q-wave MI has a minimally unfavorable effect on time-related outcome (Fig. 7-31, D). In particular, events at some time after medical treatment (PCI) over medical treatment. Comparative benefit is difference in percent freedom from cardiovascular deaths after two treatments at some time. Patient’s position on horizontal axis conceptually is determined by sum of all patient risk factors, such that the higher the percent freedom from cardiovascular death, the fewer the risk factors in the particular patient. Comparative benefit, along vertical axis, is determined by interrelationship between patient’s position along horizontal axis and number of coronary arteries with stenoses completely neutralized by interventional therapy (isobars). Values of isobars are in fact hazard ratios that represent effect on comparative benefit of number of arteries with important stenosis in patients undergoing CABG, assuming all stenoses are neutralized by interventional therapy. Nomogram pertains when time (t) is 2 to 7 years (time of approximately proportional hazards) after CABG (or PCI) and when early risks of intervention (CABG or PCI) are negligible. Abstract equation is as follows:

\[
\text{Comparative benefit} = S_{\text{CABG}}(t) - S_{\text{m}}(t)
\]

where:

- \(S_{\text{CABG}}(t)\) is survival after CABG
- \(S_{\text{m}}(t)\) is survival with medical treatment
- \(t\) is time

Key: \(CABG\), Coronary artery bypass grafting; \(h\), hazard ratio; \(LM\), left main coronary artery; \(S_{\text{CABG}}\) survival after CABG; \(SD\), vessels diseased (stenosis > 50%); \(S_{\text{m}}\) survival with medical treatment; \(t\) time. (Modified from Califf and colleagues,\textsuperscript{41} and from Califf RM, Harrell FE Jr: personal communication; 1990.)

Figure 7-30  Nomogram of an equation describing comparative benefit of coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) over medical treatment. Comparative benefit is difference in percent freedom from cardiovascular deaths after two treatments at some time. Patient’s position on horizontal axis conceptually is determined by sum of all patient risk factors, such that the higher the percent freedom from cardiovascular death, the fewer the risk factors in the particular patient. Comparative benefit, along vertical axis, is determined by interrelationship between patient’s position along horizontal axis and number of coronary arteries with stenoses completely neutralized by interventional therapy (isobars). Values of isobars are in fact hazard ratios that represent effect on comparative benefit of number of arteries with important stenosis in patients undergoing CABG, assuming all stenoses are neutralized by interventional therapy. Nomogram pertains when time (t) is 2 to 7 years (time of approximately proportional hazards) after CABG (or PCI) and when early risks of intervention (CABG or PCI) are negligible. Abstract equation is as follows:

\[
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\]

where:

- \(S_{\text{CABG}}(t)\) is survival after CABG
- \(S_{\text{m}}(t)\) is survival with medical treatment
- \(t\) is time

Key: \(CABG\), Coronary artery bypass grafting; \(h\), hazard ratio; \(LM\), left main coronary artery; \(S_{\text{CABG}}\) survival after CABG; \(SD\), vessels diseased (stenosis > 50%); \(S_{\text{m}}\) survival with medical treatment; \(t\) time. (Modified from Califf and colleagues,\textsuperscript{41} and from Califf RM, Harrell FE Jr: personal communication; 1990.)

Blackstone, working with Sergeant and colleagues\textsuperscript{16,24,28} (Table 7-7). Actual risk factors are similar to those derived from other experiences.

Strength and shape (time of maximal effect) of risk factors are best determined by nomograms that also have the advantage of presenting risk-adjusted depictions (see Chapter 6). Number of systems with important stenoses is a weak risk factor for death after CABG in the first 5 years (Fig. 7-31, A) when revascularization is complete and the ITA is used for the LAD graft. Also, number of diseased vessels and even left main coronary artery stenosis, as well as number of distal anastomoses, are not risk factors for hospital death when an adequate operation has been performed.

Pre-CABG LV function, expressed as ejection fraction, has a powerful effect on time-related outcome (Fig. 7-31, B-C), particularly when it is low.\textsuperscript{8,34} Surprisingly, some patients with low EF have none of the symptoms of chronic heart failure. Presence of this syndrome, often associated with secondary mitral regurgitation (see Chapter 10), increases the risk above that for low EF alone.\textsuperscript{11,18,66}

Unstable angina has a minimally unfavorable effect on survival (Fig. 7-31, D).

Some patients undergo CABG soon after an acute MI. Use of CABG for primary reperfusion during Q-wave MI has been largely superseded by thrombolysis and PCI. Early risks of CABG are increased only when operation is performed for acute hemodynamic deterioration after an acute (usually Q-wave) MI or for any reason within about 8 days of a Q-wave infarction.\textsuperscript{50,6,16} Early mortality in patients operated on for cardiogenic shock after an acute MI also depends on other risk factors and largely on methods of treatment. When intense resuscitative measures such as intraaortic balloon pumping stabilize the hemodynamic state before operation, early mortality may be as low as 5%.\textsuperscript{644} When cardiogenic shock is present until operation or until establishment of CPB, mortality is higher.\textsuperscript{24} However, using best available methods of myocardial management intraoperatively (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3) and with intensive postoperative care, including ventricular assist devices when needed (see “Treatment of Low Cardiac Output” in Section I of Chapter 5), at least 50% of patients survive the early postoperative period.\textsuperscript{8,14,15,15,15} Late survival depends on prevalence of other risk factors.

Nonuse of the ITA as a bypass graft to the LAD is a strong procedural risk factor and the basis for its near-routine use (Fig. 7-32) (see “Internal Thoracic Arteries” under Graft Patency later in this chapter). Older age at operation docs
<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Hazard Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
</tr>
<tr>
<td><strong>Patient Risk Factors</strong></td>
<td></td>
</tr>
<tr>
<td>DEMOGRAPHIC</td>
<td></td>
</tr>
<tr>
<td>(Older) Age</td>
<td>•</td>
</tr>
<tr>
<td>(Younger) Age</td>
<td>•</td>
</tr>
<tr>
<td>(Lighter) Weight</td>
<td>•</td>
</tr>
<tr>
<td>(Higher) Weight/height ratio</td>
<td>•</td>
</tr>
<tr>
<td>SYMPTOMS OF REVERSIBLE ISCHEMIA</td>
<td></td>
</tr>
<tr>
<td>(Higher) Canadian angina class</td>
<td>•</td>
</tr>
<tr>
<td>No angina</td>
<td>•</td>
</tr>
<tr>
<td>(Higher) Unstable angina grade</td>
<td>•</td>
</tr>
<tr>
<td>CARDIAC COMORBIDITY</td>
<td></td>
</tr>
<tr>
<td>Mitral regurgitation (mild)</td>
<td>•</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td></td>
</tr>
<tr>
<td>Chronic atrial fibrillation</td>
<td></td>
</tr>
<tr>
<td>Ventricular tachycardia/fibrillation</td>
<td></td>
</tr>
<tr>
<td>Cardiac pacemaker</td>
<td></td>
</tr>
<tr>
<td>NONCARDIAC COMORBIDITY</td>
<td></td>
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<tr>
<td>Overweight</td>
<td>•</td>
</tr>
<tr>
<td>History of vascular disease</td>
<td>•</td>
</tr>
<tr>
<td>History of cerebrovascular disease</td>
<td></td>
</tr>
<tr>
<td>Previous vascular surgery (noncarotid)</td>
<td></td>
</tr>
<tr>
<td>History of smoking</td>
<td>•</td>
</tr>
<tr>
<td>(Lower) 1-second expiratory rate (% of normal)</td>
<td>•</td>
</tr>
<tr>
<td>History of renal failure</td>
<td>•</td>
</tr>
<tr>
<td>On renal dialysis</td>
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<tr>
<td>Serum creatinine &gt; 2.5 mg · dL⁻¹</td>
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<tr>
<td>Hypertensive</td>
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<tr>
<td>(Higher, younger) Grade of diabetes and age</td>
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<td>History of malignancy</td>
<td>•</td>
</tr>
<tr>
<td>History of hepatic disease</td>
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</tr>
<tr>
<td>(Higher) Triglyceride level</td>
<td>•</td>
</tr>
<tr>
<td>LEFT VENTRICULAR FUNCTION</td>
<td></td>
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<tr>
<td>Cardiogenic shock</td>
<td>•</td>
</tr>
<tr>
<td>(Better) Clinical status</td>
<td></td>
</tr>
<tr>
<td>(Lower) Ejection fraction (lower) and</td>
<td>•</td>
</tr>
<tr>
<td>Date of operation (earlier)</td>
<td></td>
</tr>
<tr>
<td>(Greater) Limitation by heart failure</td>
<td>•</td>
</tr>
<tr>
<td>CORONARY DISEASE</td>
<td></td>
</tr>
<tr>
<td>(Earlier) 90% left main stenosis and</td>
<td>•</td>
</tr>
<tr>
<td>Date of operation</td>
<td>•</td>
</tr>
<tr>
<td>(Greater) Number of diseased systems</td>
<td>•</td>
</tr>
<tr>
<td>Three-system disease</td>
<td>•</td>
</tr>
</tbody>
</table>

*Continued*
PART II Ischemic Heart Disease

Table 7-7 Incremental Risk Factors for Death after Primary Isolated Coronary Artery Bypass Grafting—cont’d

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Hazard Phase</th>
<th>Early</th>
<th>Constant</th>
<th>Late</th>
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</thead>
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<tr>
<td><strong>Procedural Risk Factors</strong></td>
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<td></td>
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<tr>
<td><strong>CORONARY OPERATION</strong></td>
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<tr>
<td>Grafting to LAD</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of arterial grafts</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of only arterial grafts in single-system disease</td>
<td>• •</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of patch grafts</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Higher) Ratio of distals to conduits</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(More) Coronary endarterectomies</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Higher) Proportion of distals to small vessels</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete revascularization</td>
<td>•</td>
<td></td>
<td></td>
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<tr>
<td><strong>CONCOMITANT PROCEDURES</strong></td>
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<td></td>
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<tr>
<td>Left ventricular incision or plication</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>INSTITUTIONAL EXPERIENCE</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>One surgeon</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Lower) Preceding year per surgeon volume</td>
<td>•</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

Data from Sergeant and colleagues24; KU Leuven, 1971-1992; n = 9600.
Key: LAD, Left anterior descending coronary artery.

Figure 7-31 Nomograms of specific solutions of KU Leuven multivariable risk factor equation for death after coronary artery bypass grafting (CABG), illustrating strength and shape of certain risk factors for death (see Table 7-7).24 In all figures, dashed lines represent 70% confidence limits. A, Risk-adjusted effect on survival after CABG of number of stenosed systems. B, Risk-adjusted effect of moderate and severe left ventricular dysfunction. C, Risk-adjusted effect of left ventricular ejection fraction (EF), continuously represented along horizontal axis, on survival to 5, 10, and 20 years after operation. D, Risk-adjusted effect of pre-CABG unstable angina, both after “cooling” and when refractory to treatment, compared with moderately severe but stable angina.
The hazard function for return of angina, although also having a constant phase, is dominated by an early phase that peaks at about 3 months after operation and by a late, steadily rising phase that becomes evident about 3 years postoperatively (Fig. 7-33, B). The early-peaking phase is probably most often due to incomplete revascularization, as well as early graft closure. Therefore, return of angina early after CABG is an indication for restudy of the coronary circulation.

The late-rising phase of hazard for return of angina is due to progression of native-vessel disease and narrowing or closure of one or more grafts.

The most interesting aspect of risk factors for return of angina is that nonuse of the ITA has only a mild effect, at least in the KU Leuven (Katholieke Universiteit, Leuven, Belgium) experience but some studies suggest that it does. Risk of sternal wound complication is increased by the double-ITA procedure in obese or diabetic patients. Older age as a risk factor for death is receiving increasing attention as the population ages. Although hospital stay is longer and early complications more frequent in elderly patients, highly favorable results can be obtained with CABG, even in those over age 75. This situation has been well summarized in the reports by the ACC/AHA Joint Task Force Subcommittee on Coronary Artery Bypass Graft Surgery.

Return of Angina

Evidence from evaluation of symptoms and from graded exercise testing shows that CABG usually relieves angina. However, return of angina is the most common post-CABG ischemic event. In a heterogeneous group of patients, only about 60% were free of angina 10 years after CABG (Fig. 7-33, A).
Table 7-8  Incremental Risk Factors, Based on Patient, Procedure, and Institutional Variables, for Return of Angina, without Infarct or Death the Same Day, after Primary Isolated Coronary Artery Bypass Grafting

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Hazard Phase</th>
<th></th>
<th>Risk Factors</th>
<th>Hazard Phase</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Early</td>
<td></td>
<td></td>
<td>Late</td>
</tr>
<tr>
<td><strong>Patient Risk Factors</strong></td>
<td></td>
<td></td>
<td><strong>Hazard Phase</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEMOGRAPHIC</td>
<td></td>
<td></td>
<td>Absence of overweight now or previously and age (interaction)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger age</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>ANGINAL STATUS</td>
<td></td>
<td></td>
<td>Higher preoperative triglyceride level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Longer duration of angina history</td>
<td></td>
<td>•</td>
<td>History of renal failure</td>
<td></td>
<td></td>
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<tr>
<td>Higher angina class</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable ST segment at operation</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Clinically positive cycloergometric test and</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Electrocardiogram negative exercise test (interaction)</td>
<td></td>
<td>•</td>
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<tr>
<td>LEFT VENTRICULAR FUNCTION</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Absence of preoperative anterior or septal infarct</td>
<td></td>
<td>•</td>
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<tr>
<td>CORONARY DISEASE DISTRIBUTION</td>
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</tr>
<tr>
<td>Lesser stenosis of left main coronary artery</td>
<td></td>
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<tr>
<td>Multisystem coronary artery disease</td>
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<tr>
<td>COMORBIDITY (CARDIAC)</td>
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<tr>
<td>Left ventricular hypertrophy</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Aortic valve stenosis (mild)</td>
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<td>•</td>
<td></td>
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<td></td>
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<tr>
<td>COMORBIDITY (VASULAR)</td>
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</tr>
<tr>
<td>History of peripheral arterial disease</td>
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<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of noncarotid vascular operation</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcified ascending aorta</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>COMORBIDITY (NONCARDIAC, NONVASCULAR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertensive</td>
<td></td>
<td>•</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher diabetic grade</td>
<td></td>
<td>•</td>
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<td></td>
</tr>
</tbody>
</table>

**Procedural Risk Factors**

| DETAILS OF CONDUIT USED                          |              |          |                                                  |              |          |
| Nonuse of vein grafts only                       |              | •        |                                                  |              |          |
| Use of vein grafts to the LAD system             |              | •        |                                                  |              |          |
| Use of patch grafts                              |              | •        |                                                  |              |          |

| DETAILS OF DISTAL ANASTOMOSES                    |              |          | Proportion of total distal anastomoses to anastomosed vessels ≤1 mm |              |          |
| Nongrafting to the LAD                           |              | •        |                                                  |              |          |
| Ratio of number of arterial anastomoses to total number of distal anastomoses |              | •        |                                                  |              |          |

| COMPLETENESS OF REVASCULARIZATION                |              |          | Incomplete revascularization and (interaction)   |              |          |
| Use of internal thoracic artery grafts only      |              | •        |                                                  |              |          |

| OTHER SURGICAL DETAILS                           |              |          | Number of coronary endarterectomies             |              | •        |

**Institutional Risk Factors**

| SURGEONS                                         |              |          |                                                  |              |          |
| High risk for angina return surgeon              |              | •        |                                                  |              |          |
| Low risk for angina return surgeon               |              | •        |                                                  |              |          |

| EXPERIENCE                                       |              |          | Later date of operation                         |              |          |

Data from Sergeant and colleagues.\textsuperscript{276} KU Leuven, 1971-1992; \( n = 9600 \).

Key: LAD, Left anterior descending coronary artery.

Figure 7-34  Effect of use of internal thoracic artery (ITA) on return of angina after coronary artery bypass grafting, illustrated in nomograms of specific solutions of multivariable risk factor equations represented by Table 7-8.  A, Time-related, risk-adjusted freedom from return of angina.  B, Hazard function for return of angina. (From Sergeant and colleagues.\textsuperscript{276})
Patient incremental risk factors for return of angina are not powerful compared with those for death. This implies that return of angina is inherent in stenotic arteriosclerotic CAD. Procedural risk factors for return of angina are likewise not very powerful, as seen in the case of the ITA. The inference again may be that the process leading to return of angina is inherent in arteriosclerotic CAD.

Myocardial Infarction

Perioperative MI, usually defined by appearance of new Q waves in the ECG or elevation of serum levels of myocardial biomarkers, is most often related to inappropriate myocardial management, but can also result from technical problems or incomplete revascularization. Prevalence of MI is highly variable and depends on the criteria used, but it is approximately 2.5% to 5%.\(^{19,21,17,33}\) Perioperative infarction, when quantitatively more than trivial, is a risk factor for later death.\(^{8,3,39}\)

Including perioperative cases, MI is relatively uncommon after CABG, with 94% of patients in the KU Leuven experience free of infarction for at least 5 years, and 73% for at least 15 years (Fig. 7-36). However, the hazard function for MI begins to increase at about 4 years postoperatively. Risk factors for the first post-CABG infarction (excluding those that occur perioperatively) are relatively few (Table 7-9).

Survival appears to be considerably adversely affected by occurrence of post-CABG MI\(^{14,13,35}\) (Fig. 7-37). Furthermore, time-related freedom from subsequent post-CABG MI declines with each MI episode (Fig. 7-38).

Sudden Death

Time-related prevalence of sudden death is low after CABG; this may be an important factor in the survival benefit derived from CABG.\(^{18}\) In the KU Leuven experience, 97% of patients were free of sudden death 10 years after CABG (Fig. 7-39, A). The late phase of the hazard function rises more slowly than in other post-CABG ischemic events\(^{29}\) (Fig. 7-39, B). Not unexpectedly, poor LV function before CABG is statistically the most significant risk factor for sudden death.
Table 7-9  Incremental Risk Factors, Based on Patient, Procedure, and Institutional Variables, for Freedom from First Infarct after Primary Isolated Coronary Artery Bypass Grafting

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Hazard Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
</tr>
<tr>
<td><strong>Patient Risk Factors</strong></td>
<td></td>
</tr>
<tr>
<td>DEMOGRAPHIC</td>
<td></td>
</tr>
<tr>
<td>(Younger)</td>
<td>Age</td>
</tr>
<tr>
<td>(Taller)</td>
<td>Height of patient</td>
</tr>
<tr>
<td>(Shorter)</td>
<td>Height of patient</td>
</tr>
<tr>
<td>ANGINAL STATUS</td>
<td></td>
</tr>
<tr>
<td>(Higher)</td>
<td>Previous infarct within 30 days of operation</td>
</tr>
<tr>
<td>(Lower)</td>
<td>Previous infarct within 30 days of operation</td>
</tr>
<tr>
<td>(Lower)</td>
<td>Stable angina before operation</td>
</tr>
<tr>
<td>(Lower)</td>
<td>Clinic or ECG + result of preoperative cycloergometric test</td>
</tr>
<tr>
<td></td>
<td>Unstable ST segment, but not acute infarct</td>
</tr>
<tr>
<td>LEFT VENTRICULAR FUNCTION</td>
<td></td>
</tr>
<tr>
<td>(Lower)</td>
<td>Previous inferior infarct</td>
</tr>
<tr>
<td>CORONARY DISEASE DISTRIBUTION</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Two- or three-system disease</td>
</tr>
<tr>
<td>(Lower)</td>
<td>Higher percent stenosis of left main</td>
</tr>
<tr>
<td>COMORBIDITY (CARDIAC)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Aortic valve regurgitation</td>
</tr>
<tr>
<td></td>
<td>Concomitant planned pacemaker insertion</td>
</tr>
<tr>
<td>COMORBIDITY (VASCULAR)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>History of peripheral arterial disease</td>
</tr>
<tr>
<td></td>
<td>History of abdominal aortic disease</td>
</tr>
<tr>
<td></td>
<td>Cerebral, noncarotid, vessel disease</td>
</tr>
<tr>
<td>COMORBIDITY (NONCARDIAC, NONVASCULAR)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BUN &gt; 50 mg/dL</td>
</tr>
<tr>
<td>(Lower)</td>
<td>Pulmonary vital capacity as percent of normal</td>
</tr>
<tr>
<td>(Higher)</td>
<td>Grade of diabetes</td>
</tr>
<tr>
<td>(Higher)</td>
<td>Preoperative cholesterol level</td>
</tr>
<tr>
<td><strong>Procedural Risk Factors</strong></td>
<td></td>
</tr>
<tr>
<td>GENERAL TECHNICAL ASPECTS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Patch graft</td>
</tr>
<tr>
<td></td>
<td>Coronary endarterectomy</td>
</tr>
<tr>
<td></td>
<td>Incomplete revascularization</td>
</tr>
<tr>
<td>ARTERIAL GRAFTING</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Absence of at least one arterial graft</td>
</tr>
<tr>
<td></td>
<td>Absence of only arterial grafts and single-system disease</td>
</tr>
<tr>
<td></td>
<td>Nonarterial graft to the LAD</td>
</tr>
<tr>
<td><strong>Institutional Risk Factors</strong></td>
<td></td>
</tr>
<tr>
<td>SURGEONS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lower-risk surgeons for first infarct</td>
</tr>
</tbody>
</table>

Data from Sergeant and colleagues; KU Leuven, 1971 to 1992; \( n = 9600 \).
Key: BUN, Blood urea nitrogen; ECG, electrocardiogram; LAD, left anterior descending coronary artery.
Figure 7-38  Freedom from myocardial infarction after coronary artery bypass grafting (CABG) exclusive of perioperative infarction, according to number of previous post-CABG episodes of infarction. Time zero is time of CABG in depiction of freedom from first post-CABG infarction; it is time of first post-CABG infarction in depiction of time-related probability of a second post-CABG infarction; and so on. Format is as in Fig. 7-29. (Depictions from analyses of KU Leuven experience, 1971 to July 1987; n = 5880. 43,45,126)

<table>
<thead>
<tr>
<th>Years</th>
<th>Percent free of post-CABG infarct</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/12</td>
<td>100</td>
</tr>
<tr>
<td>1</td>
<td>99.8</td>
</tr>
<tr>
<td>5</td>
<td>99</td>
</tr>
<tr>
<td>10</td>
<td>97</td>
</tr>
<tr>
<td>15</td>
<td>91</td>
</tr>
</tbody>
</table>

Figure 7-39  Sudden death after coronary artery bypass grafting. Format is as in Fig. 7-26. A, Freedom from sudden death. B, Hazard function. (From Sergeant and colleagues. 129)

<table>
<thead>
<tr>
<th>Years</th>
<th>Hazard (×1000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/12</td>
<td>0.20</td>
</tr>
<tr>
<td>1</td>
<td>0.20</td>
</tr>
<tr>
<td>5</td>
<td>0.21</td>
</tr>
<tr>
<td>10</td>
<td>0.47</td>
</tr>
<tr>
<td>15</td>
<td>1.3</td>
</tr>
</tbody>
</table>

(Table 7-10). A patient with a preoperative EF of 65% has only a small probability of dying suddenly within 15 years, whereas a patient with EF of 25% before CABG has a 15% probability of sudden death within that period. 429 (Fig. 7-40).

Failure to Work

Time-related freedom from failure to work has been less well documented than for other outcome events. Its time course is probably similar to that of freedom from angina. Patients who are free of angina after CABG are more likely to be working than those with angina. 449

A common belief is that CABG does not improve prevalence of gainful employment among patients with ischemic heart disease, 47,113,114,570 but this has not been a universal finding. 123,445 Failure to take into account the differing prevalences of risk factors for failure to work after CABG explains many of the discrepancies in results. 444 Patients working before CABG have the highest probability of continued employment after operation. 47,549 Under “favorable circumstances” (as defined by risk factors listed in Table 7-11), more than 80% of patients not working at the time of CABG are working 1 year later; 20% or fewer are working after CABG when the risk factors are “unfavorable.” 420

Failure to Work

Unsatisfactory Quality of Life

Even though unsatisfactory quality of life after CABG is one of the most important unfavorable outcome events, quantifying it is difficult because it is a composite of at least three factors: (1) freedom from limiting angina or heart failure; (2) reasonable freedom from need for medication, rehospitalization, and reintervention; and (3) preservation of a reasonable exercise capacity. Most surviving patients have a satisfactory quality of life early after CABG, but the probability of retaining this gradually begins to decline after about 5 years. 440 Rate of decline is probably similar to that of freedom from angina.
Neurobehavioral and Neurologic Outcomes

Unrelated to cardiac aspects of CABG, the damaging effects of CPB usually required for operation are postulated to result in neurobehavioral disturbances and decline in cognitive function in some patients (see “Neuropsychological Subsystem” in Section I of Chapter 5). These disturbances are sufficiently mild that they might not be apparent unless patients are tested specifically for them. Their prevalence has been reduced by incorporating appropriate filters into the arterial tubing from the pump-oxygenator to the patient. As many as 75% of patients may exhibit these subtle defects when tested 8 days after CABG, but by 3 to 6 months postoperatively that proportion drops to only about 10% to 30%. Prevalence is unfavorable affected by preoperative and postoperative anxiety and depression and by older age. Only rarely are patients aware of or handicapped by these defects. Of interest, decline in cognitive function occurs in up to 45% of patients who undergo major noncardiac operations and also in patients with CAD who do not undergo CABG.

Gross neurologic defects, usually in the form of transient or permanent sequelae of strokes, are more serious but

Table 7-10 Incremental Risk Factors for Sudden Death after Primary Isolated Coronary Artery Bypass Grafting (Events = 78)

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Hazard Phase</th>
<th>Constant</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Risk Factors</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ANGINA</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>Other than stable angina</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>(Longer) Duration of anginal symptoms</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>DISTRIBUTION OF CORONARY ARTERY DISEASE</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>Three-system disease</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>Absence of left main disease &gt; 50%</td>
<td></td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>ARTERIOSCLEROTIC DISEASE</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>(Poorer) Quality of aortic anastomotic sites</td>
<td></td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>LEFT VENTRICULAR FUNCTION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Lower) Ejection fraction</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
<tr>
<td>PROCEDURAL RISK FACTOR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incomplete revascularization</td>
<td>(Longer)</td>
<td></td>
<td>•</td>
</tr>
</tbody>
</table>

Data from Sergeant and colleagues; KU Leuven, 1971 to July 1987; \( n = 5880 \).

Figure 7-40 Nomogram of specific risk-adjusted solution of multivariable equation for sudden death after coronary artery bypass grafting (CABG), illustrating effect of pre-CABG ejection fraction. Format is as in Fig. 7-31. (From Sergeant and colleagues.)

Table 7-11 Risk Factors for Time-Related Failure to Work after Coronary Artery Bypass Grafting

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Age at operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Older)</td>
<td>(Less)</td>
</tr>
<tr>
<td>Preoperative Work Conditions</td>
<td>Physical effort in job</td>
</tr>
<tr>
<td>(More)</td>
<td>(Less)</td>
</tr>
<tr>
<td>(Longer)</td>
<td>(Lower)</td>
</tr>
<tr>
<td>Clinical Status</td>
<td>Duration of preoperative angina</td>
</tr>
<tr>
<td>(Longer)</td>
<td>(Greater)</td>
</tr>
<tr>
<td>Aggressiveness of Atherosclerotic Process</td>
<td>Severity of preoperative angina</td>
</tr>
<tr>
<td>(More)</td>
<td>Peripheral arterial disease</td>
</tr>
<tr>
<td>Coexisting Disease</td>
<td>Alcohol intake</td>
</tr>
<tr>
<td>(More)</td>
<td>(Earlier)</td>
</tr>
<tr>
<td>Surgical Factor</td>
<td>(Later)</td>
</tr>
<tr>
<td>Postoperative Factors</td>
<td>Date of operation</td>
</tr>
<tr>
<td>(Shorter)</td>
<td>(Absence)</td>
</tr>
</tbody>
</table>

Data from Boulay and colleagues and Varnauskas.
Improvement in segmental wall motion 12 months after CABG has been observed even in areas of scarring from previous MI. Brundage and colleagues showed that 19 of 29 LV wall segments with asynergy at rest preoperatively had improved function, and some even had normal function late postoperatively. This finding supports the concept that viable muscle cells, which may be hibernating, are scattered through hypokinetic and, at times, akinetic and dyskinetic segments, and that wall motion in such segments can be improved by CABG. When segmental wall contraction does not occur after CABG, incomplete revascularization is the cause in some patients.

When preoperative global LV dysfunction is severe (EF < 30%), myocardial scarring is usually greater and usually limits recovery of LV function. In some patients, however, improvement in regional and global LV function occurs with CABG in this setting, and symptoms of pulmonary venous hypertension may regress. Several studies confirm that preoperatively depressed resting global LV systolic function (estimated by EF or dP/dt) is less depressed as early as 2 weeks after CABG. When this improvement fails to occur, incomplete revascularization is usually found. Hellman and colleagues have demonstrated, in a slightly different setting, that 16 of 19 post-CABG patients with preoperative resting EFs of less than 40% showed similar or increased EFs with exercise early postoperatively (±2 weeks) and no deterioration of regional wall motion. This finding supports the concept that postoperative exercise improves scarred myocardium. When segmental wall contraction does not occur after CABG, incomplete revascularization is the cause in some patients.

Use of Medication

Almost all studies report a decrease in use of vasodilators and β-blocking agents after CABG. The cooperative randomized study by the European Coronary Surgery Study Group, for example, found about 70% of patients randomized to medical treatment taking β-blockers during the first 3 years of follow-up in contrast to 25% of surgical patients. In the CASS trial, also randomized, surgically treated patients used fewer antianginal medications at 5 years than patients treated medically. By 10 years, however, the difference was likely due to chance.

Functional Capacity

Maximal exercise capacity of patients is improved by CABG, and ECG abnormalities during exercise are usually importantly reduced. Degree of recovery and ultimate exercise capacity reached depend on preoperative LV function, graft patency, and completeness of revascularization. Increase in functional capacity, as evidenced by an increase in cardiac output with exercise postoperatively, is greater in patients with complete revascularization (26% vs. 6%; P = .0001). Maximal exercise capacity generally is improved more by CABG than by medical treatment, at least for 3 to 10 years. The mechanisms of improvement in functional capacity after CABG are complex. Improvements in resting and stress LV function greatly contribute to the improved functional capacity (see next subheading). However, Serruys and colleagues found that an increase in maximal heart rate, presumably secondary to increased myocardial blood flow, is also an important determinant of increased functional capacity.

Left Ventricular Function

Resting Perfusion

Resting regional perfusion defects (at least in patients with unstable angina) are improved after CABG in at least 65% of patients, indicating that preoperative resting perfusion defects were caused at least in part by ischemia; that is, scarred areas (if present) contained considerable amounts of viable muscle. Most patients who show no improvement commonly have occluded grafts to the area. Wainwright and colleagues demonstrated that resting regional myocardial perfusion defects usually persist in areas supplied by ungrafted vessels (incomplete revascularization).

Left ventricular wall segments that are hypokinetic, akinetic, or even dyskinetic at rest preoperatively often have improved systolic function after CABG. This is associated with increased regional myocardial perfusion. Improvement in segmental wall motion 12 months after CABG.
**Ventricular Arrhythmias**

Successful CABG with relief of myocardial ischemia and its symptoms generally does not decrease frequency or severity of exercise-induced or resting ventricular arrhythmias, including ventricular tachycardia and fibrillation, although reports to the contrary exist. This lack of favorable effect occurs because areas of ventricular scarring, rather than areas of myocardial ischemia, appear to be essential to arrhythmia development.

Failure of simple CABG to abolish serious ventricular electrical instability in most patients is particularly unfortunate because exercise-induced ventricular tachycardia or ventricular fibrillation carries a poor prognosis in patients with CAD. Sudden death is one mode of death late postoperatively. Therefore, when operation is contemplated in patients with important intractable ventricular tachyarrhythmias, consideration should be given to implantation of a cardioverter-defibrillator (ICD) or procedures directed specifically at the ventricular arrhythmia, even in the absence of LV aneurysm (see Chapter 16).

Exceptions to these general statements are the few patients without ventricular scars or aneurysm in whom life-threatenning ventricular arrhythmias occur purely from reversible LV myocardial ischemia. CABG can relieve the arrhythmic tendency in these patients.

A study of 900 patients with depressed LV function (EF < 36%) and abnormalities on resting signal-averaged ECGs suggested increased risk for postoperative ventricular arrhythmias. In the Coronary Artery Bypass Graft Patch Trial, 454 patients were randomized to CABG and 446 to CABG plus ICD. During an average follow-up of 32 months, there was no evidence of improved survival among the patients in whom an ICD was implanted.

**Coronary Flow Reserve**

CABG is usually successful in improving coronary flow reserve (ability to increase flow in response to increased myocardial oxygen demand or pharmacologic vasodilatation). Surprisingly, coronary flow reserve returns to normal levels in many patients. This subject has been reviewed in detail by Wilson and colleagues. Flow reserve has been obtained from measurements made in the operating room after CABG and has been confirmed in postoperative patients. Ability to increase coronary flow is absent when there is a stenotic coronary lesion beyond the graft.

In general, a patent anastomosis between a graft and a coronary artery perfuses only that segment of myocardium to which the native artery has supplied blood. However, about 25% of grafts distribute blood well beyond the segment of myocardium that would have been expected to be supplied by the native vessel. Often the area unexpectedly perfused by the graft is in the distribution of an occluded native vessel to which there is an obstructed graft. Importantly, segmental contractility is often improved postoperatively in the unexpectedly perfused area. This phenomenon probably explains the finding of a functionally excellent result despite presence of one or two occluded grafts.

Not unexpectedly, in the few studies done late postoperatively, flow is greatest in vein grafts to the LAD system. Using a radiographic densitometric method, Hamby and colleagues found at 2 weeks after operation a mean flow of 79 mL·min⁻¹ in grafts to the LAD (range, 39-179) and 65 and

![Figure 7-41 Relationship between change in saphenous vein bypass graft flow and change in diameter between early (2 weeks) and late (average 1.5 years) postoperative study by radiographic methods. In general, decrease in diameter correlates with decrease in flow. Key: CIRC, Circumflex coronary artery; LAD, left anterior descending coronary artery; RCA, right coronary artery. (From Weisz and colleagues.)](image)

68 mL·min⁻¹ in those to the RCA and Cx artery, respectively. Flow through patent grafts during the early postoperative period is not directly related to graft size measured by cineangiographic techniques, and is presumably determined primarily by size of the arterial bed distal to the anastomosis.

An average of 2.5 years later, about 35% of vein grafts showed an important (average 45%) reduction in flow compared with early postoperatively. Thirty-five percent showed only a mild decrease during this period, and 30% showed no change. Such reductions of flow probably result largely from morphologic changes in the graft; thus, Weisz and colleagues found that change in graft flow was associated with a similar directional change in graft caliber (Fig. 7-41).

Although concern has been expressed about flow capabilities of the ITA as a bypass graft, the bulk of evidence supports the ability of this vessel to supply a normal coronary flow reserve to a LAD with distal branches that are free of disease. This evidence has been well summarized by Hodgson and colleagues, who have also shown that adequate coronary flow reserve is provided when the ITA is used for sequential grafting.

Separate ITA grafts can provide adequate flow to the entire left coronary system.

**Graft Patency**

*Internal Thoracic Arteries*

The ITA has proved an excellent conduit for use in CABG. About 90% to 95% of left ITAs whose distal end has been anastomosed end-to-side to the LAD are patent 10 to 20 years after operation (Fig. 7-42), and closure after that time is uncommon. However, up to 10% of patent grafts have stenoses late postoperatively. Accumulated information strongly suggests that most of the stenoses do not progress to occlusion. Use of the
ITA as a free graft from aorta to LAD provides patency almost as high as with an in situ graft. Favorable performance of the ITA when anastomosed to the LAD is partly related to continued function of its endothelial cells. Endothelium-derived relaxing factor and prostacyclin are produced by human ITAs, which may be an important factor in the high patency of ITAs and their excellent function as bypassing conduits. In addition, the ITA, when used for CABG as well as in its native position, has been shown to resist development of arteriosclerosis. Intimal hyperplasia develops in the ITA graft, however, and may be a cause of stenosis. Other factors contributing to occlusion or stenosis (including the “string sign”) of ITA conduits include mild target stenosis, competitive flow, and sequential grafting.

Another factor favorable to ITA patency is its grafting to the LAD, which has large runoff through the diagonal and septal branches. In support of this, ITA grafts to vessels other than the LAD have lower patency that may not be substantially different from that of vein grafts.

Use of bilateral ITA grafts has been favored by some groups, and evidence exists that use of both ITAs enhances survival of some subgroups of patients. Of interest, an analysis of the Society of Thoracic Surgeons database of 540,000 patients undergoing CABG between 2002 and 2005 indicated that bilateral ITA grafts were used in only 4.0%. Wound complications are more prevalent when bilateral ITA grafting is performed, particularly in obese and diabetic patients. Extensive surgical procedures may be required to treat them. Decreased sternal perfusion has been demonstrated after ITA harvesting using the pedicle technique. Skeletonization of the ITA results in greater sternal perfusion than the pedicle technique and may be associated with fewer sternal wound complications. A particularly beneficial effect has been observed in diabetic patients.

**Other Arterial Grafts**

The radial artery, right gastroepiploic artery, and inferior epigastric artery are used by a number of surgeons in combination with one or both ITA grafts or vein grafts and when an ITA graft is not available. Early (<13 months) patency of radial artery grafts exceeds 90% and does not differ from ITA patency. A native coronary stenosis of less than 70% is associated with lower patency of a radial artery graft than if the stenosis is 70% or greater. In a study of long-term patency of 1108 radial artery grafts, reported patency of 89% at a mean follow-up interval of 48 months. Of 318 grafts in place for more than 5 years, 294 (92%) were patent. Of 107 in place for more than 7 years, 99 (92%) were patent. Patency was highest for grafts placed to the LAD (96%) and lowest for grafts to the RCA (83%). Mechanisms of failure did not involve arteriosclerosis. For many surgical groups, the radial artery is currently the conduit of second choice behind the ITA.

In a study by Suma and colleagues of gastroepiploic artery grafts in 685 patients who underwent postoperative angiography in 122 patients early (11 ± 5 days) and in 72 patients late (11 ± 6 months) after operation. Early patency was 98%, and late patency was 93%. Of 14 grafts that were occluded or threadlike at the late study, 8 were anastomosed to arteries with a stenosis of 60% or less.

**Saphenous Vein Grafts**

Saphenous veins used as free aortocoronary grafts develop a unique remodeling and disease complex. The condition begins with diffuse intimal thickening, so-called intimal hyperplasia, which is a universal finding in vein grafts that have been in place for more than 1 month. This process is not progressive. Thickness of the intimal hyperplasia seems to be inversely related to flow in the graft, and the process appears to result in a matching of vein lumen size to that of the coronary arteries supplied by the graft. Intimal hyperplasia is thus best considered as a remodeling process.

As a result of these changes, most grafts show an angiographically detectable diffuse reduction in diameter. By 1 year afterimplantation, the diameter tends to approximate that of the recipient coronary artery; this diffuse smooth narrowing is not related to graft occlusion. Indeed, by increasing velocity of flow, remodeling may be beneficial, particularly when the vein is large initially.

Of greater importance is development of lesions in the vein graft that are indistinguishable morphologically from the fibrous plaques of arteriosclerosis. These atherosclerotic lesions are rarely found in saphenous vein grafts that have been in place for less than 3.5 years. By 10 years after CABG, however, most saphenous vein grafts have undergone at least some atherosclerotic changes that are sometimes severe. Whether this acceleration is related solely to morphologic damage to the graft caused by its removal and insertion into the arterial system, or whether it is caused by the patient’s tendency to develop arteriosclerosis, or whether
both occur, is uncertain. Both factors probably play a role, because hyperlipidemia is a risk factor for extensive vein graft atherosclerosis.\textsuperscript{C3,P3,S51,S57,S58} Also, aggressive efforts at controlling cholesterol levels retard progression of vein graft atherosclerosis.\textsuperscript{B30,C7}

About 20\% of vein grafts have proximal suture line stenosis within 1 year; about one fourth of these are found to be occluded 5 years later.\textsuperscript{G43} Almost 50\% of patients have some narrowing of the distal anastomosis within 1 year, but most have not progressed by 5 years after CABG.\textsuperscript{G43} Unfortunately, minimal information is available on the relationship of type of anastomosis (e.g., end-to-side, side-to-side) to frequency and severity of anastomotic strictures. Anastomotic strictures may result from a localized separate process or may be a local manifestation of atherosclerosis.

Thrombosis, another process that can reduce graft patency, may develop early postoperatively. Endothelial cell loss and exposure of the basement membrane and collagen to blood tend to appear early after inserting the vein graft, predisposing it to early accumulation of platelets, fibrin, and thrombus on its luminal surface.\textsuperscript{B2,S65,P3,S51,S57,S58} More often, thrombosis develops later in heavily atherosclerotic areas.

Related to all these processes, about 10\% of vein grafts close within the first few postoperative weeks, at least when antiplatelet therapy is not used. One- to 2-year patency in recently reported trials ranges from 75\% to 85\%.\textsuperscript{B17,G16,M2,Z3} Late patency is highly variable, but only 50\% to 80\% of grafts are patent in heterogeneous groups of patients.\textsuperscript{B47,G43,H1,K28} However, patency has been about 80\% when the greater saphenous vein has been used to bypass the LAD, which has a large runoff.\textsuperscript{L26,C14,K16,S3,S27} Clopidogrel, when combined with aspirin, has not been shown to increase graft patency or to reduce the frequency of adverse cardiovascular events at 1 year.\textsuperscript{G5,K38}

Other Vein Grafts

Patency of lesser saphenous vein grafts appears to approach that for the greater saphenous vein.\textsuperscript{C22} Patency is lower when the bypass graft is to a particularly small coronary artery or one that supplies a heavily scarred area, perhaps because in both circumstances there is low graft flow. Upper extremity veins have even lower patency.\textsuperscript{W14} Cryopreserved allograft veins may be used when no other suitable autologous graft is available; late patency is substantially less than that of ITA and saphenous vein grafts.\textsuperscript{L26}

Postoperative Progression of Native Coronary Artery Disease

Most important native-vessel coronary artery stenoses proximal to a bypass graft become more severe or totally obstructive within 5 years of CABG.\textsuperscript{B48,G43,H32,A4} Rates of progression of lesser stenoses proximal to a bypass graft remain uncertain. Important stenoses distal to the anastomosis also have a strong tendency to obstruct within 5 years.\textsuperscript{G43,N9} Lesser stenoses distal to a functioning bypass graft tend to remain unchanged.\textsuperscript{G43,N1} However, one study reported considerable progression of lesser distal arterial stenoses when the bypass graft to the artery was nonfunctioning.\textsuperscript{N9}

Lesser stenoses in ungrafted arteries progress in severity with less frequency than important stenoses, but 25\% to 50\% of such lesions progress within 5 years.\textsuperscript{G43,A4} In a group of patients undergoing CABG, Laks and colleagues found progression of proximal stenosis in 16 (27\%; CL 20\%-34\%) of 60 nonbypassed RCAs with less than 50\% narrowings at a mean follow-up of 20 months.\textsuperscript{A4} Two (3\%; CL 1\%-8\%) of the 60 had progressed to complete obstruction.

Important stenoses in ungrafted vessels progress after operation, presumably at about the same rate as in the natural history of CAD (see “Stenotic Coronary Artery Disease” earlier in this chapter). Controversy continues as to whether important stenoses progress less rapidly in ungrafted than in grafted vessels.\textsuperscript{E16,N9} Some information suggests that the rate is the same in both.\textsuperscript{B48,G43,P2}

New stenoses appear in apparently nonstenotic arteries that were not grafted.\textsuperscript{G48,H3} In following patients randomized to surgical vs. medical treatment, Palac and colleagues found new lesions within 5 years in about 15\% of both groups.\textsuperscript{P2} These figures may be different in patients and populations in whom risk factors for arteriosclerosis are altered.

Subsequent Reintervention

Prevalence of reintervention (repeat CABG or PCI), as with other outcome events, varies according to the patient’s characteristics before the first CABG, details of the first CABG itself, and to a lesser extent, management of the patient after the first operation. In a heterogeneous group of patients, freedom from reintervention is about 97\% 5 years after the initial operation, 89\% at 10 years, and about 72\% at 15 years.\textsuperscript{S27} (Fig. 7-43, A). Instantaneous rate of reoperation begins to rise appreciably after about 5 years (Fig. 7-43, B).

Vein graft atherosclerosis is the most common cause of reintervention, with progression of native- vessel disease the second most common.\textsuperscript{A14,L27} Thus, more frequent use of the ITA to the LAD has reduced the frequency of reoperation and lengthened the interval between first and second coronary operation.\textsuperscript{L3,L6,L27,S3} Use of both ITAs may further reduce prevalence of reintervention.\textsuperscript{B17,L31}

Results of a formal risk factor analysis for reintervention in the KU Leuven experience showed that younger age at first CABG increased risk of reoperation (Table 7-12 and Fig. 7-44, A). Young age as a risk factor is also evident in other studies.\textsuperscript{F14,K16,L3,S27} and is a surrogate for “aggressiveness of the atherosclerotic process.” In contrast to most other experiences, at KU Leuven, use of the ITA did not reduce reoperations appreciably (Fig. 7-44, B).

Operative risk of a second CABG is about twice that of the first.\textsuperscript{F14,L21,L27,Q3} Higher prevalence of risk factors in patients undergoing repeat CABG, rather than the procedure itself, is the more important reason for this increased early risk. Including hospital deaths, 10-year survival in a heterogeneous group of patients is about 65\%.\textsuperscript{L27} Considering deaths both early and late after repeat CABG, important left main coronary artery disease, three-system involvement, and severity of LV dysfunction are the most important risk factors.\textsuperscript{L27}

Symptomatic improvement is usual in surviving patients, particularly when symptoms are severe before reoperation. Thus, in the Cleveland Clinic experience, 89\% of those with severe angina before reoperation experienced either no angina or only mild angina postoperatively.\textsuperscript{L27}

Transmyocardial revascularization using a laser to create transmural channels has been applied to patients with severe angina after CABG (see Special Situations and Controversies later in this chapter).\textsuperscript{P17} It can be used as sole therapy or in combination with repeat CABG.
PCI is being used with increasing frequency in symptomatic patients after CABG. Compared with balloon angioplasty, stenting of vein graft stenoses results in higher procedural effectiveness (92% vs. 69%) and greater increase in luminal diameter early after the procedure. Freedom from death, MI, repeat CABG, or revascularization of the targeted vessel is substantially better in the stent group (73% vs. 58%).

INDICATIONS FOR OPERATION

The bases of the indications for CABG involve comparative benefits of operation relative to those of no treatment (natural history), medical treatment, or treatment by PCI. A complexity of these apparently simple propositions is that comparative benefit of CABG may be greater in one circumstance (e.g., severe vs. mild LV dysfunction) compared with another, yet the actual time-related survival after CABG is less21 (Fig. 7-45). The manner by which addition of the risk factors appears to amplify the contribution of another is explained under Multivariable Analysis in Chapter 6.)

Operation and other interventional therapies should increase regional coronary flow reserve. Small reductions in flow reserve are minimally life threatening; large reductions are life threatening. Use of techniques to quantify these reductions, such as thallium-201 single-photon emission CT and dobutamine stress echocardiography, permits predictions and comparisons of outcomes that are more accurate and precise.31

Traditionally, physicians and surgeons have talked with patients about “your chances” of “being alive” or “without pain” 1 year from now, or 5 or 15 years from now. A phrase such as “you have 95 chances out of a 100 of being alive for at least 10 more years” is frequently used, but such estimates have often been made on a qualitative basis. However, in an era when several different treatments are available, these types of predictions and comparisons for an individual patient with ischemic heart disease are often difficult to make. Fortunately, an enormous amount of information has been developed about effects of various risk factors on outcomes after different treatments for ischemic heart disease. Contrary to the belief of some, almost all this information is harmonious rather than internally conflicting. The remaining problem is efficient use of the data for (1) predicting and comparing for individual patients and (2) retrospectively evaluating quality of care and appropriateness of intervention (comparative effectiveness).23,29

For most patients with congenital heart disease and for some with other diseases, the condition that requires surgical treatment is similar from patient to patient and is the dominant risk factor. This fact makes predicting and comparing for individual patients straightforward. In contrast, stenotic arteriosclerotic CAD varies enormously from patient to patient, and the variations themselves are powerful risk factors. Therefore, recommendations to patients on the basis of predictions and comparisons of outcomes in heterogeneous groups of patients are of little value. Patient-specific predictions and comparisons are required. General indications for CABG are discussed in the text that follows.

Stable Angina

Stable angina is usually well relieved by CABG, even though not permanently so; it can also be favorably influenced by modern medical treatment, and under many circumstances by PCI.32,115,23,58,111,218 Furthermore, it is well established that CABG can accomplish considerably more than simple relief of angina. Thus, presence of chronic stable angina unrelied by medical treatment is no longer an automatic indication for CABG. Rather, duration of relief of angina and effect on time-related probability of survival must be the major considerations. These factors depend not only on presence of angina but also on all the patient-specific risk factors for unfavorable outcome events in patients with ischemic heart disease (see Box 7-1) and on procedural risk factors for the various interventions.

Patients with mild chronic stable angina (Canadian class I or II) can be considered to have mild reversible ischemia, which if confirmed by noninvasive testing, is not per se an indication for CABG or other forms of interventional therapy. However, severity and number of coronary stenoses, ischemic burden assessed by noninvasive testing, and severity of LV dysfunction may combine to give these patients better survival and relief of angina with intervention224 (see Fig. 7-6). When a clear comparative benefit of CABG over PCI or medical treatment can be predicted for an individual patient with mild reversible ischemia, such as when important stenoses in all three systems and LV dysfunction are present, operation is usually indicated.224
### Table 7-12  Incremental Risk Factors for Reintervention after Coronary Artery Bypass Grafting

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Hazard Phase</th>
<th>Early</th>
<th>Constant</th>
<th>Late</th>
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<tbody>
<tr>
<td><strong>Patient Risk Factors</strong></td>
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<tr>
<td>DEMOGRAPHIC</td>
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<td>Female</td>
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<td>(Younger) Age</td>
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<tr>
<td>SYMPTOMS OF REVERSIBLE ISCHEMIA</td>
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<tr>
<td>(Longer) Anginal history</td>
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<tr>
<td>(Higher) Unstable angina grade (not infarct)</td>
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<tr>
<td>CARDIAC COMORBIDITY</td>
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<tr>
<td>Preoperative left or right bundle branch block</td>
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<tr>
<td>Aortic valve stenosis (moderate)</td>
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<tr>
<td>Left ventricular hypertrophy</td>
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<tr>
<td>NONCARDIAC COMORBIDITY</td>
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<tr>
<td>History of peripheral arterial disease</td>
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<td>(Higher) 1-second forced expiratory volume/vital capacity</td>
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<td>(Higher) Triglyceride level</td>
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<tr>
<td>LEFT VENTRICULAR FUNCTION</td>
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<tr>
<td>Preoperative anterior and septal infarct</td>
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<tr>
<td>CORONARY DISEASE</td>
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<tr>
<td>(Lesser) Left main stenosis (%)</td>
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<tr>
<td>(Lesser) No left main stenosis &gt; 90%</td>
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<tr>
<td>(Lesser) One- or two-system disease</td>
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<tr>
<td>Procedural Risk Factors</td>
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<tr>
<td>CORONARY OPERATION</td>
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<tr>
<td>No graft to LAD</td>
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<tr>
<td>Venous graft to LAD</td>
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<tr>
<td>(Absence) Two or more internal thoracic artery anastomoses</td>
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<tr>
<td>(More) Distals from venous grafts</td>
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<tr>
<td>(More) Incomplete revascularization</td>
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<tr>
<td>INSTITUTIONAL EXPERIENCE</td>
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<tr>
<td>(Recent) Date of operation</td>
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<tr>
<td>(Lower) Preceding year per surgeon volume</td>
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</table>

Data from Sergeant and colleagues\textsuperscript{127}; KU Leuven, 1971-1992; \( n = 9600 \).

\textsuperscript{1}Includes only variables present before first CABG and procedural variables at first CABG.

Key: LAD, Left anterior descending coronary artery.

When chronic stable angina is \textit{moderate or severe} (Canadian class III or IV) despite optimal medical treatment, interventional therapy is usually advisable. When important stenoses are present in only one system, PCI often suffices.\textsuperscript{125} Although no benefit on mortality has been demonstrated with PCI compared with medical therapy in this setting, more patients treated with PCI are free from angina at 1 and 5 years.\textsuperscript{24} In patients with two-system disease without proximal LAD disease and no or minimal LV dysfunction, randomized trials and meta-analyses indicate that there is no or only a modest survival benefit with CABG compared with PCI, but up to a fivefold reduction in need for reintervention.\textsuperscript{24} For patients with high-grade stenosis of the proximal LAD in the setting of two-system disease (particularly with demonstrable ischemia on noninvasive testing and depressed LV function), CABG is preferred over PCI.\textsuperscript{24} When important stenoses are present in all three systems, or if left main coronary stenosis is present, CABG is indicated.
Figure 7-44  Nomograms illustrating strength and shape of risk factors for reintervention after coronary artery bypass grafting (CABG) in KU Leuven experience. A, Effect of age at initial CABG, depicted along horizontal axis. Predicted percent freedom is along vertical axis. Isobars represent interval between time of first CABG and time of estimation of prevalence of reintervention. B, Effect of using internal thoracic artery (ITA) as a conduit to left anterior descending coronary artery (LAD) at first CABG. (From Sergeant and colleagues; KU Leuven, 1971-1992; n = 9600.)

Figure 7-45  Comparison of survival after nonrandomly assigned coronary artery bypass grafting (CABG [Surgical]) with initial medical treatment in patients with three-system disease and severe angina, according to severity of left ventricular (LV) dysfunction. Symbols represent published nonparametric estimates. Solid line enclosed within dashed CLs are parametric estimates. For survival estimates, CLs are 70%; for survival differences, CLs are 90%. A, Survival in patients with mild LV dysfunction. B, Comparative benefit, indicating that surgical benefit is unlikely to be caused by chance alone. C, Depiction similar to A, but in patients with severe LV dysfunction. Survival 1 month and 5 years after CABG is less than when LV dysfunction is severe. D, Depiction similar to B, but in patients with severe LV dysfunction. This emphasizes that surgical benefit is greater when LV dysfunction is severe than when it is mild, even though 1-month and 5-year survival after CABG are lower than when dysfunction is mild. Key: CASS, Coronary Artery Surgery Study. (From ACC/AHA Guidelines and Indications for Coronary Artery Bypass Graft Surgery.)
and preferred because it provides a survival advantage and a marked reduction in need for repeat intervention compared with PCI.\textsuperscript{24,70}

Number of Systems with Important Stenoses

**Left Main Stenosis**

In general, stenosis of at least 50% in the left main coronary artery, either alone or in combination with stenoses in other coronary arteries, confers a sufficiently poor survival prognosis with medical treatment, and CABG is generally indicated.\textsuperscript{20,25} This is true even when the angina is well controlled by medical treatment or the patient is asymptomatic.\textsuperscript{75} The more severe the left main stenosis, the more urgent the need for CABG. There is emerging evidence that PCI in lower-risk subsets of patients with left main stenosis provides equivalent outcomes to CABG at least for the first 3 years after intervention.\textsuperscript{76} However, there is a fourfold increase in repeat revascularization with longer follow-up.\textsuperscript{24,77}

**Three-System Disease**

In general, patients with good LV function and mild or moderate reversible ischemia have a sufficiently good outlook with noninterventional therapy that CABG or PCI need not be advised as initial therapy, even with threesystem disease.\textsuperscript{B32,M34} (Fig. 7-46, A). Periodic reevaluation is clearly indicated, however, because change in any one of a number of variables may make CABG advisable. If patients in this category have impaired LV function, their long-term prognosis with medical treatment is sufficiently poor and the prognosis after CABG sufficiently good that CABG is indicated, even though survival is similar at 5 years (Fig. 7-46, B).

When one or more important proximal stenoses are part of the three-system disease, particularly when one is in the LAD, in general the prognosis with noninterventional therapy becomes less favorable, whereas that after CABG is not adversely affected.\textsuperscript{M34,V6} Thus, even with mild angina and good LV function, CABG is indicated and preferred over PCI when one or more important proximal stenoses coexist with three-system disease.\textsuperscript{E2,K24,P9}

**Two-System Disease**

In general, PCI appears to be effective interventional therapy for many patients with important (at least 50% stenoses) two-system CAD.\textsuperscript{K9,K24} Also, prognosis with medical treatment is considerably better in patients with two-system disease than in those with three-system disease.\textsuperscript{K9} Thus, CABG is not indicated in the majority of patients with mild angina and two-system disease. However, when such patients have left main equivalent disease, a severe proximal stenosis in the LAD, or impaired LV function, CABG is indicated.\textsuperscript{E2,K24,P9}

Indications for CABG are stronger when angina is more severe (Canadian class III or IV). These indications are in addition to those described for patients with two-system disease without proximal LAD stenosis, but with a large area of viable myocardium and high-risk criteria on noninvasive testing.\textsuperscript{E2,K24,P7}

**Single-System Disease**

CABG is infrequently indicated for patients with single-system disease. Results of CABG in this setting are excellent,\textsuperscript{L36} but results of medical treatment and of PCI are also good, although probably not as long lasting.\textsuperscript{F19} Bypass of the LAD with the ITA is an appropriate option in asymptomatic and symptomatic patients with proximal LAD stenosis and evidence of extensive ischemia on noninvasive testing or depressed EF (<50%).\textsuperscript{B49,R2} Results of metaanalyses comparing CABG and PCI in this setting demonstrate no significant difference in mortality or stroke, but a threefold increase in recurrent angina and a fivefold increase in repeat target-vessel revascularization with PCI at 5 years.\textsuperscript{K28,K22}

**Left Ventricular Function**

Patients with good LV function have a good prognosis with medical treatment, even in the presence of important three-system disease, but in many patients, survival is not improved by immediate CABG (see Fig. 7-46, A). Depressed LV function adversely affects outcome after CABG, even though in general the comparative benefit of CABG (vis-à-vis medical treatment) is greater the more depressed the LV function, and indications for operation are more compelling\textsuperscript{75} (Fig. 7-47). However, risks and benefits of CABG become more uncertain when resting LVEF is less than 30%, and
CABG. Exercise or resting thallium-201 scintigraphy, especially using the technique of enhancement by reinjection of thallium, may be particularly helpful in distinguishing between scar (which would contraindicate interventional therapy) and ischemia. Dobutamine stress echocardiography, positron emission tomographic (PET) scanning, and cardiac magnetic resonance imaging can also distinguish ischemic or hibernating myocardium from scar.

Performing CABG “prophylactically” in asymptomatic patients who have preserved LV function without noninvasive evidence for ischemia is undesirable from several standpoints. Medical treatment, including specific measures against unfavorable lipid profiles, may considerably or even indefinitely delay need for interventional therapy. Duration of the favorable effect of CABG appears to be finite, and for this reason alone, CABG should be delayed as long as is safe for the patient. Ideally, methods for prediction of the imminence of acute MI (the sequela of which are the usual causes of depressed LV function) should be perfected so that CABG can be performed at the most appropriate time.

Unstable Angina

Unstable angina is usually best managed initially by intense medical treatment; surgical intervention in the presence of ongoing ischemic instability is rarely required. In this discussion the description of “unstable angina” in the ACC/AHA Joint Task Force Subcommittee report is used.

Once the unstable state is controlled and the patient has been evaluated with noninvasive and invasive studies, the usual indications for CABG pertain. In some situations, however, indications for interventional therapy of some type become stronger than in patients with stable angina. Indications are particularly strong in patients with left main or left main equivalent disease, three-system disease, LV dysfunction, ongoing ischemia, or angina at rest. Indications are less strong in the subset of patients with unstable angina who have “new-onset angina.”

Uncomplicated Non–Q-Wave Myocardial Infarction or Non–ST-Segment Elevation Acute Coronary Syndrome

In general, patients with non–Q-wave MI or non–ST-segment elevation acute coronary syndrome have the same indications for CABG (and for the same reasons) as patients with unstable angina.

Uncomplicated Q-Wave or ST-Segment Elevation Myocardial Infarction

In an era of increasing success with thrombolytic therapy for acute MI, and more recently with PCI, CABG is infrequently indicated to treat patients with uncomplicated MI. However, contrary opinions to this approach exist.

When important angina persists early after an episode of acute MI, indications for operation are identical to those for unstable angina, and results are almost as good. Because early risks of undertaking CABG after acute MI are less the longer the interval since onset of the episode, delaying the procedure for a minimum of 48 hours is often advisable.
Myocardial Infarction with Hemodynamic Deterioration

Acute hemodynamic deterioration is a serious and often fatal complication of ongoing MI, and delay in interventional therapy is probably disadvantageous. There is little doubt that more than 50% of patients with this complication can be salvaged by emergency CABG. However, PCI is also effective in this setting.

When CABG is used for patients with acute hemodynamic deterioration during ongoing MI, an effective regimen of myocardial management is essential (see “Cold Cardioplegic, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Even then, recovery of some patients may not be possible, because patients in whom cardiogenic shock develops during an episode of acute MI are often elderly, have a low EF on admission, a history of previous infarctions and coronary artery interventions, and a particularly large area of acute infarction. These are all important risk factors for death in this setting.

Acute Complications during Percutaneous Coronary Intervention

Emergency CABG is indicated after unsuccessful PCI when hemodynamic compromise occurs or when there is evidence of ongoing ischemia or threatened occlusion of a major coronary artery with substantial myocardium at risk. Removal of a fractured guidewire or an underdeployed stent may occasionally be required. If the hemodynamic state is severely compromised, CPB can be initiated in the catheterization laboratory (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2). When CABG is performed under these conditions, myocardial management should be that described under “Myocardial Infarction with Hemodynamic Deterioration” earlier in this chapter.

Emergency CABG under the circumstances just described is associated with higher mortality and occurrence of perioperative infarction than elective CABG. Factors that affect outcome include presence of cardiogenic shock, older age, LV dysfunction, previous infarction, and previous CABG. With increasing use of intracoronary stents, frequency of emergency CABG after PCI has declined.

Recurring Myocardial Ischemia

Evidence of return of important myocardial ischemia and symptoms may require consideration of repeat CABG. When these symptoms develop and cineangiographic study shows evidence of ongoing ischemia or threatened occlusion of a major coronary artery with substantial myocardium at risk, PCI is indicated. PCI to the native-vessel disease for which bypass grafting was originally performed is occasionally possible, but in many cases these vessels have occluded by the time reintervention is under consideration.

When the cause of the recurring myocardial ischemia is graft disease, PCI is less effective and risks distal embolization of debris. Stenting of vein grafts is more effective in this setting than balloon angioplasty.

If PCI is not feasible, CABG is indicated in patients with moderate or severe angina despite optimal medical treatment if bypassable vessels are present in at least one system with noninvasive evidence for myocardium at risk (but preferably two or more systems). CABG may be the sole therapy or combined with transmyocardial laser revascularization.

SPECIAL SITUATIONS AND CONTROVERSIES

Coronary Artery Bypass Surgery versus Percutaneous Coronary Intervention

PCI is now an established method of management for many patients with arteriosclerotic CAD. Although initially used for treating single-system disease, PCI is currently being applied to patients with multisystem disease, including left main coronary artery stenosis. In addition to being less invasive, the advantages of PCI over CABG include shorter period of initial hospitalization and shorter recovery time. Disadvantages of PCI as the initial intervention include restenosis of the treated arteries and a higher prevalence of target-vessel revascularization. In general, a lesser degree of revascularization is achieved with PCI than with CABG in comparable patients.

During the 1990s, results of nine randomized clinical trials comparing PCI and CABG were published. Outcomes with respect to the major end points examined were summarized in a document jointly published by the American College of Cardiology and American Heart Association (Table 7-13). Several inferences can be drawn from these studies. Early mortality was comparable for the two interventions. Prevalence of early Q-wave MI was generally higher among the CABG patients, but this was unlikely due to chance in only two of the trials. Using a weighted average, prevalence was 4.1% among the CABG patients and 2.3% among the PCI patients. Initial costs and length of stay were lower for PCI than for CABG. Patients with PCI were able to exercise more at 1 month and return to work sooner.

In the Balloon Angioplasty Revascularization Investigation (BARI) and the Emory Angioplasty versus Surgery Trial (EAST), extent of revascularization achieved with CABG was higher than with PCI.

When late results were examined, there was no statistically significant difference in survival in any of the nine trials at follow-up periods ranging from 1 to 5 years (see Table 7-13). In the subset of patients with diabetes, however, all-cause mortality and cardiac mortality were higher in those treated with PCI in BARI (35% vs. 19% and 11% vs. 5.8%, respectively). A similar finding in diabetic patients was observed in the Coronary Angioplasty versus Bypass Revascularisation Investigation (CABRI), but not in EAST. No difference in prevalence of Q-wave MI or the combined end point of death and MI was demonstrated in any of the trials (see Table 7-13) or in subsequent meta-analyses. Most of the trials found that CABG resulted in greater freedom from angina.

The most striking difference between CABG and PCI was need for subsequent procedures. Prevalence was 4 to 10 times higher for PCI in every trial (see Table 7-13).

In several studies that examined quality of life and cost, physical activity and employment were similar for both procedures after 3 years, and functional status was equivalent at 5 years in BARI. Employment and emotional health were also similar. The early cost benefit of PCI decreased during follow-up because of more frequent need for repeat procedures and hospitalization.
Table 7-13  Comparison between Coronary artery Bypass Grafting and Percutaneous Coronary Intervention in Nine Randomized Controlled Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Age (% Female)</th>
<th>CAD</th>
<th>n</th>
<th>Primary End Point</th>
<th>Follow-up (Years)</th>
<th>Intervention</th>
<th>Acute Outcome (%)</th>
<th>Late Outcome (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BARI&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>61 (26)</td>
<td>MV</td>
<td>1792</td>
<td>D</td>
<td>5&lt;sup&gt;c&lt;/sup&gt;</td>
<td>CABG</td>
<td>1.3</td>
<td>4.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>1.1</td>
<td>2.1</td>
</tr>
<tr>
<td>EAST&lt;sup&gt;3&lt;/sup&gt;</td>
<td>61 (26)</td>
<td>MV</td>
<td>392</td>
<td>D+MI+T</td>
<td>3</td>
<td>CABG</td>
<td>1.0</td>
<td>10.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>1.0</td>
<td>3.0&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>GABI&lt;sup&gt;4&lt;/sup&gt;</td>
<td>(20)</td>
<td>MV</td>
<td>359</td>
<td>A</td>
<td>1</td>
<td>CABG</td>
<td>2.5</td>
<td>8.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>1.1</td>
<td>2.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Toulouse&lt;sup&gt;5,6&lt;/sup&gt;</td>
<td>67 (23)</td>
<td>MV</td>
<td>152</td>
<td>A</td>
<td>5</td>
<td>CABG</td>
<td>1.3</td>
<td>6.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>1.1</td>
<td>2.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>RITA&lt;sup&gt;7,8&lt;/sup&gt;</td>
<td>57 (19)</td>
<td>SV+</td>
<td>1011</td>
<td>D+MI</td>
<td>2½&lt;sup&gt;d&lt;/sup&gt;</td>
<td>CABG</td>
<td>1.2</td>
<td>2.4</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>0.8</td>
<td>3.5</td>
</tr>
<tr>
<td>ERACI&lt;sup&gt;9,10&lt;/sup&gt;</td>
<td>58 (13)</td>
<td>MV</td>
<td>127</td>
<td>D+MI+A+RR</td>
<td>1</td>
<td>CABG</td>
<td>4.6</td>
<td>6.2</td>
</tr>
<tr>
<td></td>
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<td>PCI</td>
<td>1.5</td>
<td>6.3</td>
</tr>
<tr>
<td>MASS&lt;sup&gt;11,12&lt;/sup&gt;</td>
<td>56 (42)</td>
<td>SV</td>
<td>142</td>
<td>D+MI+RR</td>
<td>3</td>
<td>CABG</td>
<td>1.4</td>
<td>1.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>1.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Lausanne&lt;sup&gt;13&lt;/sup&gt;</td>
<td>56 (20)</td>
<td>SV</td>
<td>134</td>
<td>D+MI+RR</td>
<td>2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>CABG</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CABRI&lt;sup&gt;14&lt;/sup&gt;</td>
<td>60 (22)</td>
<td>MV</td>
<td>1054</td>
<td>D</td>
<td>1</td>
<td>CABG</td>
<td>1.3</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>1.3</td>
<td>3.9</td>
</tr>
<tr>
<td>Weighted average</td>
<td>60 (23)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CABG</td>
<td>1.3</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>PCI</td>
<td>1.0</td>
<td>2.3</td>
</tr>
</tbody>
</table>

| Data from Eagle and colleagues.<sup>12</sup> |

Key:  A, Angina; BARI, Balloon Angioplasty Revascularisation Investigation; CABG, coronary artery bypass grafting; CABRI, Coronary Angioplasty versus Bypass Revascularisation Investigation; CAD, coronary artery disease; D, death; EAST, Emory Angioplasty versus Surgery Trial; ERACI, Estudio Randomizado Argentino de Angioplastia versus Cirugia; GABI, German Angioplasty Bypass Surgery Investigation; Hosp CABG, required CABG after PCI and before hospital discharge; LAD, left anterior descending coronary artery; MASS, Medicine, Angioplasty, or Surgery Study; MI, myocardial infarction; MV, multivessel; PCI, percutaneous coronary intervention; RITA, Randomised Intervention Treatment of Angina; RR, repeated revascularization; SV, single vessel; T, thallium defect.

<sup>a</sup>P < .05 comparing CABG and PCI cohorts.

<sup>b</sup>P < .05 comparing CABG and PCI cohorts.

<sup>c</sup>Includes total occlusion.

<sup>d</sup>Planned 5-year follow-up (interim results).
After excising arteriosclerotic debris, patch-graft enlargement of the artery is extended a variable distance onto the left main artery. An incision in the aorta just anterior to the left main coronary artery is exposed. The pulmonary trunk is dissected away from the ascending aorta, and the left main coronary artery is exposed. The surgical angioplasty for the left main coronary artery and to a lesser extent for ostial lesions of the RCA \textsuperscript{51-1,19,15,52} has been reported. Yeh and colleagues reported that anginal relief of 64% to 92% was noted when endarterectomy was done to the graft, compared with 29% when endarterectomy was not done. \textsuperscript{53} However, many studies suggest that the patency and flow in grafts to endarterectomized arteries is comparable to that of nonendarterectomized arteries. Whether perioperative MI is more likely to occur when endarterectomy is employed is controversial, \textsuperscript{52} as is the relative completeness of revascularization that can be achieved with the two techniques.

**Endarterectomy**

Although some surgeons frequently use endarterectomy, particularly in the distal RCA, most prefer to use the more distal branches of this artery for anastomosis to a bypass graft rather than endarterectomize the parent trunk and graft to it. Some surgeons continue to employ long endarterectomies, even in the LAD, and report good results. \textsuperscript{53,58,62}

Lower patency of grafts to endarterectomized arteries has been reported. Yeh and colleagues reported that graft patency of 64% when endarterectomy was done to the graft, compared with 92% when endarterectomy was not done. \textsuperscript{53} However, many studies suggest that patency and flow in grafts to endarterectomized arteries are comparable to those to nonendarterectomized arteries. Whether perioperative MI is more likely to occur when endarterectomy is employed is controversial, \textsuperscript{52} as is the relative completeness of revascularization that can be achieved with the two techniques.

**Surgical Angioplasty**

Surgical angioplasty of major coronary artery branches has limited value. However, some surgeons have successfully used angioplasty for the left main coronary artery and to a lesser extent for ostial lesions of the RCA \textsuperscript{51-1,19,15,52} has been reported. Yeh and colleagues reported that anginal relief of 64% to 92% was noted when endarterectomy was done to the graft, compared with 29% when endarterectomy was not done. \textsuperscript{53} However, many studies suggest that the patency and flow in grafts to endarterectomized arteries is comparable to that of nonendarterectomized arteries. Whether perioperative MI is more likely to occur when endarterectomy is employed is controversial, \textsuperscript{52} as is the relative completeness of revascularization that can be achieved with the two techniques.

**Small Distal Vessels**

Small distal vessel size does not represent a contraindication to operation. Levin and colleagues found that bypass grafts could be successfully placed in 73% of vessels considered inadequate because of severe distal narrowing or absence of filling on the angiogram. \textsuperscript{1,13}

**Transmyocardial Laser Revascularization**

In the 1950s, Goldman and colleagues\textsuperscript{518} and Massimo and Boffi\textsuperscript{519} proposed that conduits could be created in the subendocardium through the LV cavity to direct blood through the coronary sinusoids and into ischemic areas of the myocardium. Subsequently, Sen and colleagues used direct needle acupuncture to create communicating channels in ischemic myocardium. \textsuperscript{52} Mihoseini and Cayton\textsuperscript{528} and Okada and colleagues\textsuperscript{529} used a laser to create transmyocardial channels. Initial observational studies in patients with severe angina who underwent transmyocardial laser revascularization (TMLR) suggested that the procedure improved symptoms. \textsuperscript{522,523}

Currently, TMLR is performed with a carbon dioxide or holmium laser. In a typical procedure, 10 to 50 channels are created in areas of ischemic myocardium. If TMLR is the sole therapy, a left anterior thoracotomy is made, and the procedure is performed without use of CPB. TMLR can also be performed in conjunction with primary or repeat CABG using CPB or with OPCAB. Laser channels are created in ischemic areas that are not amenable to bypass grafting.

Four randomized clinical trials compared TMLR with medical therapy in patients with severe angina refractory to medical treatment, reversible ischemia of the LV wall, and CAD not amenable to CABG or PCI. Findings indicated that TMLR results in substantial improvement in symptoms. \textsuperscript{A1,A19,F17,S12} In three of the three trials, sustained relief of angina at 5 years was greater in the TMLR patients. \textsuperscript{A2,A17,H22} Exercise tolerance was not improved in the two studies that evaluated it. \textsuperscript{A1,S12} In two of the three trials in which myocardial perfusion was assessed at rest and during stress, TMLR did not improve it. \textsuperscript{A19,S12} In the third study, magnitude of improvement in symptoms was disproportionate to improvement in perfusion. \textsuperscript{F17} TMLR was not associated with improved LV systolic function or survival 1 year after enrollment.

Mechanisms of action for TMLR remain unclear. These include placebo effect, creating channels that provide increased blood flow to the ischemic myocardium, proliferation of new blood vessels (angiogenesis), denervation of ischemic myocardium, and infarction of ischemic myocardium.

TMLR can be performed with hospital mortality not exceeding 5% to 10% in properly selected patients. \textsuperscript{A18,A19,B68,F17,H23,S12} It can be performed as adjunctive therapy in patients undergoing CABG who would be incompletely revascularized by CABG alone. Superior relief of angina at 5 years has been demonstrated in a randomized trial. \textsuperscript{A28} Guidelines for TMLR as sole therapy or in combination with CABG have been published by the Society of Thoracic Surgeons. \textsuperscript{B31}

**Gene Therapy**

Enhanced understanding of the molecular biology of vascular cell activation and proliferation has resulted in development
of interventions at the level of gene expression to enhance the microcirculation of ischemic muscle and alter the course of vein graft atherosclerosis. Vascular endothelial growth factor (VEGF) has been administered to patients with ischemic myocardium as sole therapy by direct injection using a mini-thoracotomy or as an adjunct to CABG. Human fibroblast growth factor (FGF) has been used for a similar purpose. These studies have demonstrated evidence for improved myocardial perfusion in treated areas of the LV and improvement in symptoms early after treatment.

Ehsan and colleagues have demonstrated experimentally that a single intraoperative transfection of vein grafts with a decoy oligonucleotide that blocks cell-cycle gene transactivation, provides long-term resistance to neointimal hyperplasia and atherosclerosis. This has resulted in a reduction in primary graft failure unlikely to be due to chance when used in high-risk patients having CABG or peripheral arterial occlusions. However, a large randomized trial of more than 3000 patients whose vein grafts were treated with oligonucleotide or placebo failed to demonstrate higher patency of the treated grafts at 12 to 18 months.

Combined Carotid and Coronary Artery Disease

Carotid artery disease is an important risk factor for stroke after CABG. Hemodynamically significant carotid artery stenoses are associated with as many as 30% of strokes occurring after CABG. Prevalence of hemodynamically significant carotid artery disease among patients undergoing CABG increases with increasing age. In a nonconsecutive series of 1087 patients 65 years of age and older undergoing cardiac surgical procedures (91% with CAD) who had preoperative carotid duplex ultrasonography, prevalence of a 50% or greater stenosis of one or both carotid arteries was 17%; for an 80% or greater stenosis, it was 5.9%. Prevalence of a 50% or greater stenosis was 8% in patients between ages 65 and 69, increasing to 17% for patients age 80 and older. Incremental risk factors for presence of an 80% or greater stenosis were a previous history of transient ischemic attack or stroke, female gender, left main coronary artery disease, peripheral arterial disease, and history of smoking.

Presence or absence of a cervical bruit is poorly predictive of high-grade stenosis even in the setting of known symptomatic carotid artery disease (sensitivity 63%, specificity 61%). Carotid duplex ultrasonography is currently the most widely used preoperative screening technique to detect important carotid artery disease in patients undergoing CABG. It is used selectively in some centers and routinely in others to detect disease in older patients. If the preoperative carotid duplex study demonstrates high-grade (>75% to 80%) stenosis, and the patient's hemodynamic state is stable with no critically stenotic coronary arteries, carotid angiography is usually performed. Carotid and CABG procedures are staged, performing the carotid endarterectomy first. If the patient is hemodynamically unstable, or if there is high-grade left main coronary artery or proximal LAD disease, the carotid angiogram is often omitted, and a combined carotid and CABG procedure is performed.

This approach is justified because prophylactic carotid endarterectomy has been shown to be superior to conservative therapy for preventing stroke in symptomatic or asymptomatic patients with high-grade stenosis, and carotid artery disease is an important risk factor for stroke in patients with CAD.

When a combined procedure is performed, carotid endarterectomy may be done before CPB is established. Alternatively, endarterectomy can be performed during hypothermic CPB, which may provide additional brain protection during occlusion of the carotid artery. In patients with severe stenosis of one carotid artery and severe stenosis or occlusion of the contralateral carotid artery, deep hypothermia with or without a brief interval of circulatory arrest may be advantageous.

Superiority of the combined vs. staged approach has not been established by prospective trials. An individualized, patient-specific approach, with the decision based on symptoms and relative severity of the carotid and coronary artery disease, appears prudent and is used in many institutions. In experienced centers, staged or concomitant carotid endarterectomy and CABG can be accomplished with an early mortality that does not exceed 4%, stroke occurrence of less than 4%, and 10-year freedom from stroke of 88% to 96%.

Coronary Artery Aneurysm and Dissection

Coronary artery aneurysm is a localized dilatation that is saccular or fusiform in shape and exceeds the diameter of normal adjacent segments or the diameter of the patient’s largest coronary artery by 1.5 times. In patients undergoing coronary angiography, prevalence ranges from 0.4% to 4.9%. The majority of coronary aneurysms are arteriosclerotic in origin. These aneurysms may also be congenital, result from Kawasaki disease, or develop after PCI. Aneurysms occur most often in the RCA; the left main coronary artery is involved infrequently.

No clinical features distinguish coronary aneurysms, and the natural history is largely unknown. Diagnosis is usually made by coronary angiography. Rupture was reported in 12% of a series of 53 autopsied cases reported by Daoud and colleagues in 1963. In CASS, however, which included more than 20,000 patients who underwent coronary angiography, no case of rupture was observed among 978 patients in whom coronary artery aneurysms were detected. Thrombus develops in these aneurysms and may be a source for distal embolization. Bypass grafting of an artery containing an aneurysm, with or without ligation of the artery distal to the aneurysm, may be indicated in patients who have important occlusive disease in the artery or evidence of distal embolization in the absence of occlusive disease.

Coronary artery dissection is a rare cause of ischemic heart disease and sudden death. Coronary dissection can occur spontaneously or result from aortic dissection, blunt chest trauma, cardiac catheterization, coronary angioplasty, or CABG. Dissection has been observed after intense physical exercise and cocaine abuse. Predisposing factors include arteriosclerotic CAD, pregnancy, and Marfan and Ehlers-Danlos syndromes. Sudden death is the most frequent clinical presentation. In patients who survive the initial event, medical therapy is appropriate for those without ongoing ischemia. Stenting or CABG is advisable for symptomatic patients. Patients with dissection of the left main coronary artery should undergo CABG.
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M


PART II Ischemic Heart Disease

Chapter 7  Stenotic Arteriosclerotic Coronary Artery Disease


Chapter 7: Stenotic Arteriosclerotic Coronary Artery Disease


Y


Z


**Definition**

A postinfarction left ventricular (LV) aneurysm is a well-delineated transmural fibrous scar, virtually devoid of muscle, in which the characteristic fine trabecular pattern of the inner surface of the wall has been replaced by smooth fibrous tissue. In such areas, the wall is usually thin, and both inner and outer surfaces bulge outward. During systole, the involved wall segments are akinetic (without movement) or dyskinetic (paradoxical movement).

Scars and infarcts are not considered aneurysms. Unlike aneurysms, they are not discrete, the LV wall is not thin, and the scar is interspersed with muscle. The definition of aneurysm and the criteria for separating an aneurysm from other types of LV scars are controversial, and some clinicians have adopted a broader, non-morphologic definition rather than the one given earlier. Johnson and colleagues defined aneurysm as “a large single area of infarction (scar) that causes the LV ejection fraction to be profoundly depressed (to approximately 0.35 or lower).” Although realistically the definition of LV aneurysm is less important to the surgeon than are criteria for and results of surgical excision of LV scars, lack of uniformity of definition complicates almost all discussions of this entity. For example, many reports indicate that most patients with LV aneurysms have single-system left anterior descending coronary artery (LAD) disease, whereas others find that nearly all patients have multiple-system disease. Many patients with multiple-system disease have scars rather than true aneurysms.

**Historical Note**

Although John Hunter and others recognized that LV aneurysms occurred, it was not until the 1880s that the relationships among stenotic coronary artery disease, myocardial infarction (MI), myocardial fibrosis, and LV aneurysm were recognized. Until about 1950, few cases were diagnosed during life, but thereafter the ability to diagnose LV aneurysms improved. In 1967, Gorlin and colleagues reported that a strong suspicion of aneurysm could be obtained in 75% of patients with this complication of MI based on history, physical examination, and apex cardio, electrocardiographic, and radiologic studies. Many clinicians believe the prevalence of LV aneurysms has been decreasing since about 1980. Surgical treatment of postinfarction LV aneurysm probably began in 1944 when Beck reinforced such a lesion with fascia lata in an effort to reduce...
expansile pulsation and prevent rupture. A closed ventriculoplasty, done with a special side-biting LV clamp, was reported in 1955 by Likoff and Bailey. A few years later, Bailey reported five survivors among six patients treated by this method. In 1959, Cooley and colleagues in Houston reported the first successful open excision of an LV aneurysm using cardiopulmonary bypass (CPB).^13^

**MORPHOLOGY**

**Gross Pathology**

The wall of a mature aneurysm is a white fibrous scar, visible externally on the cut surface as well as endocardially. Characteristically, the aneurysmal portion of the LV wall is thin, the endocardial surface is smooth and nontrabeculated, and the area is clearly demarcated. In more than half of patients, varying amounts of mural thrombi are attached to the endocardial surface. The mural thrombus may calcify, as may the overlying pericardium, which is often densely adherent to aneurysm’s epicardial surface.^39,54^ Such classic LV aneurysms are at one end of the spectrum of postinfarction LV scars. At the other end the diffuse, scattered, and at times sparse punctate scars, frequently visible at operation in areas of previous MI. These scars are usually not transmural, and the LV wall is not thinned or only minimally so. The endocardium beneath retains its trabeculations, and the area of scarring is not clearly demarcated from the rest of the wall. Mural thrombi are not commonly present, and the pericardium is not commonly adherent to the area. Between these extremes is a continuous spectrum of postinfarction LV scarring, because in an area of MI, myocardial necrosis is rarely homogeneous (see “Myocardial Infarction and Morphologic Sequelae” in Chapter 7).

**Microscopic Pathology**

A mature aneurysm consists almost entirely of hyalinized fibrous tissue. However, a small number of viable muscle cells are usually present. Fibrous tissue of the type present in aneurysms takes at least 1 month to form, although collagen is present within 10 days of infarction. Thus, when an aneurysm is said to be present (based on wall thinning and dilatation) within 1 week or so of a first infarction, the wall is composed largely of necrotic muscle and is not therefore by definition a true (mature) aneurysm.

**Location**

About 85% of LV aneurysms are located anterolaterally near the apex of the heart. Few are confined to the lateral (obtuse marginal) area, and only 5% to 10% are posterior, near the base of the heart. Posterior, or inferior, aneurysms (i.e., those occurring in the diaphragmatic portion of the LV) are in some ways different from apical and anterolateral aneurysms. Nearly half of posterior aneurysms are false aneurysms (see “False Left Ventricular Aneurysm” under Special Situations and Controversies), whereas nearly all anterolateral and apical aneurysms are true aneurysms.^15^ Virtually all lateral aneurysms are false aneurysms. True posterior wall postinfarction aneurysms are associated with a high prevalence of postinfarction mitral regurgitation secondary to ischemia or necrosis of the papillary muscle.^15,51^ (see Chapter 10).

**Coronary Arteries**

Somewhat less than half of patients undergoing resection of classic LV aneurysms or scars have stenotic coronary artery disease confined to the left anterior descending coronary artery (LAD).^5,18,14,2,12,5,7,19,3,5,1,1,13,1,16,18,1,19,3,4,9^ More often, multiple-system disease is present. The discrepancy between the reported prevalence of single- and multiple-vessel disease may be related to differences in the definition of LV aneurysm, to different sources of the material (clinical, surgical, or postmortem), and in the case of surgical material, to case selection. A patient with single-system disease is more apt to survive an acute infarction and appear in a surgical series than is a patient with multiple-system disease.

**Left Ventricle**

Postmortem studies indicate that most patients with classic LV aneurysms have increased cardiac volume and weight.^39,4,4^ The increase in volume is in part the result of simple thinning and bulging of the aneurysmal portion of the LV wall. However, nonaneurysmal portions of the LV also increase in volume and thickness secondary to hemodynamic stress placed on them by akinesia of the aneurysmal segment (remodeling) and by the Laplace law. Inactivation (by akinesia or dyskinesis) of at least 20% of the LV wall area is required for LV enlargement to occur.^2,4^ The larger the akinetic or dyskinetic area, the greater the enlargement of the rest of the ventricle. The time course of these events has not been clearly defined.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Morphologic diagnosis of postinfarction LV aneurysm can be made with assurance only at operation or autopsy. This is because the akinetic or dyskinetic segmental wall motion of an LV aneurysm can be mimicked by nontransmural scars or early infarcts that are not morphologic aneurysms. Thus, Froehlich and colleagues found no aneurysm at operation in 3 of 18 patients (17%; CL 7%-31%) with a preoperative diagnosis of aneurysm and only a questionable aneurysm, which was plicated, in an additional 4 patients (22%, CL 12%-37%).^17^ Small and moderate-sized aneurysms are often associated with no specific symptoms, although the patient may experience angina because of stenoses in other portions of the coronary arterial tree. Patients with large LV aneurysms, however, usually present with dyspnea that often has persisted from the time of infarction. Heart failure requiring medication for control may have appeared by the time of presentation to the physician.^25,3^ (Table 8-1). Symptoms related to ventricular tachycardia occur in 15% to 30% of patients and may become intractable to medical treatment and cause death.^23,6^ Although about half of aneurysms contain thrombus, thromboembolism occurs in only a small proportion of patients. On physical examination, palpation over the heart often demonstrates a diffuse, sustained apical systolic thrust and a double impulse. On auscultation, usually a third heart sound and often a fourth (atrial) sound are present. There may be an apical pansystolic murmur if mitral regurgitation is present. Chest radiography and fluoroscopy may show an external bulge or convexity when the aneurysm is large enough and profiled. Methods of LV imaging—namely, left ventriculography, two-dimensional and transesophageal...
Table 8-1  Symptoms in Patients Operated on for Left Ventricular Aneurysm

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No.</th>
<th>% of 145</th>
</tr>
</thead>
<tbody>
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<td>Severe angina* alone</td>
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<td>31</td>
</tr>
<tr>
<td>Heart failure alone</td>
<td>30</td>
<td>21</td>
</tr>
<tr>
<td>Heart failure + severe angina</td>
<td>27</td>
<td>19</td>
</tr>
<tr>
<td>Ventricular tachycardia* + other symptoms</td>
<td>22</td>
<td>15</td>
</tr>
<tr>
<td>Heart failure + mild angina</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Mild angina* alone</td>
<td>8</td>
<td>5.5</td>
</tr>
<tr>
<td>Mild effort dyspnea</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>145</td>
<td>100</td>
</tr>
</tbody>
</table>

*Severe = Canadian angina class 3 or 4.
*Severe dyspnea, orthopnea, paroxysmal nocturnal dyspnea, fluid retention, hepatomegaly.
*Two or more episodes of documented ventricular tachycardia or ventricular fibrillation despite treatment with antiarrhythmic drugs.
*Mild = Canadian angina class 1 or 2.

Modified from Barratt-Boyes and colleagues.13

echocardiography, radionuclide cardiac blood pool imaging, computed tomography (CT), and magnetic resonance imaging (MRI)—are all useful diagnostic techniques (Fig. 8-1).13,16,16 However, an incorrect preoperative or preoperative diagnosis of aneurysm is still sometimes made. Ventriculography is a sensitive imaging method. When there is akinesia or dyskinesia of the wall segment during systole, a permanent outward bulging or convexity, thinning of the wall and lack of inner wall trabeculation, and clear demarcation of the area from the remaining ventricle, the diagnosis is probably correct. Wall thinning and even bulging of the contrast-medium–lined LV cavity may not be detected when there is extensive smooth mural thrombus, and it is often difficult to define the margins of an area with akinesia. Identification of significant mural thrombus adds to the probability of aneurysm, as does presence of calcification in the wall. Right heart catheterization is useful because it enables measurement of pulmonary artery pressure and calculation of cardiac output. From the left heart study, LV end-diastolic pressure, ejection fraction, and end-diastolic volume are measured or calculated. Coronary angiography is always performed.

Figure 8-1  Cine (ultrafast) computed tomographic images at four adjacent anatomic levels (upper left, cranial, to lower right, caudal) demonstrate an anterior left ventricular (LV) aneurysm. There is severe thinning of the anteroseptal and anterior walls and bulging of the LV anteriorly. (From Higgins.15)
Development of Left Ventricular Aneurysm

Historically, about 10% to 30% of patients who survived a major MI developed an LV aneurysm.\textsuperscript{A3, N1} Today, the prevalence appears to have lessened thanks to improved treatment of patients with acute MI. The most important development may be widespread use of thrombolytic therapy and percutaneous coronary interventions, which have reduced the prevalence of permanently occluded LADs. Other improvements include better management of hypertension and avoidance of corticosteroids, both of which are risk factors for development of aneurysms.\textsuperscript{B16, M12} The mechanisms by which LV aneurysms form are not completely elucidated. Occurrence of a large transmural infarction is a prerequisite. It has been suggested that patients who develop LV aneurysms have few intercoronary collateral arteries.\textsuperscript{B14, C6, J15} It is postulated that a rich collateral blood supply to an area of MI tends to increase the number and size of the islands of viable myocardial cells in the area and decrease the probability that the necrosis is extensive enough to result in a thin-walled transmural scar. This hypothesis is supported by Forman and colleagues, who studied 79 patients undergoing cardiac catheterization 6 months after a first MI.\textsuperscript{J9} They found total occlusion of the LAD and poorly developed collateral flow to be the determinants of LV aneurysm formation. Apparently, normal or supranormal systolic function in adjacent ventricular segments is necessary for generating sufficiently high intraventricular pressure and wall tension in the infarcted area to result in aneurysm formation.\textsuperscript{A3}

Pathophysiologic Progression of Aneurysm

Whether large LV aneurysms are large from inception or gradually enlarge once formed is uncertain. The mechanism for increasing symptomatology that characterizes the life history of many patients with large LV aneurysms has not been clearly established.\textsuperscript{C2, C14, J6} It may be due to a gradual increase in the size of the area of akinesia or dyskinesia and to a consequent gradual reduction in stroke volume and global ejection fraction.\textsuperscript{A7, J6} The nonaneurysmal portion of the LV wall is subjected to increased systolic wall stress as ventricular size increases (as described by the Laplace law) and may ultimately lose its systolic reserve and contribute to LV enlargement and failure.\textsuperscript{J6} This process is aggravated by any myocardial ischemia that develops in the nonaneurysmal portion of the ventricular wall.

Left Ventricular Function

An aneurysm changes the curvature and thickness of the LV wall, and because these are determinants of LV afterload (wall stress), global LV performance is altered.\textsuperscript{D10, N2} Also, a large LV aneurysm leads to global cardiac remodeling with generalized dilatation.\textsuperscript{N2} Variations in intrinsic properties of scar, muscle, and border-zone tissue can affect both systolic and diastolic function.\textsuperscript{K5} Finally, paradoxical movement in the aneurysmal portion of the wall reduces efficiency of the ventricle because systolic work is wasted on expansion of the aneurysm.\textsuperscript{J15}

Function in uninvolved segments of the LV per se (segmental ejection fraction) has been difficult to study because of the complexities of assessing ventricular function in this setting. However, when echocardiographically determined wall thickening is used as a measure of regional systolic function, it appears that systolic function is maintained in the remote nonaneurysmal portions of the ventricle.\textsuperscript{N2} Early in systole, the aneurysm and border zones bulge outward (paradoxical movement) as systolic intraventricular pressure rises to a maximum. Later in systole, after the aortic valve has opened and wall stress is falling, some wall thickening occurs in the border zones, contributing to ejection.\textsuperscript{N2}

Right Ventricular Function

Right ventricular (RV) function may be impaired in patients with LV aneurysm. This may result from akinesia or dyskinesia of the ventricular septum, impaired RV wall motion near the apex, increased pulmonary artery pressure, occlusive disease of the right coronary artery, and increased volume of the LV within the pericardial cavity.\textsuperscript{B13, C1, G6}

Survival

The complexities of ischemic heart disease in general and the difficulties in identifying true LV aneurysms have mitigated against achieving a clear understanding of survival and risk factors for death of patients with LV aneurysms. Patients with an LV akinetic area (not all of which are true aneurysms) are reported to have a 5-year survival without operation of 69%,\textsuperscript{B12} perhaps only a little less than that dictated by their coexisting coronary artery disease. Patients with a dyskinetic area of LV wall (many of which are probably aneurysms) have a 54% 5-year survival, which is reduced to 36% when myocardial function in the remainder of the ventricle is reduced.\textsuperscript{N12} Size of the aneurysm is a risk factor for premature death in surgically untreated patients. In patients with small aneurysms (usually without symptoms of heart failure), the probability of surviving is dictated primarily by severity and extent of the coronary arterial stenoses and is greater in asymptomatic than in symptomatic patients (Fig. 8-2).\textsuperscript{G3} Prognosis is adversely affected by dyskinesia rather than akinesia in the aneurysm; the former is usually associated with a low global LV ejection fraction.\textsuperscript{F3} The functional characteristics of the remainder of the ventricle are also major determinants of survival. In addition, all the usual risk factors for premature death in patients with ischemic heart disease (see Table 7-2 in Chapter 7) pertain to patients with LV aneurysm.\textsuperscript{F2}

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**Figure 8-2** Five-year survival with left ventricular aneurysm but without operation for 20 patients with few or no symptoms and for 20 symptomatic patients. (Modified from Grondin and colleagues.\textsuperscript{G1})
TECHNIQUE OF OPERATION

Most patients who undergo resection of postinfarction LV aneurysms or other scars also require coronary artery bypass grafting (CABG). The following discussion augments the description of CABG in Chapter 7.

Preoperative and operating room preparations, removal or preparation of grafts, and median sternotomy are accomplished as described in Chapters 2 and 7. The pericardial adhesions over the LV are not lysed at this point. If CABG is to be performed, and if the proximal anastomoses are to be placed first, this is done now. If the LAD is to be revascularized, the left internal thoracic artery is prepared. Moderately hypothermic CPB is established using double venous cannulation and caval taping or a single venous cannula. A left atrial or LV vent is not inserted. Dissection of adhesions between the LV and pericardium is deferred until the aorta is clamped, to avoid dislodging and embolizing mural thrombus.

Because patients with large LV aneurysms usually have heart failure and the operation may be prolonged, warm induction of cardioplegia after aortic occlusion and controlled reperfusion with initially hyperkalemic, modified, and enriched blood may be used (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Retrograde cardioplegia (see “Technique of Retrograde Infusion” under Methods of Myocardial Management during Cardiac Surgery in Chapter 3) and a “no-touch” technique may be particularly useful.57 Adhesions, if thin, can be mobilized over the entire aneurysm. If the classic method of repair is anticipated and the aneurysm is densely adherent to the pericardium, the LV can be separated from the aneurysm without disturbing these adhesions. The aneurysm is incised at some convenient point, and loose thrombus is sought and removed. When the aneurysm contains considerable thrombus and debris, a sponge is placed deep inside the ventricle over the aortic and mitral valves to prevent debris from entering the aorta and left atrium. This sponge is removed after the dissection is completed. A small sump sucker is placed through the incision into the ventricle and is positioned so as to maintain a pool of blood within the open ventricle below the level of the ventriculotomy. This prevents air from entering the aorta, coronary ostia, and left atrium. The incision is extended around the entire aneurysm, leaving a thin rim of scar tissue to facilitate closure.

A true aneurysm has a smooth endocardial surface. Additional endocardial tissue may be removed and other procedures done if the patient has a history of life-threatening ventricular arrhythmias (see Section V, “Ventricular Tachycardia and Ventricular Fibrillation in Ischemic Heart Disease,” in Chapter 16). When large amounts of thrombus are present, the ventricular cavity is carefully inspected and thoroughly irrigated to remove all debris. If the aneurysm wall is left adherent to the pericardium, thrombotic material is removed from it (this can be done later during rewarming, after the ventricle is closed), and the avascular fibrous tissue is left attached to the pericardium.

Reconstruction of the Left Ventricle

Anterior Aneurysm

When reconstruction is performed with the classic technique (linear closure), a line of closure is selected that will least distort the LV. After opening the ventricle and excising the scar (Fig. 8-3, A), a stay suture is placed at each end of the line of closure (Fig. 8-3, B). If the aneurysm is small, closure of the LV can be accomplished with two rows of a simple continuous suture using No. 0 or 1 polypropylene on a large curved needle. More often, closure is performed with heavy double-armed sutures (No. 1 or 2 silk or polyester) that are placed horizontally immediately adjacent to one another, incorporating strips of polytetrafluoroethylene (PTFE) felt (see Fig. 8-3, B). These sutures are placed deep into the ventricular septum (see Fig. 8-3, B [inset]) to exclude as much septal scar as possible.314 As these sutures are tied, beginning at the basal portion of the ventricle, volume from the pump-oxygenator is infused, and the lungs are gently inflated to evacuate air from the pulmonary veins and left atrium. Saline can also be infused into the open LV. When this suture line is completed, it is reinforced with two continuous No. 0 or 1 polypropylene sutures that are positioned at each end of the incision, placed through the felt and through the edges of the myocardium superficial to the mattress sutures, and tied to each other (Fig. 8-3, C). Incorporation of the distal portion of the LAD into the suture lines should be avoided.

An alternative procedure is patch closure of the defect in the LV (Fig. 8-4).11,64 This technique has been termed “endoaneurysmorrhaphy” by Cooley11 and “endoventricular circular patch plasty repair” by Dor.65 The rationale for this technique is based in part on the fact that, coexisting with anterior LV aneurysm, scar tissue and akinesis or dyskinesis are present in the anterior portion of the LV septum. When a patch is used for closure, the area of septal scarring can be excluded from the reconstructed LV. This may result in improved LV function.11,6,52 Furthermore, curvature of the left anterior wall may be maintained.18 Based on echocardiographic measurements in normal hearts, Fontan determined that the patch should be oval and should have a long diameter of 2 to 2.5 cm in situ. Thus, it should be made 2.5 to 3 cm in length to compensate for the space taken up by the suture line.14 A patch that is too large may result in too large an end-diastolic LV volume and thus a reduced global ejection fraction. A patch that is too small may reduce LV volume and compliance.52 A preshaped balloon of known volume (50 to 60 mL) can be inserted into the opened LV cavity to facilitate creating a chamber of appropriate size and shape.53 After opening the LV, the line of demarcation between scar and contractile LV myocardium is identified (Fig. 8-4, A [inset]). This may be facilitated by palpation if cardioplegia is not used during this portion of the operation.52 A purse-string suture of No. 2-0 polypropylene is placed at the junction of scar and contractile septal and free wall myocardium (Fig. 8-4, B). The longitudinal and transverse dimensions of the resulting defect are measured. A patch of gelatin or collagen-impregnated polyester (that can be lined with autologous pericardium) with slightly larger (0.5 cm) dimensions is fashioned and then sutured into place with slightly larger (0.5 cm) dimensions is fashioned and then sutured into place with a continuous No. 3-0 polypropylene suture (Fig. 8-4, C). Before completing the suture line, air is evacuated from the LV by infusing volume from the pump-oxygenator, gently inflating the lungs, and injecting saline into the ventricle. This suture line must be watertight to avoid formation of a false aneurysm. The remnant of the aneurysm is trimmed, if necessary, and is closed securely over the patch with a continuous No. 2-0 polypropylene suture (Fig. 8-4, D).

A second alternative procedure in patients without a calcified aneurysm, and the rare patient with a small LV cavity, is
Figure 8-3  Technique for repair of anterior left ventricular aneurysm by linear closure. A, After the aorta is clamped and cardioplegic solution has been infused, an incision is made in the thinnest portion of the aneurysm parallel to the interventricular groove. If pericardial adhesions are dense, the aneurysm can be left attached to the pericardium. The scar is excised (inset). B, After all the scar has been excised, traction sutures are placed at each end of the anticipated line of closure. The defect is closed with No. 1 or 2 double-armed silk or polyester sutures placed horizontally and immediately adjacent to one another. These sutures are placed deep into the ventricular septum to exclude as much septal scar as possible (inset). C, Suture line is reinforced with two continuous No. 0 or 1 polypropylene sutures positioned at each end of the incision, placed in scar tissue superficially to the mattress sutures, and tied to each other. Key: LV, Left ventricle; RV, right ventricle.
Figure 8-4  Technique for repair of anterior left ventricular aneurysm by patch closure. A, After the aorta is clamped and cardioplegic solution has been infused, an incision is made in the thinnest portion of the aneurysm parallel to the interventricular groove (inset). B, A purse-string suture of No. 2-0 polypropylene is placed at the line of demarcation between scar and contractile myocardium on the septum and free wall (inset). Longitudinal and transverse dimensions of the resulting defect are measured.

Continued
C. A patch of gelatin- or collagen-impregnated polyester or of polyester backed with pericardium (inset) is fashioned with slightly larger dimensions (0.5 cm) and is sutured into place, incorporating the purse-string suture, with a continuous No. 3-0 polypropylene suture. D. Remnant of the aneurysmal wall is trimmed and sutured securely over the patch with a continuous No. 2-0 polypropylene suture (inset). Key: LV, Left ventricle; RV, right ventricle.
direct LV reconstruction using multiple concentric purse-string sutures without a patch.\textsuperscript{C4,K8}

**Posterior Aneurysm**

The techniques described for repairing anterior LV aneurysms are also applicable to posterior aneurysms. However, the defects remaining after excision of the scar or after circular reduction with a suture are generally smaller. Injury to the posterior papillary muscle at the lateral edge of the defect and to the posterior descending coronary artery on the medial edge of the defect must be avoided.

**Associated Mitral Regurgitation**

Mitral regurgitation of variable degree is often present in patients with LV aneurysm. If repair of the valve is possible, it may be accomplished with standard techniques through a left atrial approach (see Technique of Operation in Chapter 11). Alternatively, the “edge-to-edge” repair technique proposed by Alfieri and colleagues can be performed through the ventriculotomy.\textsuperscript{M1}

If valve replacement is indicated, it can be performed through the opened LV for posterior as well as anterior aneurysms (Fig. 8-5). The ventricle is opened through the aneurysm as previously described, and the mitral valve is examined (Fig. 8-5, A). If replacement is indicated, the mitral valve leaflets are excised, and all chordae tendineae are transected. A small remnant of anterior leaflet is left adjacent to the aortic valve cusps (Fig. 8-5, B). The valve holder apparatus is removed from the appropriately sized mechanical or bioprosthetic valve, and the valve is inverted and suspended by two hemostats. Interrupted pledgeted mattress sutures of No. 2-0 polyester are placed through the mitral anulus, with the pledgets positioned on the atrial side (Fig. 8-5, C). These sutures are placed through the sewing ring of the prosthesis on the undersurface of the flanged portion (see Fig. 8-5, C). The valve is then lowered into the anulus and the sutures tied (Fig. 8-5, D). A soft rubber catheter is used to keep the prosthesis leaflets in the open position until air is evacuated from the pulmonary veins and left atrium. The LV is then reconstructed using one of the techniques previously described.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Postoperative care is the same as that for other patients after intracardiac operations (see Chapter 5) and particularly after CABG. The detailed late-postoperative care required for patients undergoing CABG (see Special Features of Postoperative Care in Chapter 49) should also be applied to patients whose operation has included resection of a postinfarction LV aneurysm.

**RESULTS**

Survival

**Early (Hospital) Death**

Hospital mortality after LV aneurysm repair, with or without concomitant CABG, is about 5% to 7%\textsuperscript{C3,E2,F4,J2,J4,J5,K4,K7,M9,S6,V5,Z1} down from 10% to 20% in the earlier era (1958-1978) of cardiac surgery.\textsuperscript{B5,B18,C12,C14,M13,R3,R8}

Reduced mortality is related to improved surgical techniques, better myocardial management, greater efforts to perform concomitant CABG, better protection against embolization during operation, and use of adjunctive measures in patients with associated intractable ventricular tachycardia. No consistent difference in early mortality has been demonstrated between the classic (linear closure) and endoaneurysmorraphy (circular or patch closure) techniques.\textsuperscript{J2,K4,K7,M9,R3,S6,V5,Z1}

**Time-Related Survival**

Overall time-related survival of heterogeneous groups of patients undergoing resection of LV aneurysms has varied, but in general, 30-day and 1-, 3-, and 5-year survival has been about 90%, 85%, 75%, and 65%, respectively.\textsuperscript{B5,B18,C13,E2,F6,K7,S6} Several studies\textsuperscript{M9,V5} report higher 5-year survival (80% to 88%). In the Surgical Treatment for Ischemic Heart Failure (STICH) trial, the only randomized trial to compare CABG with CABG plus surgical ventricular reconstruction in patients with an ejection fraction of 35% or less and dominant anterior LV dysfunction (akinesia or dyskinesia), 5-year survival among the 501 patients randomized to CABG plus surgical ventricular reconstruction was 67%.\textsuperscript{K6} It did not differ significantly from survival of 499 patients randomized to CABG alone (Fig. 8-6). Not unexpectedly, differences in outcome after surgical and nonsurgical treatment are particularly evident in patients with coexisting three-system disease.\textsuperscript{F1}

**Modes of Death**

The most common mode of death early after operation is acute cardiac failure.\textsuperscript{S6,V3,V5} Late postoperatively, the mode of death is progressive chronic heart failure in about one third of patients and acute heart failure after another MI in another third. Intractable ventricular tachycardia and sudden death have been the mode in about 15% of patients in the past, but the prevalence may be lower now as a result of more effective intraoperative management and medical and surgical treatment.

**Incremental Risk Factors for Premature Death**

In patients undergoing LV aneurysmectomy, risk factors for premature death and other unfavorable outcomes are generally the same as those in other patients with ischemic heart disease. The lower probability of time-related survival of patients undergoing LV aneurysmectomy (with or without concomitant CABG) is explained for the most part by their greater likelihood of having risk factors relating to myocardial scarring.\textsuperscript{C8}

**Severity and Extent of Coronary Arterial Stenoses**

When complete revascularization is not accomplished in operations for ischemic heart disease, severity and extent of residual coronary arterial stenoses may appear as risk factors for most unfavorable outcome events. In surgical series in which the severity and extent of coronary artery disease have not been identified as risk factors for death early or late after operation,\textsuperscript{B10,C13,F3,K7,R3,W1} the presumption is that complete revascularization was accomplished. In other studies, preoperative severity and extent of coronary arterial stenoses have been risk factors.\textsuperscript{B5} Presumably, they represent groups of patients in whom revascularization was necessarily incomplete.
surrogates identified as risk factors include preoperatively reduced cardiac output, elevated LV end-diastolic pressure, impaired septal systolic function, higher New York Heart Association (NYHA) functional class (Fig. 8-8), poor segmental wall motion, and ventricular tachycardia. Also related to the extent and location of myocardial scarring is the complication of life-threatening ventricular tachycardia. This is clearly a risk factor for death, both early and late

Extent and Location of Myocardial Scar

By definition, patients with LV aneurysm have considerable myocardial scarring, and the scar often is neither completely removed nor exteriorized by the operation. New scar formation occurs at the suture lines. Nonaneurysmal muscle may be scarred as well. Risk factors for death both early and late after resection of LV aneurysms that are surrogates for myocardial scar include preoperative resting LV dysfunction and chronic heart failure (Fig. 8-7). Other

Figure 8-5 Replacement of mitral valve through left ventricle (LV). A, An incision is made in the thinnest portion of the aneurysm parallel to the interventricular groove, and the mitral valve is examined. Chordae tendineae are divided at the tips of the papillary muscles. B, Mitral valve leaflets are excised. A small rim of anterior leaflet is left adjacent to aortic valve cusps. C, Valve holder apparatus is removed from mechanical valve or bioprosthesis, and valve is inverted and suspended by two hemostats. Interrupted, pledgeted mattress sutures of No. 2-0 polyester are placed through the mitral anulus, with pledgets on atrial side of anulus. These sutures are then placed through the sewing ring of the prosthesis on the underside of the flanged portion. D, The valve is lowered into the anulus and the sutures tied. The LV is reconstructed using one of the techniques described in Figs. 8-3 and 8-4.
or observational study has demonstrated a favorable effect of this procedure on late survival when compared with linear closure or other techniques.\textsuperscript{2,4,6,9}

**Other Risk Factors**

Other risk factors for death and other unfavorable outcome events after CABG (see Tables 7-2, 7-7, and 7-8 in Chapter 7) also pertain to patients undergoing LV aneurysmectomy. For example, older age at operation is clearly a risk factor for death, both early and late after aneurysmectomy.\textsuperscript{7,6,9}

**Symptomatic Results**

Most long-term survivors have substantial improvement in symptoms. The majority are in NYHA functional class I or II.\textsuperscript{6,8,16,33,37,38,39,54} Improvement has also been demonstrated with exercise testing.\textsuperscript{32} Several\textsuperscript{30,33,35} but not all\textsuperscript{54} comparative studies have demonstrated greater symptomatic improvement among patients undergoing patch closure than among those who had linear closure of the ventriculotomy.

**Late Postoperative Left Ventricular Function**

Determining LV function late after resection of LV aneurysms presents the same problems and complexities as it does in the case of the aneurysmal LV before operation (see “Left Ventricular Function” under Natural History earlier in this chapter). However, a reasonable amount of information is available. The relationship between improvement in LV
performance and symptomatic improvement is not entirely clear. Some patients with symptomatic improvement are without demonstrable improvement in LV function.\textsuperscript{14,17} It is possible that current techniques of studying LV function do not identify the small increases in LV function that allow symptomatic improvement. Although improvement is often noted in indices of LV function after aneurysmectomy without or with CABG,\textsuperscript{13,17} it does not always occur. Possible mechanisms for failure to improve include:

- incomplete aneurysm resection (e.g., Froehlich et al. found in most of their patients that only 50\% of the noncontractile area visualized by left ventriculography was resected\textsuperscript{17});
- small size of the aneurysm, leading to small changes in function after resection; and
- intraoperative damage to nonaneurysmal portions of the ventricle.

Also, despite improved resting LV function, some patients show no improvement in exercise ejection fraction or stroke volume.\textsuperscript{31,18} Often, however, the improvement in global and regional ejection fraction during exercise is striking.\textsuperscript{32,33} Paradoxical movement in the segments in the border zone during isovolumic contraction is usually eliminated by aneurysmectomy.\textsuperscript{34} This effect may be the result of more favorable geometry in these segments, a reduction in wall stress related to decreased chamber size, or better coronary perfusion produced by CABG. Wall thickening increases in some but not all uninvolved (remote) segments; in some improved segments, operation fails to increase blood supply.\textsuperscript{35} Improvements in LV function are most evident in patients with heart failure preoperatively.\textsuperscript{32}

A reduction in end-diastolic pressure is well correlated with clinical improvement in some patients.\textsuperscript{87} In 1969 in three patients with single-system LAD disease and classic aneurysm, Harman and colleagues demonstrated that simple resection without CABG increased LV ejection fraction, stroke volume and stroke work, and cardiac index and reduced LV end-diastolic pressure and volume.\textsuperscript{34} Two of the three patients were also relieved of angina pectoris. The data suggest that the resection and resultant decrease in LV volume decreased wall force according to the Laplace law. The decreased tension (afterload) during systole probably increased the rate of fiber shortening, thereby increasing stroke volume, and decreased myocardial oxygen consumption, thereby decreasing angina pectoris (see “Ventricular Afterload” under Cardiac Output and Its Determinants in Section I of Chapter 5).

INDICATIONS FOR OPERATION

A large LV aneurysm in a symptomatic patient, particularly one with angina pectoris but also in one with heart failure, is an indication for operation. Appropriate CABG is indicated at the time of aneurysmectomy, as described in Chapter 7. Currently, the patch closure technique for remodeling ventriculoplasty is the most widely used for repair of anterolateral aneurysms or areas of akinesis. In view of the high risk of operation in patients with advanced chronic heart failure, operation may not be indicated when the known risk factors are highly unfavorable to survival. It is apparent (see Fig. 8-8) that a patient with an LV aneurysm, NYHA class V, a myocardial score of 8 (two-system disease) or more, and severe heart failure has an 80\% probability of hospital death (CL 55%-90\%); if the myocardial score is 11 or greater, the risk approaches 100\%. In these circumstances, operation may be contraindicated, although current methods of myocardial management may allow some such patients to survive operation and be clinically improved. The risk is lower when heart failure is less severe; under such circumstances, operation is clearly advisable. In borderline cases, coexisting akinesia or dyskinesia of the posterior-basal segment of the LV is recognized as an additional risk factor.

When the LV aneurysm is small or moderate in size, its presence is not an indication for operation per se. This conclusion is based in part on the fact that many preoperatively diagnosed aneurysms are not found to be aneurysms at operation or autopsy. Patients in such situations are advised about operation based on their coronary artery disease and LV function (see Chapter 7) rather than on their aneurysm. In this regard, it is noteworthy that an aneurysm that remains small 1 year after MI is unlikely to enlarge progressively thereafter, and embolization from it is unlikely. When indications for resection of an LV aneurysm or akinetic area are present, operation need not be deferred to permit maturation of the aneurysm. Walker and colleagues reported one hospital death among 20 patients (5\%; CL 0.6%-16\%) undergoing operation within 8 weeks of acute infarction.\textsuperscript{89} Six of the patients underwent early operation because of recurrent ventricular tachycardia. The long-term results were excellent, with 92\% survival at 5 years. Similar results (low operative mortality, satisfactory 3- to 5-year survival) have been reported by Di Donato and colleagues\textsuperscript{85} and Battaloglu and colleagues.\textsuperscript{86}

LV scars encountered in the operating room during surgery for coronary artery disease may require excision if they clearly contain little muscle and are of important size. Di Donato, Dor, and colleagues have demonstrated comparable improvement in resting ejection fraction in patients with akinetic scars and those with dyskinetic scars (aneurysms) following endoventricular circular patch plasty repair.\textsuperscript{14,84} They and others\textsuperscript{56,81} have postulated that patients with heart failure, previous anterior MI, and LV dilatation or akinesia may benefit from this type of repair as well. Results from a multicenter registry of 1198 patients undergoing endoventricular patch plasty repair indicate a 30-day mortality of 5.3\% (CL 4.6%-6.0\%) and 5-year survival of 69\%.\textsuperscript{84} Among a cohort of the surviving patients, mean LV ejection fraction increased from 30\% ± 11\% to 40\% ± 12\% (P < .001), and mean LV end-systolic volume index decreased from 80 ± 51 mL · m⁻² to 56 ± 34 mL · m⁻². The STICH trial demonstrated comparably low 30-day mortality (6\% in 501 patients having the combined procedure, CL 4.9%-7.3\%) and comparable 5-year survival (67\%).\textsuperscript{85} Mean LV end-systolic volume index decreased from 83 mL · m⁻² to 67 mL · m⁻² (P < .001).

SPECIAL SITUATIONS AND CONTROVERSIES

Intractable Ventricular Tachyarrhythmias

Although intractable ventricular tachyarrhythmias occur in patients with ischemic heart disease in the absence of areas of LV scarring, they are more common in patients with LV aneurysms or extensive fibrosis. However, only a small proportion with LV aneurysms develop intractable ventricular tachycardia.\textsuperscript{89} Most patients in whom such an arrhythmia
develops have poor global LV function, and it has been suggested that ventricular tachyarrhythmias are particularly likely to occur when the ventricular septum has been involved in the infarction. As a corollary, poor LV function and nonresponsiveness to drug therapy for ventricular tachycardia have been identified as risk factors for sudden cardiac death. Management of patients with the combination of LV aneurysm and intractable ventricular tachyarrhythmias is discussed in detail in Section V, “Ventricular Tachycardia and Ventricular Fibrillation in Ischemic Heart Disease,” in Chapter 16.

False Left Ventricular Aneurysm

The aneurysms discussed in this chapter, so-called true aneurysms, are formed by scarring, thinning, and stretching of an infarcted area of LV wall. This process generally produces a wide-mouthed aneurysm. By contrast, a false aneurysm may develop after acute rupture of an infarcted area of LV. Such ruptures are usually fatal, but when the pericardium is sufficiently adherent to the epicardium, rupture may result only in a localized hemopericardium. Persistent communication of the hemopericardium with the LV cavity results in gradual expansion of the hemo-pericardium into a false aneurysm whose wall is composed of pericardium and adhesions and occasionally of myocardium, and whose mouth is usually narrow. These aneurysms have a strong tendency to rupture in contrast to true aneurysms. False aneurysms are much more likely than true aneurysms to occur posteriorly (on the diaphragmatic surface of the LV) or laterally.

Differentiation between true and false aneurysms can be difficult because the imaging characteristics of the two entities are often similar. However, Doppler color flow imaging and transesophageal echocardiography are useful techniques for demonstrating the presence of a false aneurysm.

Resection of an LV false aneurysm is clearly advisable. The resection may pose formidable problems when the aneurysm sac extends anteriorly beneath the sternum. It is then necessary to begin CPB via cannulae introduced into the femoral artery and vein. If the false aneurysm is very large, the patient is cooled to 20°C before the sternum is opened. As soon as possible, the aorta is clamped, cardioplegia induced (see Chapter 3), and the operation begun. The false sac is entered, and blood from this sac is returned to the circuit using cardiotomy suckers. The aneurysmal wall is resected or left alone, and the LV is reconstructed using techniques described earlier in this chapter (see Technique of Operation). When indicated, CABG is also performed.

Postinfarction Left Ventricular Free Wall Rupture

Acute rupture of the free wall of the LV is an infrequent but serious complication of acute MI, occurring in 2% to 4% of patients. Among 1048 patients with acute infarction and cardiogenic shock evaluated in the SHOCK (SHould we emergently revascularize Occluded Coronaries in cardiogenic shock?) trial and registry, free wall rupture or tamponade was present in 28 (2.7%). It is the second most common cause of death following acute infarction (behind acute cardiac failure), accounting for up to 20% of early deaths. Occasionally the rupture is massive, and death quickly results from exsanguination. Cardiac rupture is more often a gradual process, beginning with small areas of endocardial necrosis. These permit formation of hematomas, which gradually dissect through the necrotic myocardium into the pericardium, resulting in tamponade and cardiogenic shock. If rupture is massive (the so-called blowout phenomenon), death occurs suddenly. If it is not, tamponade develops more slowly, allowing time for diagnosis and surgical treatment. Rupture occurs most commonly on the lateral or anteroapical wall of the LV and generally in the middle of the ventricle along the axis from base to apex. Myocardial free wall rupture should be suspected in patients with recent MI who have recurrent or persistent chest pain, hemodynamic instability, syncope, signs of pericardial tamponade, or transient electromechanical dissociation. Diagnosis can be made most expeditiously with echocardiography, which demonstrates a pericardial effusion or pericardial thrombus (Fig. 8-9). Operation is indicated unless the patient is moribund. If the patient is hemodynamically unstable with evidence of tamponade, rapid infusion of fluids and pericardiocentesis may permit stabilization. An intraaortic balloon should be inserted. If the hemodynamic state does not improve, CPB should be established by peripheral cannulation (see

Figure 8-9 Echocardiographic apical two-chamber view of left ventricular (LV) free wall rupture. A, Apical LV expansion with mild pericardial effusion. B, Fifteen hours later, echocardiogram shows apical expansion with an apical fibrotic cap (arrow), and larger pericardial effusion with signs of cardiac tamponade. (From Haddadin and colleagues.)

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“Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2). Preoperative coronary angiography is not advisable unless the hemodynamic state is stable. Several techniques have been used for surgical treatment. The traditional approach has involved use of CPB, infarctectomy, and closure of the defect directly with pledged sutures or a polyester patch. More recently, sutureless techniques have been used. Patches of PTFE felt, polyester, or pericardium (autologous or bovine) have been placed over the site of rupture and secured with various glues (gelatin-resorcin-formaldehyde-glutaraldehyde [GRF], fibrin, cyanoacrylate) with or without suturing the patch to the adjacent noninfarcted myocardium. A number of these procedures have been performed without CPB. This technique appears to be particularly valuable when there is no obvious rupture or “blowout” site. CABG can be added to all these procedures when appropriate.

Operative mortality is substantial and is related principally to hemodynamic status at time of operation. Among a group of 66 patients surgically treated by Loiance and colleagues and followed up to 16 years postoperatively, actuarial survival was 44% at 5 years and 26% at 10 years.1,3

Congenital Left Ventricular Aneurysm

Congenital LV aneurysm is a rare malformation characterized by thinning of the myocardium, with layers of myocardial cells intermingled with various amounts of fibrous tissue.3,6 It is usually located at the apex of the LV and has a broad neck.6 This entity differs from a congenital diverticulum of the LV, which is a noncontractile bulging of the LV into the epigastrum.12 The latter is characterized by an elongated shape and a narrow connection with the LV cavity.6 It is also associated with midline thoracic and anterior abdominal defects. Both conditions are rare and have been treated surgically with good results.3,15,58

Traumatic Left Ventricular Aneurysm

Rarely, violent nonpenetrating chest trauma produces such a severe contusion of the heart that a localized aneurysm forms.2,10 Vascular injury and intramyocardial dissection resulting from blunt trauma may also lead to aneurysm formation.5,55 The aneurysm, which is usually well localized and often thin walled, may be detected early after the trauma or several years later.8,17,51 Because of the thin wall and propensity for rupture, a posttraumatic LV aneurysm should be resected whenever possible.

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A

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C


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Chapter 8 Left Ventricular Aneurysm


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2. Ziegler E. Uber die Ursachen der Nierenschlimpfung nebst hemer-kungen fiber die Unterschiedung Verschiedener Formen de Nebritis. Freiburg, West Germany, 1879, p. 886.
Postinfarction ventricular septal defect (VSD) is an opening in the ventricular septum resulting from rupture of acutely infarcted myocardium.

**HISTORICAL NOTE**

In 1847, Latham first described a postinfarction VSD at autopsy, but it was not until 1923 that Brunn made the diagnosis clinically. In 1957, Cooley and colleagues first reported surgical repair of a postinfarction VSD 11 weeks after myocardial infarction (MI). The patient died 6 weeks later. The first long-term survivor of such repair was reported by the Mayo Clinic in 1963. Approach through the left ventricle (LV) was described in 1969 by Kay and Dubost and subsequently by Kitamura and colleagues, Javid and colleagues, and others. The double-patch method was described by Iben and colleagues and subsequently modified by Gonzalez-Lavin and Zajtchuk and by Daggett and colleagues. Repair of the ruptured septum through a right atrial approach was reported by Filgueira and colleagues in 1986. In 1987, David and colleagues introduced the concept of endocardial patch repair with infarct exclusion using autologous pericardium.

**MORPHOLOGY**

Postinfarction VSD is usually located in the anterior or apical portion of the ventricular septum (=60% of cases) as a result of a transmural anterior MI. About 20% to 40% of patients have a VSD in the posterior portion of the ventricular septum as a result of an inferior MI. Ventricular septal rupture usually occurs as a complication of a first acute MI. Also, a well-developed collateral coronary circulation is uncommon in hearts with a postinfarction VSD. The defect is generally associated with complete occlusion (rather than severe stenosis) of a coronary artery, usually the left anterior descending coronary artery. Important stenoses often coexist in the right coronary artery system. VSDs may be multiple, and rather than occurring simultaneously, they may develop separately several days apart. The importance of concomitant right ventricular (RV) infarction in patients with postinfarction VSD is now evident. For many years, evidence of RV dysfunction was thought simply to represent poor “adaptation” of the RV to the sudden increase in pulmonary blood flow imposed by the postinfarction VSD. Accumulated information indicates that actual infarction of the inferior RV wall, or at least severe ischemia of that area, is responsible for the dysfunction. A posterior VSD, in particular, may be accompanied by mitral valve regurgitation secondary to papillary muscle infarction or ischemia (see Chapter 10). In about 40% of patients who survive the early period after ventricular septal rupture, the remainder of the infarcted septum and adjacent ventricular wall may become aneurysmal.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

The first sign of ventricular septal rupture in a patient who has recently sustained an MI is development of a pansystolic murmur, usually at the left lower sternal border, with or without radiation to the axilla, and of varying intensity. If the murmur is overlooked or its importance ignored, most patients with ventricular septal rupture die undiagnosed. The chest radiograph provides evidence of pulmonary venous hypertension and increased pulmonary blood flow. A systolic murmur can result from acute mitral regurgitation secondary to MI as well as from postinfarction VSD, and the two conditions may coexist. Thus, after detection of the murmur, an
examination with two-dimensional echocardiography (either transthoracic or transesophageal) with Doppler color flow imaging is performed to define the site of the VSD, quantify the magnitude of left-to-right shunt, and ascertain presence or absence of mitral regurgitation. Echocardiography is highly sensitive and specific and provides safe and rapid diagnosis. It also permits preoperative analysis of wall motion abnormalities in a high percentage of patients.

Magnitude of left-to-right shunt can also be quantified by the Fick principle (see “Whole Body Oxygen Consumption” under Cardiovascular Subsystem in Chapter 5). A pulmonary artery (Swan-Ganz) catheter is introduced at the bedside. Blood samples are obtained from the right atrium, the pulmonary artery, and a peripheral artery. The left-to-right shunt is usually large, with a pulmonary-to-systemic blood flow ratio \((Q_p/Q_s)\) of 2.0 or greater. Both pulmonary artery wedge pressure, reflecting left atrial and LV end-diastolic pressures, and pulmonary artery pressure are usually elevated. Once the presence of a left-to-right shunt is demonstrated and initial management implemented (see “Preoperative Preparation” under Technique of Operation), coronary angiography should be performed if the patient is hemodynamically stable.

Although some patients with postinfarction VSD will do well without addition of invasive studies, there is accumulating evidence that bypass grafting of stenotic coronary arteries supplying the noninfarcted areas of myocardium is associated with improved early and late survival. Multiple-system coronary artery disease is present in more than 50% of patients. If echocardiographic studies have adequately identified the VSD, presence or absence of mitral regurgitation and LV wall motion abnormalities, intracardiac pressure measurements, and left ventriculography are unnecessary.

**NATURAL HISTORY**

Before the advent of thrombolytic therapy and acute percutaneous coronary artery interventions, postinfarction VSD developed in approximately 1% to 3% of patients. Following introduction of these therapeutic interventions, the frequency has been substantially reduced to less than 0.5% of patients. Ventricular septal rupture generally occurs during the first week after acute MI. There is a high incidence in the first day (94% in the GUSTO-I trial); median time for presentation in the SHOCK trial was 16 hours. Without surgical treatment, early death is common; less than 30% of patients survive 2 weeks, and only 10% to 20% survive more than 4 weeks. Risk of death is greatest immediately after myocardial rupture and then gradually declines. Women and the elderly may be more susceptible.

**TECHNIQUE OF OPERATION**

**Preoperative Preparation**

Because most patients with postinfarction VSD are seriously ill and require operation early after septal rupture, their management before operation is of critical importance. Once the diagnosis of acute postinfarction VSD has been confirmed by echocardiography and a pulmonary artery catheter has been inserted, additional diagnostic studies must be considered before proceeding with operation. (The only exception to this is the occasional patient with essentially no systemic hemodynamic disturbance, as described in “Indications for Operation.”) An intraaortic balloon catheter (IABP) should be inserted urgently, because these patients can deteriorate rapidly. If the patient remains hemodynamically unstable, cardiopulmonary bypass (CPB) can be established by peripheral cannulation (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2). If indicated, the patient is taken immediately to the cardiac catheterization laboratory for special studies (see “Clinical Features and Diagnostic Criteria” earlier in this chapter), with the IABP or CPB in place and functioning. When the studies have been completed, or if they are not performed, operation is undertaken immediately, because permanent improvement is generally not achieved with support devices alone.

**Initial Steps**

After the usual initial preparations in the operating room (see “General Comments and Strategy” in Section III of Chapter 2), a median sternotomy incision is made. The heart
is disturbed as little as possible before CPB is established. While performing the median sternotomy, removal and preparation of saphenous vein is accomplished in the usual manner (see Chapter 7). Because of the length and complexity of the operation, the surgical plan must be efficient so that aortic-clamp and CPB times are kept to a minimum. CPB is promptly established using two venous canulae and caval tapes. If CPB is established percutaneously before or immediately after the patient is brought to the operating room, central cannulation should be performed and CPB established using a pump-oxygenator designed for operating room use. The femoral lines are clamped and removed, and the femoral artery and vein are repaired at the end of the procedure. The aorta is clamped. Myocardial management may include warm induction of cardioplegia and controlled aortic root reperfusion (see “Cold Cardioplegia, Controlled Aortic Root Perfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Because an acute coronary occlusion is typically present, the coronary sinus route of administration should be employed for at least part of the cardioplegic infusion (see “Technique of Retrograde Infusion” under Cold Cardioplegia [Multidose] in Chapter 3). The caval tapes are secured. A left atrial venting catheter may be inserted, but usually is not necessary.

Repair of Defect

The VSD is usually approached through the LV. When located anteriorly, it is approached through the anterolateral infarction (or aneurysm) that is generally present (Fig. 9-2, A). The defect in the septum is typically found immediately beneath this area (Fig. 9-2, B). It is repaired using a collagen- or gelatin-impregnated polyester patch or a patch of autologous or bovine pericardium. The patch is made sufficiently large to cover the adjacent intact but infarcted portion of the septum as well as the VSD. No part of the ventricular septum is resected. The patch is sewn into place on the LV side of the septum, with pledgeted mattress sutures placed away from the edge of the defect into noninfarcted myocardium. The sutures are placed close together and the pledgets placed on the RV side of the defect (Fig. 9-2, C). Alternatively, the patch can be sutured into place with a continuous No. 3-0 or 4-0 polypropylene suture, securing the patch to noninfarcted myocardium on the ventricular septum (Fig. 9-2, D). Infarcted or aneurysmal myocardium on the anterolateral wall of the LV is excised, avoiding the anterolateral papillary muscle. If more than a small amount of tissue is removed from the anterolateral wall, it may be necessary to close the defect in the LV wall with a polyester or pericardial patch. If this is not necessary, the incision in the LV is closed with interrupted heavy (No. 0 or 2-0) silk or polyester sutures placed through strips of polytetrafluoroethylene (PTFE) felt and through the patch that has closed the VSD (Fig. 9-2, E). This suture line is reinforced with a continuous suture of No. 0 or 2-0 polypropylene, which is passed through both strips of PTFE felt, both edges of the myocardium, and the ventricular septal patch (Fig. 9-2, F).

An alternative technique involves suturing a pericardial patch to the LV endocardium adjacent to the area of the infarction. The LV is opened through an incision in the infarcted anterolateral wall. An oval patch (approximately 4 × 6 cm) of bovine pericardium is sutured to the endocardium of the inferior portion of the noninfarcted endocardium of the ventricular septum with a continuous No. 3-0 polypropylene suture (Fig. 9-3, A). The suture line is continued into the noninfarcted endocardium of the anterolateral ventricular wall (Fig. 9-3, B). When placing the continuous suture through the transition zones (superiorly and inferiorly) between the septum and the free wall of the LV, care must be taken to anchor the patch securely to the myocardium to prevent residual communications between the LV and RV. Separate interrupted sutures may be required. Once the patch is completely secured to the LV endocardium, the LV cavity is essentially excluded from the infarcted myocardium (Fig. 9-3, C). The ventriculotomy is closed using two strips of bovine pericardium or PTFE felt (Fig. 9-3, D).

When the VSD is in the apical portion of the septum and is associated with an apical MI, the operation consists of amputating the apex of the ventricle, including the involved portion of the ventricular septum (Fig. 9-4, A). The LV is opened through the infarcted myocardium and the septum examined. If the VSD is immediately adjacent to the area of apical infarction, the apex of the heart is excised, including the involved portion of the septum and adjacent RV (Fig. 9-4, B). Using strips of PTFE felt on each side of the septum and on the edges of the right and left ventricular myocardium, heavy mattress sutures of silk or polyester are placed through these four layers of felt as well as through the right and left ventricular myocardium and the ventricular septum (Fig. 9-4, C). These sutures are tied, thus excluding the interventricular communication and the openings into both ventricles. The resulting suture line is reinforced with a continuous No. 0 or 2-0 polypropylene suture (Fig. 9-4, D).

VSDs located in the posterior septum are more difficult to expose and repair. The heart is lifted out of the pericardium with traction on the LV apex. The defect is approached through a vertical incision in the infarcted LV myocardium (Fig. 9-5, A). If the VSD is relatively small, the necrotic tissue can be excised, including the infarcted free wall of both the RV and LV, often with the overlying occluded posterior descending coronary artery (Fig. 9-5, B). The VSD patch (collagen- or gelatin-impregnated polyester or bovine or autologous pericardium) is placed on the LV side of the septum and secured using mattress sutures of No. 2-0 polyester, with pledgets placed on the RV side of the septum (Fig. 9-5, C). If little or no free wall myocardium has been excised, LV and RV edges are approximated, incorporating the septal patch and two strips of PTFE felt. A large defect in the free wall requires a second patch. The free edge of the septal patch is sutured to the free wall of the LV with interrupted mattress sutures of No. 2-0 polyester using pledgets on the patch and a strip of PTFE on the ventricular wall (Fig. 9-5, D). The patch for closure of the RV is attached to the septal patch already in position and to the free wall of the RV. Pledgets of felt are placed on the inner surface of the RV, and a strip of felt is placed on the outer surface (see Fig. 9-5, D).

Muehrcke and colleagues describe an alternative technique for closure of the free wall when there is extensive infarction. No infarcted muscle on the RV or LV free walls is excised. The septal patch is sutured to the RV edge of the incision that was made to expose the septum. This suture line incorporates the infarcted free wall and a patch of polyester placed over the entire infarcted muscle of the free wall (Fig. 9-5, E).
Figure 9-2  Repair of anterior postinfarction ventricular septal defect. A, Incision is made through the anterolateral infarcted myocardium that is usually present or, if some weeks have elapsed, through the scar or aneurysm that has formed. B, Defect is located immediately beneath incision. C, If interrupted sutures are used, the patch is sewn into place on left ventricular (LV) side of septum, with pledged mattress sutures placed away from the edge of the defect into noninfarcted myocardium (dashed line). Sutures are placed close together, and pledgets are placed on the right ventricular side of the defect. Key: APM, Anterior papillary muscle; LV, left ventricle; RV, right ventricle; VSD, ventricular septal defect.
If a continuous suture technique is used, the patch is sutured to noninfarcted myocardium on the ventricular septum adjacent to the area of infarction using a No. 3-0 or 4-0 polypropylene suture. If patch repair of anterolateral wall is not required, the incision in the LV is closed with interrupted heavy silk or polyester sutures placed through strips of polytetrafluoroethylene (PTFE) felt, edges of the myocardium, and patch that has closed the ventricular septal defect. Suture line is reinforced with a continuous suture of No. 0 or 2-0 polypropylene, which is passed through both strips of PTFE felt, both edges of the myocardium, and ventricular septal patch.
Figure 9-3  Infarct exclusion technique with endocardial patch for repair of anterior postinfarction ventricular septal defect. **A,** Left ventricle (LV) is entered through an incision in the infarcted anterolateral wall. An oval patch of bovine pericardium is sutured to the endocardium of the posterior, noninfarcted portion of the ventricular septum with a continuous No. 3-0 polypropylene suture. **B,** Suture line is continued into the noninfarcted endocardium of the anterolateral ventricular wall.
Figure 9-3, cont’d  
**C.** The LV cavity is thus excluded from the infarcted myocardium.  
**D.** Ventriculotomy is closed using two strips of bovine pericardium or polytetrafluoroethylene (PTFE) felt and a continuous polypropylene suture. Key: LV, Left ventricle; RV, right ventricle.

**Figure 9-4**  
Repair of postinfarction ventricular septal defect in apical portion of septum.  
**A.** Location of infarction at apex of heart.  
**B.** Line of excision through left ventricle, septum, and right ventricle. Key: LV, left ventricle; RV, right ventricle.  
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Pledged sutures are placed circumferentially around the area of infarcted muscle and through the polyester patch, then tied over a strip of PTFE felt (Fig. 9-5, F).

The technique developed by David and colleagues involves an incision in the inferior wall of the LV parallel to the posterior descending coronary artery. The traction sutures are placed on the edges of the ventriculotomy to facilitate exposure (Fig. 9-6, A). The VSD is identified, and a triangular patch of bovine pericardium approximately 4 × 7 cm is sutured first to the fibrous anulus of the mitral valve using a continuous No. 3-0 polypropylene suture. The medial margin of the patch is sutured to noninfarcted muscle of the septum adjacent to the defect (Fig. 9-6, B). The lateral edge of the patch is then sutured to the endocardium of the LV free wall adjacent to the posterior papillary muscle (Fig. 9-6, C). This excludes all infarcted muscle from the LV cavity (Fig. 9-6, D). The ventriculotomy is closed with two layers of sutures buttressed with strips of bovine pericardium or PTFE felt (Fig. 9-6, E).

Associated Procedures

Occasionally, mitral regurgitation may be associated with acute septal rupture, particularly when the infarction is posterior. The mitral valve is replaced (or occasionally repaired) under such circumstances. Replacement is usually best performed through the left ventriculotomy, using interrupted pledged mattress sutures with the pledgets on the atrial side of the anulus. It can also be replaced (or repaired) through a left atrial or biatrial incision (see Chapter 10).

When an LV aneurysm coexists with a postinfarction VSD, it is excised as the initial step in the operation. Then after repair of the VSD, the aneurysm is generally repaired as usual (see Chapter 8). However, improvisation in the repair may be necessary. Rarely, patients with postinfarction VSD are also found to have free wall rupture of the infarct. In surgical

Completion

An essential part of the operation is controlled aortic root reperfusion (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). During this maneuver, all suture lines are examined. Additional measures are used, if necessary, to establish hemostasis. The remainder of the operation is completed in the usual manner (see “Completing Operation” in Section III of Chapter 2). Particular care is taken to achieve hemostasis. Two right atrial and two RV temporary pacing wires are placed so that atrioventricular sequential pacing can be established, if needed. IABP is resumed during the rewarming phase of CPB and usually is continued into the postoperative period. If CPB cannot be discontinued after about 30 minutes of normothermic partial CPB, temporary ventricular assistance may be required (see “Temporary Ventricular Assistance” in Chapter 5).

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is conducted as described in Chapter 5. IABP is continued in a one-to-one mode until cardiac output is adequate; it is then gradually discontinued and the balloon catheter removed. If ventricular assist devices are in place, flow through them is gradually decreased as ventricular function and cardiac output improve (see “Temporary Ventricular Assistance” in Chapter 5). Because patients are often critically
Figure 9-5 Repair of posterior postinfarction ventricular septal defect (VSD). A, Heart is lifted out of pericardial cavity, and VSD is approached through a vertical incision in infarcted left ventricular myocardium. B, Infarcted tissue (right ventricle [RV], left ventricle [LV], and septum) is excised. Dashed lines indicate limits of excision. C, Septal patch is placed on LV side of septum and secured using polyester mattress sutures, with pledgets placed on RV side of septum.

Continued
ill during the early postoperative period, with low cardiac output and often with complicating arrhythmias, a full therapeutic regimen is usually required. This includes optimizing preload with infusion (or removal) of volume, enhancing contractility with inotropic agents, and reducing afterload, if indicated. Attaining a heart rate that results in optimal cardiac output by pacing or pharmacologic agents is also important. Using the technique described earlier under “Clinical Features and Diagnostic Criteria,” measurements are made to detect residual shunt, which can be present because of friability of the septum and relative insecurity of the repair. Transesophageal echocardiography is also useful for this purpose. If the $\frac{Q_p}{Q_s}$ is 1.5 to 2.0 or greater and the hemodynamic state is poor, prompt reoperation should be considered.

Care required late postoperatively by patients undergoing isolated CABG should be applied to those who have undergone repair of a postinfarction VSD (see “Special Features of Postoperative Care” in Chapter 7).
Figure 9-6  Infarct exclusion technique with endocardial patch for repair of posterior postinfarction ventricular septal defect. A, Left ventricle (LV) is entered posteriorly through an incision parallel and adjacent to the posterior descending coronary artery. Traction sutures are placed through edges of the myocardium. B, Triangular-shaped patch of bovine pericardium is first sutured to the fibrous anulus of the mitral valve using a continuous No. 3-0 polypropylene suture. Medial edge of patch is then sutured to noninfarcted muscle of the septum adjacent to the defect. Key: IVC, Inferior vena cava; RV, right ventricle; VSD, ventricular septal defect.
Chapter 9 Postinfarction Ventricular Septal Defect

Time-Related Survival

Time-related survival after repair of postinfarction VSD is less than optimal. In large series of patients with long-term follow-up, 5-year survival ranged from 44% to 57% and 10-year survival from 29% to 36% \(^{(D5,D8,D9,J2,L4,M7)}\) (Fig. 9-7, A). The hazard function for death after repair of postinfarction VSD has not only a high and rapidly declining early phase, but also an appreciable constant phase that is approximately five times greater than that after isolated CABG (Fig. 9-7, B).

RESULTS

Early (Hospital) Death

Hospital mortality after VSD repair is approximately 30% to 40% \(^{(A3,A4,D5,D8,D9,E1,J2,L4,M7,P1,P3)}\). Death may be difficult to prevent because of the extent of myocardial necrosis associated with rupture of the ventricular septum. However, mortality might be reduced by prompt surgical repair, better methods of myocardial management, and more aggressive use of ventricular assistance in the postoperative period.

Figure 9-6, cont’d  

C, Lateral edge of patch is next sutured to endocardium of the LV free wall adjacent to posterior papillary muscle. 

D, This technique excludes all infarcted muscle from LV cavity. 

E, LV is closed with two layers of sutures buttressed with strips of bovine pericardium or polytetrafluoroethylene (PTFE) felt.
Modes of Death

The mode of death in more than half and up to 90% of patients dying early after operation for postinfarction VSD is cardiac failure. This relatively high prevalence is related to extensive MI, complexity of operation, and preoperative organ system dysfunction. Bleeding, sepsis, stroke, gastrointestinal bleeding, and recurrent VSD are other modes of early death. Cardiac failure is also the most common mode of late death. Other modes of late death include sudden death, stroke, sepsis, and MI.

Incremental Risk Factors for Death

Mortality is influenced by several factors that have been identified by a number of multivariable analyses. From these and other studies in the literature, and from knowledge of the risk factors for death and other adverse outcomes in patients with ischemic heart disease (see “Results” in Chapter 7), some inferences can be made. The most important risk factors for death in the early hazard phase are poor hemodynamic state (cardiogenic shock) at operation and acute RV dysfunction (Fig. 9-8). Amount and distribution of myocardial necrosis and scar are responsible for both factors. Poor hemodynamics becomes an even more severe risk factor when present for many hours before surgical intervention. Operation early after rupture of the septum typically carries a higher risk than that undertaken many days or weeks later, principally because of the high prevalence of hemodynamic instability and extensive myocardial necrosis. RV dysfunction results from ischemic injury or frank infarction of the RV and thus is more likely to be present when stenosis or occlusion in the right coronary artery system is located proximally. RV dysfunction may also occur after anterior MI. The higher mortality associated with repair of defects located inferiorly in the septum reported in some series probably relates to the higher prevalence of important right coronary stenosis and RV dysfunction in this group. Mortality may also be related to the greater complexity of posterior repairs and to more frequent involvement of the mitral valve. Severity and distribution of coronary artery disease are also risk factors, but are overshadowed by the patient’s hemodynamic status at operation and amount of damaged myocardium. Comorbidities such as older age at operation, diabetes, and preinfarction hypertension are likely risk factors for death in the early and constant hazard phases. The relatively small number of patients in most reported series has made identification of these and other factors difficult.

Functional Status

The functional status of most patients surviving the period of hospitalization is good. The majority of patients (70% to 95%) are in New York Heart Association (NYHA) functional class I or II.

Residual and Recurrent Defect

A residual VSD has been noted early or late postoperatively in 3% to 40% of patients. Residual VSD may be caused by (1) reopening of a closed defect, (2) presence of an overlooked VSD, or (3) development of a new VSD during the early postoperative period. Reoperation is required for closure of such residual defects when Qp/Qs is greater than 1.
INDICATIONS FOR OPERATION

Postinfarction VSD is almost always an indication for operation, because it produces a large left-to-right shunt and outcome without intervention is extremely poor.

A persisting question is the timing of operation. Repair of postinfarction VSD 2 to 3 weeks or more after septal rupture is relatively safe. By then, edges of the defect have become more fibrotic, and repair is more securely and safely accomplished. Therefore, when the patient presents with satisfactory hemodynamics, repair can be delayed, but there must be a high degree of certainty that the hemodynamics will remain stable. Criteria for deferment include (1) adequate cardiac output, with no evidence of cardiogenic shock; (2) absence of symptoms of pulmonary venous hypertension, or easy control of initial symptoms with appropriate drug therapy; (3) absence of fluid retention, or easy control by diuretics; and (4) adequate renal function, with stable blood urea nitrogen (BUN) and creatinine levels. The natural history of postinfarction VSD suggests that such circumstances are uncommon.

In the vast majority of patients, septal rupture rapidly leads to deteriorating hemodynamics with cardiogenic shock, marked and intractable symptoms of pulmonary venous hypertension, and fluid retention. Immediate study and urgent operation are then indicated. Even if these signs and symptoms are absent and renal function deteriorates, as evidenced by rising BUN and creatinine levels, surgical intervention should be promptly undertaken. The increased risk of early repair is accepted because of the high risk of death without operation.

Delayed detection and referral for surgical treatment of seriously ill patients may make recovery so unlikely that it is appropriate to allow the natural history of the disease to unfold without surgical intervention. For example, the surgeon might see a patient only after profound cardiogenic shock has led to neurologic unresponsiveness, ischemic compromise of a limb or the bowel, or severe impairment of renal function with anuria or greatly elevated BUN and creatinine levels.

SPECIAL SITUATIONS AND CONTROVERSIES

Repair of Defect Through a Right Atrial Approach

Repair of postinfarction VSD can be accomplished through a right atrial or bialtral approach. The potential advantage of this technique is that an incision in the LV myocardium is avoided. Experience with this procedure is limited. Massetti and colleagues have reported one of the larger series (12 patients). There were three early deaths (25%) and one late death. One patient required reoperation for a residual defect 3 months postoperatively, and one had a small residual left-to-right shunt. Of the eight surviving patients who were followed for a mean of 5 years, three were in NYHA functional class I, four in class II, and one in class III.

Percutaneous Closure of Defect

Percutaneous techniques have been used successfully to close congenital VSDs (see “Percutaneous Closure of Ventricular Septal Defects” under Special Situations and Controversies in Section I of Chapter 35). Lock and colleagues achieved successful percutaneous transcatheter closure of postinfarction VSDs in four patients with cardiogenic shock using the Rashkind double-umbrella device. The device emboled to the pulmonary artery in one patient, and the remaining three patients died with evidence of increased shunting across the defect over the ensuing several days. A Rashkind patent ductus arteriosus occluder system has also been used.

Balloon catheters, which are inserted through the LV via the aorta or through the RV and then inflated, and other occluders have been successful in temporarily reducing or eliminating the left-to-right shunt, thereby improving hemodynamic status and permitting a delay in surgical treatment. Percutaneous devices have also been used to close residual septal defects after open repair. Wider use of these or other minimally invasive techniques could substantially improve outcome.

Use of percutaneous closure as the definitive treatment for postinfarction VSD has been reported by Maltais and colleagues using the Amplatzer septal occluder device. Early mortality was 42% among 12 patients. One patient (8%) had a residual septal defect.

Postoperative Mechanical Circulatory Support

Mechanical circulatory support following surgical repair of postinfarction VSD should be considered for patients who cannot be weaned from CPB with maximal inotropic and IABP support (see “Temporary Ventricular Assistance” in Chapter 5).}

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10 Mitral Regurgitation from Ischemic Heart Disease

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Mitral regurgitation due to ischemic heart disease (ischemic mitral regurgitation) is mitral regurgitation caused by ischemic heart disease. This entity must not be confused with mitral regurgitation from other causes that coexist with ischemic heart disease.

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Mitral regurgitation resulting from rupture of a papillary muscle has been long recognized as a rare and frequently catastrophic complication of acute myocardial infarction (MI). A case was identified at autopsy at Johns Hopkins Hospital in 1935, but apparently the diagnosis was first made antemortem in 1948. Mitral regurgitation without papillary muscle rupture, occurring as an acute or chronic complication of ischemic heart disease with or without MI, was described in 1963 by Burch and colleagues. These authors referred to this type of ischemic mitral regurgitation as “papillary muscle dysfunction,” the presence of which was surmised rather than proved. The first successful surgical correction of papillary muscle rupture was reported by Austen and colleagues at Massachusetts General Hospital in 1965. Surgeons at Massachusetts General were also among the first to replace the mitral valve for ischemic mitral regurgitation, beginning in 1970.

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DEFINITION

Mitral regurgitation due to ischemic heart disease (ischemic mitral regurgitation) is mitral regurgitation caused by ischemic heart disease. This entity must not be confused with mitral regurgitation from other causes that coexist with ischemic heart disease.

HISTORICAL NOTE

Mitral regurgitation resulting from rupture of a papillary muscle has been long recognized as a rare and frequently catastrophic complication of acute myocardial infarction (MI). A case was identified at autopsy at Johns Hopkins Hospital in 1935, but apparently the diagnosis was first made antemortem in 1948. Mitral regurgitation without papillary muscle rupture, occurring as an acute or chronic complication of ischemic heart disease with or without MI, was described in 1963 by Burch and colleagues. These authors referred to this type of ischemic mitral regurgitation as “papillary muscle dysfunction,” the presence of which was surmised rather than proved. The first successful surgical correction of papillary muscle rupture was reported by Austen and colleagues at Massachusetts General Hospital in 1965. Surgeons at Massachusetts General were also among the first to replace the mitral valve for ischemic mitral regurgitation, beginning in 1970.

MORPHOLOGY

Acute Mitral Regurgitation Complicating Myocardial Infarction

Rupture of Papillary Muscle

Rupture of a papillary muscle occurs as an acute complication of MI, but its prevalence among patients with acute mitral regurgitation in the early stages of infarction is uncertain. About half of these patients have an actual rupture. About one third of patients with rupture may have a complete disruption of the papillary muscle, resulting in flailing of both the anterior and the posterior mitral leaflets. About two thirds of patients have rupture of one or more heads of the papillary muscle rather than a complete rupture of the entire muscle. The posteromedial papillary muscle is ruptured in about 75% of patients and the anterolateral muscle in about 25%. Correspondingly, most patients with acute mitral regurgitation resulting from MI have an inferoposterior left ventricular (LV) infarction. Also, at least in the study of Coma-Canella and colleagues, many have coexisting right ventricular infarction. Regardless, when the LV infarction is located inferoposteriorly rather than anterolaterally, the reason for more frequent rupture of the adjacent papillary muscle is not clear. The difference in collateral circulation to the two areas may play a role. The size and nature of the coexisting acute LV infarction vary, perhaps because of the...
small number of cases in most series. Nishimura and colleagues reported that the infarction is often small, whereas Barbour and colleagues found infarction in more than 20% of the LV wall and septum in the majority of patients. The infarction may be subendocardial or transmural.

Occasionally, papillary muscle rupture is associated with rupture of the ventricular septum as well as with rupture of the free wall of the LV.

Papillary Muscle Necrosis without Rupture

About half the patients who develop severe mitral regurgitation during acute MI do not have papillary muscle rupture, only papillary muscle necrosis. Papillary muscle dysfunction may contribute to resultant mitral regurgitation. However, contiguous MI probably plays a more important role. The distribution of necrotic changes and extent of MI are similar to those described for papillary muscle rupture.

Other Causes

Mitral regurgitation is a frequent complication of acute MI. When Doppler echocardiography is used for diagnosis, mitral regurgitation has been detected in up to 39% of patients early after an infarction. Substantial (moderate or severe) mitral regurgitation is present in 3% to 19% of patients and is an important predictor of mortality. Because papillary muscle rupture or necrosis occurs infrequently after acute infarction, other important causes of mitral regurgitation include (1) changes in configuration of the LV (remodeling), (2) global or segmental LV dysfunction, and (3) changes in function of the mitral valve resulting from leaflet prolapse, abnormal closure, or anular dilatation. Although papillary muscle dysfunction has been implicated as an important cause of ischemic mitral regurgitation, experimental and clinical studies employing two-dimensional (2D) echocardiography have demonstrated that it rarely is causative. LV systolic dysfunction, increased LV chamber sphericity, and regional asynergy of the inferoposterolateral wall overlying the posterior papillary muscle may be important determinants of developing mitral regurgitation. Van Dantzig and colleagues found that changes in the mitral valve anulus and leaflets were of limited importance in the pathogenesis of ischemic mitral regurgitation early after MI. Thus, although there is often no apparent structural abnormality of the mitral valve, changes in configuration and contractile function of the LV after an acute infarction prevent adequate coaptation of the leaflets and result in mitral regurgitation.

Chronic Mitral Regurgitation from Ischemic Heart Disease

Many patients with ischemic heart disease and chronic mitral regurgitation have coexisting mitral regurgitation caused by rheumatic fever, myxomatous degeneration, or other conditions. At operation, distinction between mitral regurgitation coexisting with ischemic heart disease and that caused by ischemic heart disease can be difficult because papillary muscle scarring or fibrosis is not always the result of earlier necrosis or adjacent MI. Chronic regurgitation through the mitral valve apparatus does follow acute MI in some patients. Causes include underlying papillary muscle ischemic dysfunction, papillary muscle scarring and shortening or even lengthening, previous rupture of a portion of the papillary muscle, asynergy of the adjacent LV wall, and LV remodeling, all of which can result from an earlier MI. Chronic regurgitation may also occur through the central part of the valve. This can result from restricted leaflet motion with increased leaflet tethering (Figs. 10-2 and 10-3) and from anular dilatation secondary to ischemic LV dysfunction. Severity and degree of the dysfunction may vary over time according to the degree of remodeling (increased sphericity) that occurs in the individual patient after infarction.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Acute Mitral Regurgitation Complicating Myocardial Infarction

Papillary muscle rupture presents as an acute event within a few hours to 14 days after an MI in 1% to 3% of patients. The onset is usually characterized by pulmonary edema, hypotension, or both, typically 2 to 7 days after acute infarction.

Rupture is signaled by worsening of the patient’s clinical condition. Profound shock indicates gross mitral regurgitation from total rupture; less severe signs suggest less severe mitral regurgitation from partial rupture or LV dysfunction. A new apical systolic murmur can be heard provided cardiac output is adequate and the regurgitation is not severe. The murmur is frequently absent in total rupture and usually present in partial rupture. An apical third heart sound is common, and pulmonary edema is often seen on chest radiography. The heart is usually normal in size or only slightly enlarged, and the left atrium is small.

A pulmonary artery (Swan-Ganz) catheter can provide important information (e.g., excluding the presence of left-to-right shunting) and, when it is in the pulmonary artery wedge position, may demonstrate a prominent v wave on the pressure tracing. Echocardiography (2D or transesophageal) is a valuable diagnostic tool in mitral regurgitation associated with MI. It is used to differentiate between papillary muscle rupture and LV dysfunction. In the latter condition, extensive wall motion abnormalities are usually present. With papillary muscle rupture, the mitral leaflet becomes flail and prolapses into the left atrium during systole. The ruptured portion of the muscle may be directly visualized as a separate mass attached to the chordae.
performed to confirm the diagnosis of mitral regurgitation (or ventricular septal defect or occasionally both) and to define areas of impaired LV contraction or aneurysm formation. In critically ill patients, however, left ventriculography is unnecessary when precatheterization studies have established the diagnosis and only coronary angiography is performed. When the patient is seriously ill, an intraaortic balloon pump (IABP) should be used. If the patient’s hemodynamic state remains unstable, cardiopulmonary bypass (CPB) can be established using a percutaneous technique (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2). These devices can be left in place until cardiac catheterization is completed and the patient is taken to the operating room.

**Chronic Mitral Regurgitation from Ischemic Heart Disease**

Usually the patient presents with gradually increasing mitral regurgitation. When the murmur dates from an MI, an ischemic etiology is assumed. There may be cardiac enlargement, including left atrial enlargement, hypokinesia, and akinesia at the infarction site. An LV aneurysm may coexist (see Chapter 8). Positron emission tomography (PET) or dobutamine echocardiography may reveal chronically ischemic, hibernating myocardium that may respond to increased blood flow from coronary artery bypass grafting (CABG) alone. Gadolinium contrast-enhanced cardiovascular magnetic resonance reveals myocardial scarring, and if the posterior papillary muscle is extensively scarred (nonviable), mitral annuloplasty may be insufficient to eliminate ischemic mitral regurgitation. Other diagnostic criteria are the same as for other types of chronic mitral regurgitation (see Chapter 11).

**NATURAL HISTORY**

**Acute Mitral Regurgitation Complicating Myocardial Infarction**

Rupture of a papillary muscle is an uncommon complication of acute MI and currently is probably even less common, given the widespread use of thrombolytic and percutaneous interventional therapy for acute infarction. It is, however, a life-threatening complication, with only about 25% of patients treated nonsurgically surviving more than 24 hours after total rupture. Survival after partial papillary rupture is better; more than 70% of patients survive the first 24 hours, and about 50% survive more than 1 month. They are then considered to have chronic mitral regurgitation.
When the papillary muscle remains intact, the natural history of acute mitral regurgitation is less well defined. As previously noted, however, moderate or severe mitral regurgitation in the absence of papillary muscle rupture is present in 3% to 19% of patients early after an acute infarction and is an important predictor of mortality.\(^{1,14,15,15,15}\) Using multivariable analysis, Lehmann and colleagues found that mitral regurgitation of any degree (as detected by left ventriculography) was a predictor of cardiovascular mortality at 1 year (relative risk 7.5; CI 2%-29%; \(P = .0008\)).\(^{1,16}\) In the study of Lamas and colleagues, cardiovascular mortality during 3\(^1/2\) years of follow-up was also higher in patients who developed mitral regurgitation early after acute infarction than in those who did not (29% vs. 12%; \(P < .001\)).\(^{1,17}\) Grigioni and colleagues observed a direct and significant correlation between severity of mitral regurgitation as determined by echocardiography and long-term survival\(^{1,18}\) (see Fig. 10-1). They also observed that mitral regurgitation predicts mortality in excess of that anticipated on the basis of patient characteristics and degree of LV dysfunction.

Chronic Mitral Regurgitation from Ischemic Heart Disease

Mild or moderate mitral regurgitation without papillary muscle rupture is episodic in some patients, presumably a result of changing prevalence and distribution of ischemic myocardium, loading characteristics of the LV, and variations in LV function.\(^{1,14}\) Persistent and severe mitral regurgitation, often associated with moderate or severe LV dysfunction, worsens the prognosis for patients with poor LV function.\(^{1,15}\) Furthermore, increasing severity of mitral regurgitation has an increasingly adverse effect on survival, regardless of type of treatment\(^ {1,18,1,15,1,14,1,12}\) (Fig. 10-4).

TECHNIQUE OF OPERATION

Acute Mitral Regurgitation Complicating Myocardial Infarction

In critically ill patients with this complication of acute MI, IABP is begun as soon as the condition is recognized,\(^{1,13}\) or CPB is established by percutaneous technique if indicated (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2). In the operating room, the patient is prepared and draped for CABG; the sternotomy, graft preparation, and preparation for CPB are expeditiously accomplished. CPB is established using two venous cannulae. If CPB was established percutaneously before bringing the patient to the operating room, the cannulations just described should be made and CPB established by a pump-oxygenator designed for use in the operating room. The peripheral lines are clamped but left in place. These cannulae are removed in the operating room at the end of the cardiac procedure.

Myocardial management may include warm induction of cardioplegia and controlled aortic root reperfusion (see “Cold Cardioplegia, Controlled Aortic Root Perfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Because an acute coronary occlusion is typically present, the coronary sinus route of administration should be employed for part of the cardioplegic infusion (see “Technique of Retrograde Infusion” under Cold Cardioplegia [Multidose] in Chapter 3). The distal anastomoses of the bypass grafts are performed before the mitral valve is repaired or replaced to avoid retracting the heart after a mitral prosthesis (valve or ring) has been inserted and thus prevent possible rupture of an area of infarcted LV.\(^{1,11}\) The proximal anastomoses of the grafts can be performed either immediately after completing the distal anastomoses and before opening the left atrium, or after closing the left atrium. If the left atrium has been closed, these anastomoses can be performed with the aorta still occluded or after removing the aortic clamp and placing a partially occluding clamp on the aorta while rewarming is completed.

The approach to the mitral valve is generally through the left atrium, although an approach through the right atrium may be useful (see “Approach Across the Atrial Septum” under Special Situations and Controversies in Chapter 11). With acute total papillary muscle rupture, the mitral valve is replaced with a mechanical prosthesis or bioprosthesis. Because the mitral annular tissue is usually not thickened and may be more friable than normal, great care must be taken to (1) obtain adequate bites of tissue when placing the annular sutures and (2) avoid excessive traction on these sutures as the valve is lowered into position, to prevent them from pulling through the tissue. Pledged mattress or nonpledgeted simple interrupted sutures are preferred.

When the papillary muscle is not ruptured and the chordal mechanism is intact, or if only one head is ruptured and there is annular dilatation, reparative techniques and anuloplasty with or without use of an anuloplasty ring are preferable to valve replacement\(^ {1,15,1,3}\) (see “Mitral Regurgitation Repair” under Technique of Operation in Chapter 11). If an anuloplasty ring or band is inserted, it is probably preferable to use one that is smaller than the sizer that fits the annulus. After CPB is discontinued and with cannulae still in place, competence of the valve is assessed, preferably by transesophageal echocardiography (TEE). Left atrial pressure should be at least 15 mmHg and systolic arterial pressure above 120 to 130 mmHg during the assessment. If the valve is not competent, CPB is reestablished, cardioplegia is reinfused, and the valve is either repaired again or replaced. The remainder of the operation is completed as usual. An IABP or temporary ventricular assistance may be needed (see “Treatment of Low
Cardiac Output” under Cardiovascular Subsystem in Section I of Chapter 5).

Chronic Mitral Regurgitation from Ischemic Heart Disease

The techniques of repair and replacement of the chronically regurgitant mitral valve are described under “Technique of Operation” in Chapter 11. Difficulties in intraoperative decision making result from (1) time-related variability in the magnitude of regurgitation caused by ischemic heart disease, (2) uncertainty about the precise morphologic basis of the regurgitation, and (3) frequency with which regurgitation is associated with poor LV function. These considerations require careful evaluation of regurgitation and need for mitral repair or replacement preoperatively, in the operating room before CPB is established, after repair while CPB is still in place, and after CPB is discontinued.

Evaluation includes careful assessment of the intraoperative TEE, visual examination of the morphology of the valve, and identification of the location and magnitude of the regurgitation. Identifying the location and assessing the magnitude of regurgitation are accomplished by TEE, recognizing that this technique may overestimate or underestimate the degree of regurgitation (see Fig. 10-2). When the circulation is intact, echocardiographic assessments should be made with left atrial pressure at least 12 to 15 mmHg and systolic pressure above 120 to 130 mmHg.

On direct visualization of the valve, diagnosis of an ischemic etiology for regurgitation is generally made by exclusion. The anulus appears normal or is only slightly dilated. The leaflets are usually normal in appearance, and the chordae tendineae are usually not shortened or elongated. The papillary muscles may be pale, scarred, or normal in appearance. In this setting, repair of the valve with some form of annuloplasty is usually possible (see Chapter 11). When regurgitation is severe both preoperatively and intraoperatively and dominates the clinical picture, mitral repair or replacement is indicated. When severity of regurgitation is variable preoperatively and variable and no more than moderate intraoperatively (particularly when severity lessens after the CABG portion of the operation is completed), and signs and symptoms of myocardial ischemia are dominant, the mitral valve may be left alone. However, this recommendation is controversial. Intermediate situations demand individual intraoperative decision making.

When a repair is performed, the functional status of the mitral valve is evaluated by TEE after discontinuing CPB, with the cannulae still in place and with the systolic arterial pressure above 120 to 130 mmHg. If the hemodynamic situation or the repair is unsatisfactory, CPB can be reestablished and the mitral valve repaired again or replaced. If mitral replacement is necessary, every effort should be made to preserve the chordae tendineae to the posterior leaflet or to both leaflets.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

The usual management protocols are followed (see Chapter 5). Because patients with mitral regurgitation from ischemic heart disease are apt to have low cardiac output postoperatively, catecholamine support and IABP are required more often than after other procedures.

**RESULTS**

**Early (Hospital) Death**

**Acute Mitral Regurgitation Complicating Myocardial Infarction**

Because of the rarity of the condition, only a few surgical series have been reported. Among those with the largest numbers of patients (between 21 and 55), early mortality ranged from 18% to 22%. For patients without rupture of a papillary muscle who require operation for ischemic mitral regurgitation, hospital mortality is substantial, particularly for patients in cardiogenic shock. With use of appropriate myocardial management (see “Technique of Operation”), early mortality should depend primarily on extent of MI. Chevalier and colleagues and Russo and colleagues reported lower early operative mortality among patients who had concomitant CABG. This supports the earlier observation of Hickey and colleagues that early reperfusion of ischemic myocardium in this setting is beneficial.

**Chronic Mitral Regurgitation from Ischemic Heart Disease**

Recent experience indicates that hospital mortality for patients with chronic ischemic mitral regurgitation who undergo valve repair or replacement, usually in combination with CABG, and who are not in cardiogenic shock, is approximately 3% to 11%. Incremental risk factors for increased hospital mortality include low ejection fraction, extensive coronary artery disease, advanced age, renal disease, lower hematocrit, LV end-diastolic dimension greater than 65 mm, longer CPB time, and need for inotropic support. Among patients who had concomitant CABG, hospital mortality in several large series has not been consistently lower among patients who underwent repair. Concomitant procedures such as LV aneurysmectomy may be associated with increased hospital mortality.

**Time-Related Survival**

When the operation is done acutely for rupture of papillary muscle, late results are favorable. In three of the largest reported series, despite substantial early mortality, 5-year survival was 68%, 65%, and 65%. In the largest reported series (54 patients from Mayo Clinic), 5-year survival was 65 ± 7%, and survival free of heart failure was 52 ± 7% (Fig. 10-5). In this study, 5-year survival of 30-day operative survivors was 79 ± 4%, identical (P = .2) to that of matched controls with MI but without rupture of the papillary muscle. Survival free of heart failure was also similar (10-year survival, 28 ± 8% vs. 36 ± 6%; P = .5).

Overall survival after CABG, including hospital mortality, is distinctly poorer in patients with ischemic mitral regurgitation than in those without it. Also, survival after CABG plus mitral valve replacement or repair is poorer when the regurgitation is ischemic in origin rather than rheumatic or degenerative. These differences probably relate to more LV dysfunction in patients with ischemic mitral regurgitation. Nonetheless, survival of patients with chronic ischemic mitral regurgitation who are treated surgically is better than that of those treated medically.
Risk factors for poor outcomes in patients with ischemic heart disease in general apply to this group as well (see Chapter 7).

Addition of LV aneurysmectomy to the procedure adversely affects long-term survival. Miller and colleagues found poor late results in this group, with only 35% (CL 4%-25%) of hospital survivors alive 3 years later. In a longer experience with valve replacement as an isolated or combined procedure, Karp and colleagues found that preoperative LV aneurysm was a significant incremental risk factor for premature late death.

In the study of Hickey and colleagues, mitral valve repair was associated with better long-term survival than mitral valve replacement. In a more recent nonrandomized study of surgery for ischemic mitral regurgitation, however, Hausmann and colleagues observed similar early and late survival among 197 patients treated by mitral valve replacement and 140 patients treated by mitral valve repair. Seven-year survival was 67% and 62%, respectively, although it was better among patients who had no or minimal mitral regurgitation after the repair (77% at 7 years) than among those who had more extensive regurgitation or mitral valve replacement.

Gillinov and colleagues, using propensity analysis and multivariable hazard function regression, observed that in patients with ischemic mitral regurgitation who were not at high risk (younger age, lower New York Heart Association [NYHA] functional class, fewer wall motion abnormalities, no renal dysfunction), mitral valve repair was associated with higher survival at 5 years (58%) than was valve replacement (36%) (P = .08). There was no survival benefit for mitral valve repair among higher-risk patients. A randomized trial of valve repair vs. valve replacement for patients with severe chronic ischemic mitral regurgitation is ongoing (2010) in the National Heart, Lung, and Blood Institute (NHLBI)-sponsored Cardiothoracic Surgery Network. A concurrent randomized trial of CABG alone vs. CABG plus mitral anuloplasty for moderate chronic ischemic mitral regurgitation is ongoing as well.

INdICATIONS FOR OPERATION

When a patient with an acute MI suddenly develops acute mitral regurgitation, operation is advisable, recognizing that hospital mortality under such circumstances may be substantial. As with acute rupture of the ventricular septum (see Chapter 9), operation should be done before severe hemodynamic deterioration occurs. When the hemodynamic state is stable, one strategy has been to delay operation about 2 weeks to 2 months. However, Nishimura and colleagues reported sudden deterioration followed by death in five patients whose condition had initially stabilized with medical therapy. Therefore, all patients with papillary muscle rupture complicating acute MI should have prompt investigation and operation. Operation should be avoided only when the patient is moribund.

When chronic mitral regurgitation results from ischemic heart disease, indications for operation are less well defined. Infrequently, and particularly when it develops acutely from partial rupture of a papillary muscle after MI, mitral regurgitation dominates the clinical picture and causes the symptoms and disability. Then the decision for operation on the mitral valve is straightforward and based on the usual indications (see Chapter 11). Concomitant CABG is performed if indicated. More often, however, patients with usual symptoms of ischemic heart disease requiring CABG have some signs of...
LV failure and clinical and angiographic evidence of mitral regurgitation. As already mentioned, the degree of regurgitation may fluctuate, but it may be constant and moderate or severe. In the latter circumstance, mitral valve repair or replacement is indicated.

When the severity of regurgitation varies over time, it is more difficult to know when mitral valve surgery should be done at the time of CABG. The effect of CABG alone on this form of mitral regurgitation is not known with certainty. If mitral regurgitation is at least moderate (grade 3 or more on a scale of 1 to 6), however, as determined by intraoperative TEE, and under the appropriate loading conditions, mitral repair or replacement is usually indicated (see “Technique of Operation”). If mitral regurgitation is severe in patients with a low ejection fraction (10%-20%), mitral valve replacement rather than repair may be preferable, because persistent mitral regurgitation after repair is associated with substantial early and late mortality. Patients with severe LV dysfunction and mitral regurgitation who are suitable candidates should be considered for transplantation as an alternative to myocardial revascularization and mitral repair or replacement.183,31

SPECIAL SITUATIONS AND CONTROVERSIES

Controversy persists regarding the role of mitral valve repair or replacement in patients undergoing CABG who have ischemic mitral regurgitation. No randomized trials comparing CABG vs. CABG plus mitral valve repair or replacement in patients with mild or moderate mitral regurgitation, or comparing mitral valve repair vs. mitral valve replacement in patients with severe ischemic mitral regurgitation with or without concomitant CABG, have yet been reported. Until the results of such studies become available, management of patients with these conditions will continue to be individualized, relying on currently available information. Accumulating evidence, however, suggests that in carefully matched patients with severe functional ischemic mitral regurgitation (LV ejection fraction ≤ 45%), long-term survival and functional status are not improved by adding mitral valve anuloplasty to CABG34 (Fig. 10-7). Other observational studies support these findings.

Types of Mitral Anuloplasty Devices

A number of devices have been devised and evaluated for the treatment of ischemic mitral regurgitation. These include posterior anuloplasty bands (flexible or rigid) and complete rings, which can be flexible, semi-rigid, rigid, flat, or shaped. No large trials comparing the relative efficacy of these devices have been performed. An observational study of 169 patients who received either a flexible (n = 117) or rigid (n = 52) ring and who had similar baseline characteristics demonstrated a similar degree of improvement in LV dimensions in the two groups, although systolic function did not improve.34 Fewer patients with rigid rings remained in NYHA class III or IV. Improvement in the degree of mitral regurgitation was better in the rigid-ring group (P = .006). There was also a lower prevalence of recurrent mitral regurgitation in the rigid-ring group.

Restrictive Anuloplasty

Restrictive anuloplasty, a technique for reducing the size of the mitral anulus initially reported by Bolling and colleagues, is widely used for treating ischemic mitral regurgitation.188 Standard sizers are used to determine the size of a ring that conforms to the anterior mitral leaflet and the intertrigonal distance of the mitral valve. A ring two or more sizes smaller than this is selected and used for the repair. Proponents of this technique cite as possible advantages the elimination of mitral leaflet tethering and mitral regurgitation in a sheep model. Division of secondary chords (chordal cutting) has been shown experimentally to decrease mitral regurgitation and reverse remodeling, particularly in patients with LV end-diastolic dimensions of 65 mm or less.34,81,62 Functional mitral stenosis has been reported to occur with this technique.31

Alternatives to Isolated Anuloplasty

for Surgical Treatment

Several alternative strategies have been proposed to address ischemic mitral regurgitation. Division of secondary chords (chordal cutting) has been shown experimentally to decrease leaflet tethering and mitral regurgitation in a sheep model.34 The largest clinical experience with this technique is that of Borger and colleagues.39 Secondary chords to the anterior leaflet, posterior leaflet, and the commissure arising from one or both papillary muscles affected by infarcted myocardium

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**Figure 10-7** Survival after coronary artery bypass grafting (CABG) either alone or with concomitant mitral valve (MV) anuloplasty for functional ischemic mitral regurgitation. Symbols represent deaths positioned according to the Kaplan-Meier estimator, vertical bars are 68% CLs, and numbers in parentheses are patients still alive. Solid lines are parametric estimates enclosed within 68% CLs. A, Unadjusted survival, based on 37 deaths after CABG alone and 92 after CABG + MV anuloplasty. B, Propensity-matched survival based on 19 deaths after CABG alone and 19 after CABG + MV anuloplasty. (From Mihaljevic and colleagues,34)
were severed and a posterior undersized anuloplasty band inserted in 43 patients. In comparison with 49 control patients in whom only an anuloplasty band was used, the chordal cutting group had greater mobility of the anterior leaflet ($P = .01$) and less recurrent mitral regurgitation (15% vs. 37%) during the 2-year follow-up interval.

Posterior mitral leaflet extension with pericardium has been evaluated as a method to reduce the severity of ischemic mitral regurgitation. This technique was used by deVarennes and colleagues in 44 patients with severe (4+) ischemic mitral regurgitation, enlarging the posterior half of the posterior leaflet (half of P2 and all of P3) with a 1.0 3.5- to 4.5-cm patch of bovine pericardium. An anuloplasty ring (not downsized) was also used. Actuarial freedom from moderate or severe recurrent mitral regurgitation was 90% 2 years postoperatively, and 92% of the patients were in NYHA class I.

Relocation of the posterior papillary muscle in conjunction with a partially flexible anuloplasty ring (not downsized) has been used in a small number of patients by Kron and colleagues. A 3-0 polypropylene suture is passed twice through the fibrous portion of the tip of the posterior papillary muscle. It is then passed through the adjacent mitral anulus just posterior to the right fibrous trigone. The suture is tightened until leaflet coaptation is achieved. In a series of 18 patients with 2+ to 3+ mitral regurgitation preoperatively, 3 had trace and 15 had no mitral regurgitation 2 months postoperatively.

A papillary muscle sling has been proposed and evaluated by Hvass and Joudinaud to correct ischemic mitral regurgitation. After mobilizing the trabeculations of the posterior papillary muscle through the mitral valve, a 4-mm tube of polytetrafluoroethylene is drawn around the two papillary muscles, forming an intraventricular sling that is secured with sutures so that there is no gap between the muscles. An anuloplasty ring (not or only moderately downsized) is then inserted. Among 37 patients with moderate or severe mitral regurgitation, mean ejection fraction of 30%, and a mean LV end-systolic and end-diastolic dimensions were reduced, ejection fraction increased, and 5-year survival was 80%. Other interventions (edge-to-edge (Alfieri) mitral repair: results in diverse clinical settings. Ann Thorac Surg 2004;77:1598-606.


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Mitral Valve Disease with or without Tricuspid Valve Disease
Section I Mitral Valve Disease

DEFINITION
This chapter describes surgical aspects of acquired mitral valve disease, excluding ischemic mitral regurgitation (see Chapter 10). Associated or secondary tricuspid valve disease is also considered (see Section II of this chapter and Chapter 14), as is concomitant coronary artery surgery in patients with nonischemic mitral valve disease (see Section III of this chapter).

HISTORICAL NOTE
Mitral Stenosis
Sir Lauder Brunton was among the first to consider surgical treatment of mitral stenosis in his “preliminary note” in *The Lancet* in 1902. Cutler, then at Western Reserve University Medical School in Cleveland and later the Mosley Professor of Surgery at Harvard Medical School and Peter Bent Brigham Hospital in Boston, did experimental work on surgical approaches to mitral stenosis. In 1923, he and Levine reported an operation via median sternotomy in which a special curved knife was inserted through the left ventricular (LV) apex to cut a stenotic mitral valve.

In 1925, Souttar digitally opened a stenotic mitral valve through the left atrial appendage.

An effective closed surgical approach to mitral stenosis began with Harken and colleagues and Bailey in the United States and Brock and colleagues in London. Harken had been doing animal experiments involving mitral valve surgery at the Boston City Hospital in 1939 before serving with the United States Army in World War II, during which time he became well known for successful removal of missiles and shell fragments from the heart. After the war he continued his work on mitral valve surgery at the Boston City and Peter Bent Brigham Hospitals. Bailey was working primarily at Hahnemann Hospital in Philadelphia. Although their techniques and terminology were somewhat different, their approaches to opening the valve through the left atrial appendage were similar. Technical modifications subsequently
added to closed commissurotomy included Tubb’s transventricular dilator, used with digital control by a finger inserted through the left atrial appendage.\textsuperscript{2}\textsuperscript{2}\textsuperscript{3}

In 1955, surgeons began to think of opening stenosed mitral valves by intracardiac techniques on cardiopulmonary bypass (CPB). However, closed heart operations produced such generally good results that the open heart technique did not come into wide use until after 1970.

Mitral Regurgitation

Although a few ingenious closed methods of surgically improving mitral regurgitation were reported during the 1950s, particularly by Bailey, Davila, Nichols, and their colleagues,\textsuperscript{B1,D11,N9} an effective open approach using CPB was not made until 1957 by Lillehei and colleagues\textsuperscript{4}\textsuperscript{11} and Merendino and Bruce.\textsuperscript{M19} McGoon described an effective repair for mitral regurgitation due to ruptured chordae in 1960.\textsuperscript{M15} In subsequent years, a number of surgeons have contributed technical advances in the repair of mitral regurgitation, particularly Carpentier, Duran, Frater, Reed, and their colleagues.\textsuperscript{C11,D16,L7,R13}

Mitral Valve Replacement

A number of surgeons realized very early the need for replacing at least some diseased mitral valves. However, it was Starr and Edwards from the University of Oregon Medical Center who, in 1961, first reported successful mitral valve replacement using a mechanical prosthesis.\textsuperscript{S32}

Although the Starr-Edwards valve became the “gold standard” in prosthetic valves for most of the next decade, it soon became apparent that aggressive anticoagulation was necessary to control the marked thromboembolic tendency. Valve design focus subsequently was redirected toward lower-profile valves with novel occluder designs. The Bjork-Shiley prosthesis, designed by cardiac surgeon Viking Bjork of Sweden and Earl Shiley in California,\textsuperscript{B20,E44} was the first successful tilting disc valve. It emerged as the leading prosthesis in the 1970s. It was first marketed in 1971 with a carbon-coated disc and both inflow and outflow struts welded to the chromium alloy orifice. The hemodynamics and freedom from hemolysis were superior, but strict anticoagulation was required to prevent valve thrombosis. When a later design change (convexo-concave disc)\textsuperscript{15} was associated with strut fracture,\textsuperscript{11} the valve was eventually taken off the market.\textsuperscript{B27,C34,H16} Enduring bileaflet valves would await the application of pyrolytic carbon technology from the space industry in about 1977. The bileaflet St. Jude Medical valve developed in the late 1970s became the dominant prosthetic valve of the 1980s,\textsuperscript{E10,E11} offering further improvement in hemodynamics, less blood stagnation, greater opening of the leaflets, and a lower risk of thromboembolism.\textsuperscript{C21,C42}

Biological or tissue prosthetic valves had been in development since the 1950s, and in the 1960s formalin fixation was introduced to sterilize and fix heterograft tissue.\textsuperscript{16} When investigators became aware of the tendency of formalin fixation to induce collagen breakdown in valve cusps—with resultant fibrosis, calcification, and degeneration—tissue fixation of porcine valves with glutaraldehyde rapidly became the standard. The first commercially available bioprosthetic valves were developed by Hancock in the United States (1970) and Carpentier in Paris.\textsuperscript{C4,C7,K2}

MORPHOLOGY

Anatomy of the mitral valve is discussed in detail in Chapter 1. Several features are of particular importance in considering valve pathology and reparative techniques. The anterior leaflet is conveniently divided into three sectors: \( A_1 \) laterally, \( A_2 \) centrally, and \( A_3 \) medially. The posterior leaflet is also divided into three sectors: \( P_1 \) laterally, \( P_2 \) centrally, and \( P_3 \) medially\textsuperscript{12} (Fig. 11-1). When the cause of regurgitation is prolapse of the posterior leaflet, sectors \( P_2 \) and \( P_3 \) are usually involved. Additionally, there is usually some degree of annular dilatation.

The right fibrous trigone is adjacent to the posteromedial commissure and is part of the central fibrous body located at the intersection of the membranous septum, mitral and tricuspid anulus, and aortic anulus (Fig. 11-2). The left fibrous trigone is located near the aortic anulus under the left aortic cusp and adjacent to the anterolateral commissure. The posteroanterior and anterolateral papillary muscles give rise to chordae tendineae going to both leaflets. The chords are generally categorized into three groups: first-order chordae originate near tips of the papillary muscles and insert on the free edge of the leaflets. These chordae prevent valve edge prolapse during systole and, when elongated or ruptured, produce mitral regurgitation. Second-order chordae (including two or more longer strut chordae) insert on the ventricular surface of the leaflets at the junction of the rough zone (closer to the free edge) and clear zone, which is demarcated by a ridge that corresponds to the line of leaflet coaptation. Third-order chordae originate from the underlying ventricular wall and insert on the posterior leaflet near the anulus. In addition, distinct commissural chordae exist at the commissures.

Mitral Stenosis

Acquired mitral stenosis usually results from rheumatic heart disease, as does mixed stenosis and regurgitation. It occurs as an isolated valvar condition in 40% of patients with rheumatic heart disease.\textsuperscript{W9}

Commisural fusion and leaflet thickening are the dominant features in clinically important mitral stenosis. The characteristic fusion of the edges of the mitral leaflets in

\[ \text{Figure 11-1} \text{ Segmental leaflet anatomy of mitral valve. Anterior leaflet has three sectors: } A_i, \text{ nearest the anterolateral commissure (labeled by star on left side of diagram); } A_m, \text{ in the mid-leaflet; and } A_s, \text{ nearest the posteromedial commissure (right-side star). Corresponding sectors of posterior leaflet are } P_i, \text{ } P_m, \text{ and } P_s. \text{ (From Quill and colleagues.\textsuperscript{Q1})} \]
Mitral valve and subvalvar apparatus.

Mitral valve prolapse is a billowing of one or both leaflets into the left atrium during ventricular systole, with or without mitral regurgitation. Prolapse of a mitral valve leaflet occurring as an isolated abnormality is a relatively common and complex entity occurring in 1% to 2.5% of the population. Familial mitral valve prolapse is inherited as an autosomal trait. Primary mitral valve prolapse occurs with left atrial hypertension. Organic pulmonary vascular disease may also increase Rp and is often found in young Polynesian and Asian patients, as well as in a small proportion of other patients with long-standing mitral stenosis. Rarely, the vascular disease may progress to obliteration of pulmonary arterioles. Increased Rp produces a rise in pulmonary artery and right ventricular pressure out of proportion to the valve stenosis and left atrial pressure increase, which leads to right ventricular (RV) hypertrophy and secondary tricuspid regurgitation.

Mitrail Stenosis and Regurgitation

Mixed mitral stenosis and regurgitation is primarily rheumatic in origin. Stenosis is produced by varying degrees of commissural fusion and chordal thickening. Regurgitation results from fibrous retraction of the central unfused portion of the leaflets and either chordal shortening or chordal elongation. Shortening restricts leaflet motion and increases the gaping central orifice, whereas elongation permits cusp prolapse. Occasionally, chordae rupture as a result of the rheumatic process.

Endocarditis on a rheumatic stenotic valve adds regurgitation by eroding leaflet or chordal tissue.

Mitrail Regurgitation

Regurgitation may be due to rheumatic valve disease, but has numerous other causes and morphologic patterns.

Rheumatic Mitral Regurgitation

Mitrail regurgitation may occur as a severe lesion (sometimes combined with aortic regurgitation) during the acute rheumatic process in association with extensive myocarditis and sometimes pericarditis and pancarditis. Anular dilatation is the primary cause of regurgitation in this circumstance, with the valve leaflets frequently showing edema only and virtually normal chordae. After remission of the acute process, regurgitation may spontaneously regress, presumably because the myocarditis heals, the heart becomes smaller, and anular dilatation regresses. In most cases, however, there is progressive leaflet thickening, particularly of the posterior leaflet, which becomes retracted and rolled with shortening of chordae. The anterior leaflet is less thickened, and major chordae are frequently elongated, allowing leaflet prolapse. The posterior chordae may also elongate, and occasionally one or more may rupture. Commissural leaflets are obliterated and fused, but the commissures remain more or less open. Calcification is uncommon. Anular dilatation is almost invariably progressive and produces increasing regurgitation.

Mitrail Valve Prolapse

Mitrail valve prolapse is a billowing of one or both leaflets into the left atrium during ventricular systole, with or without mitral regurgitation. Prolapse of a mitral valve leaflet occurring as an isolated abnormality is a relatively common and complex entity occurring in 1% to 2.5% of the population. Familial mitral valve prolapse is inherited as an autosomal trait. Primary mitral valve prolapse occurs with

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1Variously termed myxomatous mitral valve prolapse, myxomatous mitral valve degeneration, floppy valve, “the symptom complex of midsystolic click and late systolic murmur,” and Barlow syndrome.26
increased frequency in patients with Marfan syndrome and certain other connective tissue disorders.\textsuperscript{1,13}

Our understanding of the anatomic details of prolapsing anterior and posterior leaflet components has been enhanced by the classification of Carpentier\textsuperscript{28,29,425} and others. In a pathologic study, Quill and colleagues identified abnormal (“deviant”) clefts in all valve segments, but most commonly in the P\textsubscript{2} region.\textsuperscript{91} Such abnormal clefts may contribute to mitral regurgitation observed in degenerative mitral valve disease.

Infrequently, in its severe form, mitral prolapse results in important mitral regurgitation (10% of patients).\textsuperscript{425} Nonetheless, in the United States mitral valve prolapse has been reported as the most common cause of surgically treated isolated mitral regurgitation.\textsuperscript{830} The basic pathologic conditions are mitral leaflet redundancy and myxomatous leaflet thickening, resulting at least partly from myxomatous proliferation of the acid mucopolysaccharide within the spongiosa, which replaces collagen in the leaflets. The redundant and elongated leaflets no longer meet properly to support each other during systole, and they begin to overshoot into the left atrium. Not only is the valve thereby rendered regurgitant, but abnormal strain is placed on the chordae as well. The chordae elongate, and ultimately some rupture, producing more regurgitation. These histologic changes and severe valve redundancy are especially pronounced in younger patients with Barlow syndrome. Older patients with degenerative mitral regurgitation are more likely to have fibroelastic deficiency and less redundant valve tissue. These differences have important surgical implications because marked leaflet redundancy with more severe myxomatous changes requires more extensive reconstructive techniques. Calcifications may occur in the mitral anulus, but do not appear to contribute to mitral valve dysfunction.\textsuperscript{347}

	extit{Idiopathic} Chordal Rupture

“Idiopathic” and more or less localized chordal rupture is usually a variant of mitral valve prolapse syndrome,\textsuperscript{13} in which a considerable portion of leaflet tissue is uninvolved by the myxomatous process. In most cases, the posteromedial portion of the posterior leaflet is involved; after chordal rupture, this becomes redundant and flail. More extensive posterior chordal rupture sometimes occurs. Localized chordal rupture may also occur in patients with Marfan syndrome.

Mitral Anular Calcification

Mitral anular calcification may occur in older patients without evident disease of the leaflets or chordae, but it may be more common in patients with myxomatous degeneration and prolapse of the mitral leaflets.\textsuperscript{28,46,57} Anular calcification is probably a degenerative disease, more common in elderly patients and apparently more common in women.\textsuperscript{28} It is also seen in patients with LV hypertrophy, particularly those with hypertrophic obstructive cardiomyopathy (HOCM; see Chapter 19). The process involves the posterior or mural portion of the anulus more often than other portions. Degenerative anular calcification often extends into the adjacent ventricular myocardium, and it may secondarily produce mitral regurgitation or stenosis by displacing or immobilizing the mitral leaflets. Anular calcification considerably complicates mitral repair or replacement.\textsuperscript{1,14}

Ischemic Papillary Muscle Dysfunction or Rupture

Papillary muscle dysfunction or rupture resulting from myocardial infarction or ischemic fibrosis can produce severe mitral regurgitation (see Chapter 10).

Infective Endocarditis

Endocarditis is a relatively uncommon cause of pure mitral regurgitation compared with its etiologic frequency in aortic regurgitation. When the aortic valve is infected and regurgitant, vegetations may drop down onto and infect the central portion of the anterior mitral leaflet, producing perforation and mitral regurgitation. In the absence of aortic valve disease, a normal or abnormal mitral valve may become infected,\textsuperscript{345} with destruction of cusps, chordae, or both (see Chapter 15).

Submitral Left Ventricular Aneurysms

Submitral LV aneurysms frequently result in mitral regurgitation. This unusual type of aneurysm is not ischemic in origin and occurs most often among the southern and western African black population.\textsuperscript{118} It may be multiloculated and have a well-defined neck situated immediately beneath the posterior mitral leaflet. Mitral regurgitation often coexists because of aneurysmal distortion of the posterior leaflet and leaflet prolapse. In rare instances, the aneurysm bulges into the left atrium from behind, partly obstructing the mitral orifice.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Mitral Stenosis

The normal mitral valve orifice area in an adult is 4.0 to 5.0 cm\textsuperscript{2}. Most asymptomatic patients have a mitral valve area less than 2.5 cm\textsuperscript{2}.\textsuperscript{423} The diastolic transmirtal gradient is the fundamental physiologic expression of mitral stenosis. At any given orifice size, the transmirtal gradient is a function of the square of the transvalvar flow rate and diastolic filling time. Thus, for example, doubling the flow rate quadruples the transvalvar gradient. This explains the importance of exertion or other causes of increased cardiac output in development of dyspnea (induced by increased left atrial and pulmonary venous pressure) during the initial stages of mitral stenosis. As heart rate increases, during atrial fibrillation for example, diastolic filling time is greatly reduced, thereby increasing the gradient and left atrial pressure.

Effective atrial contraction during sinus rhythm has a major lessening effect on dyspnea with severe mitral stenosis, because the left atrial pressure is lower than during atrial fibrillation, and the loss of atrial contribution during atrial fibrillation results in about a 20% reduction in cardiac output.

Although the clinical condition of mitral stenosis is a continuum without discrete hemodynamic abnormalities corresponding to functional state, the following hemodynamic guidelines are useful in defining severity of mitral stenosis:\textsuperscript{31}:

- **Mild**: valve area 1.5 to 3.5 cm\textsuperscript{2} and mean diastolic gradient less than 5 mmHg
- **Moderate**: valve area 1.0 to 1.5 cm\textsuperscript{2} and mean diastolic gradient 5 to 10 mmHg


■ Severe: valve area less than 1.0 cm² and mean diastolic gradient greater than 10 mmHg

Patients with moderate mitral stenosis are often asymptomatic at rest or with ordinary activities, particularly until the third or early part of the fourth decade of life. With severe exertion, pulmonary edema may develop suddenly.

Patients with severe mitral stenosis and without important elevation of Rp (“unprotected” mitral stenosis) have easy fatigability and effort dyspnea, orthopnea, and paroxysmal nocturnal dyspnea. As the disease progresses in duration and severity, structural changes (alveolar basement membrane thickening, increased lymphatic drainage, adaptation of neuroreceptors) may allow patients to remain functional for prolonged periods. When Rp rises, the alveolar bed is protected from sudden rises in capillary pressure with exertion, so pulmonary edema does not occur, and orthopnea and paroxysmal nocturnal dyspnea disappear. Hemoptysis is more common in this setting. When the reduction in mitral valve orifice size reaches severe levels, resting cardiac output becomes subnormal, which is usually accompanied by varying degrees of increased Rp (see also Morphology). The patient with advanced mitral stenosis who has low cardiac output and chronic heart failure secondary to high Rp is seldom seen today in developed countries. These patients tend to be women who have marked mitral facies, peripheral coldness, cyanosis, hepatic enlargement and pulsation, high jugular venous pressure with waves of tricuspid regurgitation, and sometimes ascites and peripheral edema.

In most patients, mitral stenosis can be diagnosed clinically based on history, physical examination, chest radiograph, and electrocardiogram (ECG). Auscultatory findings provide good evidence of mitral stenosis when they include a loud first sound, an opening snap, and the characteristic diastolic rumble with a presystolic crescendo when sinus rhythm is present. In severe stenosis the mid-diastolic murmur occupies more than half of diastole, and the opening snap is early.

In surgical candidates with important mitral stenosis, the chest radiograph typically shows some left atrial enlargement, although it is often only about grade 2 (on a scale of 1 to 6, with 6 being most severe). The left atrial appendage may or may not appear prominent along the left upper border of the cardiac silhouette. The LV is normal in size, but the RV and pulmonary trunk are usually somewhat enlarged. When Rp is elevated, the pulmonary trunk, branches, and hilar arteries are more enlarged; once tricuspid regurgitation occurs, there is considerable right atrial and RV enlargement. The lung fields also show varying degrees of pulmonary venous hypertension on the plain chest radiograph (large pulmonary veins in upper lung fields, interstitial pulmonary edema, Kerley B lines, or alveolar pulmonary edema).

The ECG is not diagnostic but often shows P-wave abnormalities characteristic of left atrial enlargement (P mitrale) or atrial fibrillation, and evidence of RV hypertrophy when pulmonary hypertension is present.

Two-dimensional (2D) echocardiography is highly reliable for diagnosing and quantifying severity of mitral stenosis. It demonstrates degree of stenosis, leaflet mobility, thickening and probable calcification, and any subvalvar obstruction. Doppler echocardiography, enhanced by color flow imaging to identify precise flow direction, is valuable for estimating severity of stenosis. Currently these methods suffice for estimating mitral valve area as well as morphology and gradient across the valve. An echocardiographic grading system for mitral stenosis has been endorsed in the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, which is useful for identifying patient suitability for valvotomy (balloon catheter), surgical commissurotomy, or valve replacement (Table 11-1). Greater leaflet mobility, less subvalvar involvement, and less leaflet calcification (grade 1) increases the likelihood of successful valvotomy or commissurotomy.

Cardiac catheterization is usually unnecessary for diagnosing mitral stenosis and estimating its severity. Catheterization is necessary in patients older than about age 35 to study the coronary arteries, however, because about 25% of patients older than 40 with mitral stenosis without angina have important coronary artery disease. When balloon valvotomy is used, prevalvotomy and postvalvotomy measurements are easily made by classic catheterization techniques or by echocardiography. Pulmonary capillary wedge pressure (PCPW) is measured to determine severity of pulmonary venous hypertension. PCPW (which is similar to left atrial pressure) is compared with directly measured LV diastolic pressure to determine transmural gradient; a resting end-diastolic gradient of 10 mmHg or more indicates important mitral stenosis. Mitral valve area is calculated from Gorlin’s modified orifice equation.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Mobility</th>
<th>Subvalvar Thickening</th>
<th>Thickening</th>
<th>Calcification</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Highly mobile valve with only leaflet tips restricted</td>
<td>Minimal thickening just below mitral leaflets</td>
<td>Leaflets near normal in thickness (4 to 5 mm)</td>
<td>A single area of increased echo brightness</td>
</tr>
<tr>
<td>2</td>
<td>Leaflet mid and base portions have normal mobility</td>
<td>Thickening of chordal structures extending up to one third of the chordal length</td>
<td>Midleaflets normal, considerable thickening of margins (5 to 8 mm)</td>
<td>Scattered areas of brightness confined to leaflet margins</td>
</tr>
<tr>
<td>3</td>
<td>Valve continues to move forward to diastole, mainly from the base</td>
<td>Thickening extending to distal third of the chords</td>
<td>Thickening extending through entire leaflet (5 to 8 mm)</td>
<td>Brightness extending into midportion of leaflets</td>
</tr>
<tr>
<td>4</td>
<td>No or minimal forward movement of the leaflets in diastole</td>
<td>Extensive thickening and shortening of all chordal structures extending down to papillary muscles</td>
<td>Considerable thickening of all leaflet tissue (&gt;8 to 10 mm)</td>
<td>Extensive brightness throughout much of leaflet tissue</td>
</tr>
</tbody>
</table>

From Bonow and colleagues.831
In a patient coming to treatment for mitral stenosis, the possibility of left atrial myxoma must always be considered. Echocardiography can detect a left atrial myxoma\(^ {\text{24}}\) and is the type of screening performed when further information is needed (see Section I, Myxoma, in Chapter 18).

**Mitral Regurgitation**

**Chronic**

Patients with mitral regurgitation are often asymptomatic for many years, during which time LV size may steadily increase and LV contractility decrease. Eventually, effort intolerance develops, and symptoms of pulmonary venous hypertension evolve. Fluid retention and chronic heart failure, occasionally with cardiac cachexia, are characteristic of the late stage of the disease; by then, secondary tricuspid regurgitation is usually evident.

As with mitral stenosis, important mitral regurgitation can usually be diagnosed based on history, physical examination, chest radiograph, and ECG. The classic apical systolic murmur of mitral regurgitation is pansystolic, loudest at the apex, and radiates to the left axilla and left lung base. Classical auscultatory findings in mitral valve regurgitation from prolapse include one or more mid-systolic clicks and a late or holosystolic murmur of mitral regurgitation. When regurgitation is the result primarily of ruptured chordae and prolapse of the posterior leaflet, however, the regurgitant jet is directed toward the roof (superior aspect) of the left atrium and is transmitted to the aortic root. Therefore, the murmur is maximal in the parasternal aortic area and may radiate into the carotid arteries. In contrast to the anterior radiation of posterior leaflet prolapse, the murmur of anterior prolapse radiates posteriorly to the infracostal and posterior cervical area.\(^ {\text{218}}\) As a result of large and rapid mitral valve flow during diastole, an LV filling sound (S\(_3\)) and a diastolic rumble may be present. Two important signs of the severity of regurgitation are an overactive LV impulse at the apex (from LV enlargement) and a precordial lift, the latter the result of systolic pulsation in the enlarged left atrium and right ventricle. There is no correlation between intensity of the murmur and severity of mitral regurgitation, but a true holosystolic murmur is indicative of more severe regurgitation.\(^ {\text{216,88}}\)

In severe chronic mitral regurgitation, the chest radiograph usually is highly characteristic. The left atrium generally is more enlarged than in patients with mitral stenosis, and the left atrial appendage is usually prominent. The LV may be enlarged, and there may be varying degrees of right atrial enlargement, depending on the amount of associated tricuspid regurgitation.

The ECG may remain normal even in the presence of severe mitral regurgitation. However, a pattern of LV hypertrophy is common.

As with mitral stenosis, 2D echocardiography demonstrates the details of leaflet pathology. Both transthoracic (TTE) and transesophageal echocardiography (TEE) are useful. Echocardiographic diagnosis of mitral valve prolapse requires prolapse of 2 mm or more above the anulus in the long-axis parasternal view.\(^ {\text{39}}\) Leaflet thickness of 5 mm or more increases the likelihood of mitral valve prolapse. Prolapse of a specific leaflet can be visualized, and Doppler color flow imaging can identify the location and magnitude of the mitral regurgitant flow. Echocardiography may also be used to estimate both the degree of LV enlargement and, by quantification of shortening fraction, ventricular contractility. Newer echocardiographic methods using 3D techniques offer precise and accurate evaluation of leaflet physiology and specific areas of regurgitation within the valve apparatus. The effective regurgitant area and regurgitant volume can be measured echocardiographically and have been identified as predictors of outcome following mitral valve repair (see Indications for Operation later in this section). The American Society of Echocardiography has recommended grading mitral regurgitation as mild, moderate, and severe (grades 1-3). For refinement of intermediate levels, the terms mild to moderate and moderate to severe can be used.\(^ {\text{22}}\)

Left ventriculography also demonstrates the regurgitant process at the mitral valve and can show leaflet prolapse. Degree of regurgitation can usually be estimated with reasonable accuracy, although if left atrial or LV enlargement is severe, the estimate is less valid. Fairly accurate calculations of regurgitant flow can be made from measurements of LV stroke volume by quantitative left ventriculography, and of forward flow by some measurement of cardiac output.\(^ {\text{33}}\) LV ejection fraction (EF) can also be calculated by quantitative cineangiography or radioisotope techniques. Decisions about treatment of patients with mitral regurgitation may require additional studies from which inferences can be made about LV contractility (see “Mitral Regurgitation” under Natural History later in this section).

**Acute**

Mitral regurgitation may develop acutely as a result of chordal rupture or infective endocarditis or may complicate the course of acute myocardial infarction (see Chapter 10). Symptoms and signs of severe pulmonary venous hypertension suddenly appear. The left atrium and LV are normal in size or only slightly enlarged. The chest radiograph is dominated by signs of pulmonary venous hypertension, and left atrial pressure is high, as is the v wave. A mitral regurgitation murmur is often pansystolic and higher pitched compared with the pansystolic murmur of chronic mitral regurgitation.

**NATURAL HISTORY**

**Mitral Stenosis**

Rheumatic mitral stenosis develops slowly after initial rheumatic involvement of the valve. In the New England area of the United States, the average age of the initial attack of rheumatic fever is 12 years, average age of onset of clinical signs of mitral stenosis 20 years, and age at onset of symptoms 31 years.\(^ {\text{228}}\) Progression of valve fibrosis and calcification is related in part to repeated episodes of rheumatic fever, but mechanical trauma and deposition of platelets and other blood substances resulting from stenosis-induced alterations of flow patterns also play a role.\(^ {\text{54}}\) This progression is a major factor in increasing symptoms, ultimately causing death.

Most patients with mitral stenosis have normal LV wall thickness, volume, and systolic and diastolic function\(^ {\text{510}}\) but do not increase cardiac output under stress, such as when LV afterload is acutely reduced by infusion of sodium nitroprusside.\(^ {\text{339}}\) These findings suggest that the major cause of chronically reduced cardiac output in these patients is obstruction at the mitral valve.\(^ {\text{339,110,212}}\) In some patients with long-standing mitral stenosis, however, minor posterobasal
Mitral Regurgitation

The natural history of mitral regurgitation is difficult to define because (1) etiology is variable, (2) age at onset is variable, (3) mitral regurgitation may be mild and nonprogressive for many years, and (4) LV function, an important determinant of symptoms and survival, deteriorates at different rates.

Patients with mild to moderate mitral regurgitation may remain asymptomatic for many years. Even when mitral regurgitation becomes severe, the effect of changes in global LV function is modified by the fact that total LV load resisting shortening (afterload) is abnormally low in these patients (see “Ventricular Afterload” under Cardiac Output and Its Determinants in Chapter 5). Afterload is low as a result of ejection of part of the LV stroke volume into the low-pressure system.

Regional wall contraction abnormalities develop, perhaps from a rigid mitral valve complex. In a small proportion of patients with apparently isolated mitral stenosis (usually older persons), EF is substantially reduced. Such patients have severe posterobasal segmental wall contraction abnormalities, sometimes anterolateral segmental contraction abnormalities, and occasionally diffuse hypokinesis. Anterolateral segmental contraction abnormalities may be caused by papillary muscle scarring and immobilization. Diffuse hypokinesia may result from scarring and decreased LV compliance secondary to chronic low cardiac output and low coronary blood flow.

Once symptoms develop after the so-called latent period, their progression to a state of total disability (New York Heart Association [NYHA] functional class IV) requires an estimated 7 to 10 years (Fig. 11-3). Average age of death of patients with surgically untreated mitral stenosis is estimated to be 40 to 50 years.

This general pattern of evolution is considerably shorter in some parts of the world and in some races. Polynesians in New Zealand, African Americans in south-central Alabama, Inuits in Alaska, and Asians experience a greatly accelerated evolution of signs, symptoms, and disability. Many reports suggest that in addition to possible genetic factors, economic underdevelopment may play a role.

Other events tend to occur during the lifetime of patients with surgically untreated mitral stenosis, and these in turn may alter the natural history of the disease. Atrial fibrillation usually develops, often occurring first in paroxysmal form. The first paroxysm, usually with tachycardia, may initiate symptoms because patients with mitral stenosis are particularly sensitive to loss of the atrial contribution to ventricular filling and to shortening of ventricular filling. Although originally incited by left atrial hypertension and hypertrophy, atrial fibrillation eventually becomes persistent because of disintegration of the architecture of atrial muscle. Because it reduces cardiac output and elevates left atrial pressure, atrial fibrillation accelerates clinical deterioration of patients with mitral stenosis and indicates a relatively advanced stage of the disease. It is an incremental risk factor for premature death of these patients. Olesen found that in patients with atrial fibrillation, 10- and 20-year survival was 25% and 10%, respectively, whereas in patients in sinus rhythm at initial observation, survival was 46% and 29%, respectively.

Systemic arterial emboli, most of which lodge in cerebral arteries, can suddenly complicate or kill patients with mitral stenosis. Most emboli originate in the left atrial appendage or left atrium, yet often no residual thrombus remains in the heart after embolization. Hoeksema and colleagues found that only 25% of patients with a history of arterial emboli had left atrial thrombi detected at closed commissurotomy. Also, some patients with large left atrial thrombi never have demonstrable embolization. Left atrial thrombosis and embolization are much more common when atrial fibrillation is present than in patients in sinus rhythm. At least 10% of surgically untreated patients develop arterial embolization during their lifetime, and a massive cerebral embolus may suddenly kill a mildly symptomatic patient.

Infectious endocarditis is unusual in patients with mitral stenosis. Massive pulmonary hemorrhage may occasionally develop in patients otherwise mildly symptomatic from mitral stenosis. The association between mitral stenosis and hemorrhage is strongly suggested by its prompt and long-standing remission after surgical treatment of the stenosis.

In fact, the aforementioned features and criteria do not truly represent the “natural” (i.e., untreated) history of mitral stenosis, but rather the spectrum of mitral stenosis in surgically untreated patients receiving medical treatment available in the mid-20th century. The end stage of the disease in many patients is characterized by cardiac cachexia, a state infrequently seen before diuretic therapy became available. The true natural history of mitral stenosis in the first quarter of the 20th century must have been different from that portrayed here, with the interval between onset of symptoms and death much shorter and with different patterns of death.

Likewise, evolution of the rheumatic disease complex is different in patients with mitral stenosis treated surgically vs. medically. The course of the disease varies because the increased lifespan due to surgery now results in development of hemodynamically important rheumatic aortic valve disease and important tricuspid regurgitation in a considerably greater proportion of patients with mitral stenosis (Fig. 11-4).
left atrium; because of this, the LV becomes small, and its wall thickens very early in systole. The resulting favorable relationships in the Laplace law reduce wall stress and afterload. Because of this, LV contractility may gradually deteriorate while LV systolic function (EF) is maintained, the mechanism being reduction in afterload. The EF may even increase during exercise under these circumstances while symptoms remain mild. This compensated period of mitral regurgitation may last for years. Later, as the regurgitation becomes severe and LV contractility decreases, EF may diminish during exercise, even in asymptomatic patients.

These considerations have led to development of techniques for estimating LV function that are independent of preload and afterload. Foremost among these are those that use ventricular end-systolic pressure-volume relations (see “Mitr al Regurgitation” under Indications for Operation, Selection of Technique, and Choice of Device later in this section and “Cardiac Output and Its Determinants” in Section I of Chapter 5).

Patients with mitral regurgitation may develop tricuspid regurgitation, which also affects natural history (see Section II).

Rheumatic Mitral Regurgitation

Patients with rheumatic mitral regurgitation are more likely to have had a previous severe attack of rheumatic fever than those with mitral stenosis. The interval before the appearance of regurgitation also is shorter than for stenosis. Patients with surgically untreated but hemodynamically important rheumatic mitral regurgitation survive similarly to those with mitral stenosis. Furthermore, the curve is different in different environmental and genetic situations, as it is in mitral stenosis. In San Francisco, for example, survival of such patients 5 years after initial evaluation was 80%, with 10-year survival of 60%, whereas in Venezuela, 5-year survival was only 46%. Accelerated forms of rheumatic mitral regurgitation also occur in the same geographic areas where severe mitral stenosis appears in the pediatric population, with important symptoms by age 10 years.

Mitral Valve Prolapse

The natural history of isolated mitral valve prolapse without regurgitation is highly variable, with the majority of patients having age-adjusted survival similar to that of the general population. However, the major predictor of cardiac mortality is moderate to severe mitral regurgitation. Mitral regurgitation associated with mitral valve prolapse has a complex natural history that entails more than leakage at the mitral valve. The mitral leaflets not only prolapse in this condition but are usually thickened as well. Mitral valve regurgitation is not the only event in patients with mitral prolapse. Serious but rarely fatal arrhythmias may occur in patients with only mild regurgitation, and psychiatric disturbances may develop. Symptoms may mimic thyrotoxicosis, hyperadrenergic states, or hypoglycemia.

Patients with the classic form of mitral prolapse, which includes thickening of the leaflets as well as prolapse, have an increased prevalence of infective endocarditis; those with normal leaflets (in the absence of regurgitation) do not. Both groups have a higher prevalence of stroke.

Severe mitral regurgitation requiring valve repair or replacement rarely develops before age 50. Thereafter, the prevalence increases steeply, particularly in men. However, even men with mitral valve prolapse who have reached age 70 years have only about a 5% chance of requiring mitral valve repair or replacement. Once important mitral regurgitation appears, however, it tends to progress just as it does in patients with rheumatic mitral regurgitation. Presumably, as prolapse worsens, support in systole provided by closing of the two leaflets against each other (“stacked rifle effect”) is lost. This puts an abnormally large load on the chordae, which elongate, become thick, and eventually rupture. This process worsens the regurgitation and accelerates the natural history of the disease.

In view of the increasing ability of cardiac surgeons to repair mitral regurgitation, the natural history of severe mitral regurgitation secondary to mitral valve prolapse is of considerable importance. Two Mayo Clinic studies in the mid-1990s called attention to the increased mortality in patients with chronic flail leaflets treated medically.

A 2008 multicenter European study examined the natural history of severe regurgitation caused by one or both flail leaflets (failure of leaflet coaptation with rapid systolic movement of the involved leaflet tip in the left atrium). Involvement was confined to the posterior leaflet in 314 patients (79%), anterior leaflet in 31 (8%), both in 46 (12%), and unspecified in 3 (1%). The long-term outcome with medical treatment included an important likelihood of major adverse events by 8 years, including atrial fibrillation, heart failure, and cardiovascular death. Need for mitral valve surgery (or death from cardiovascular causes) was nearly unavoidable by 8 years after diagnosis. A subgroup analysis of asymptomatic patients with normal ventricular systolic function revealed a 5-year survival of 97% with medical treatment, but the combined occurrence of atrial fibrillation, heart failure, or cardiovascular death was 42% at 8 years. A Mayo Clinic analysis of asymptomatic patients with severe organic mitral regurgitation identified an effective regurgitant orifice (by echocardiography) of at least 40 mm² as a major predictor of late mortality.
Ruptured Chordae Tendineae

Patients with mitral regurgitation and ruptured chordae tendineae may have a slow, insidious development of symptoms. Ruptured chordae of the anterior or posterior leaflet or both are often found at operation, and the mitral valve leaflets have the appearance of myxomatous degeneration. These patients probably represent a subgroup of individuals with mitral valve prolapse. In fact, ruptured chordae may be present in patients with prolapse without important symptoms. Grenadier and colleagues found 11 (8%) of 134 patients with mitral regurgitation due to flail leaflet. (From Grigioni and colleagues."

By contrast, important mitral regurgitation produced acutely by chordal rupture may occur in patients with no previous valve leakage. This happens predominantly in middle-age men. Often it is a complication in the life history of patients with mid-systolic clicks and only trivial murmurs, but without previous evidence of mitral regurgitation. The anterior mitral leaflet and its chordae are frequently entirely normal, with the disease process limited to the medial aspect of the posterior mitral leaflet. In this group of patients with acute and severe symptoms, presumably initiated by sudden chordal rupture, the left atrium and LV are small, left atrial pressure is high, the v wave is greatly accentuated, and there is substantial clinical and radiologic evidence of pulmonary venous hypertension. TTE and TEE are diagnostic. The posteromedial segment of the valve (P2, P3) prolapses, and the ruptured chordae are flail or seen as thickened stubs on the affected portion of the leaflet. If the patient survives the acute event, the LV and left atrium enlarge moderately over time, and symptoms may lessen with appropriate medical management (as has been shown experimentally as well). The patient gradually regains a feeling of well-being. One year later, left atrial and ventricular enlargement may not have progressed, the LV and left atrium seemingly adapting to the volume overload. Years may pass before the self-aggravating tendency of mitral regurgitation results in increased regurgitation volume. After this, the classic natural history of important mitral regurgitation evolves.

In other patients with severe acute manifestations, symptoms improve only mildly with intense medical treatment. Although most patients survive, LV and left atrial enlargement progress steadily in the months after onset. Such patients have a large mitral regurgitant flow. When untreated surgically, they progress through the life history of severe mitral regurgitation more rapidly than most patients; without surgical intervention, they die within 2 to 5 years.

Infective Endocarditis

Infective endocarditis on a previously mildly abnormal mitral valve may produce acute mitral regurgitation. The natural history of that condition is similar to that described for acute chordal rupture, except that early mortality is higher. Infrequently, death is related to uncontrolled infection. Infective endocarditis is discussed in detail in Chapter 15.

TECHNIQUE OF OPERATION

Tricuspid valve regurgitation may be associated with any type of mitral valve disease. Consequently, tricuspid annuloplasty or rarely replacement may have to be performed concomitantly with mitral valve surgery. Techniques for these operations are described in Chapter 14.

Closed Mitral Commissurotomy

After the usual preparations, including placing an arterial catheter in the right radial artery, the patient is positioned in the right lateral decubitus position. The hips are rotated to the patient’s left. The left arm is placed at the patient’s side and hanging slightly over the edge of a well-padded portion of the operating table, with the left hand beneath the hips. This position permits good access to the operative area.

After appropriate skin preparation and patient draping, an anterolateral incision is made over the interspace, through which the impulse of the apex of the LV can be palpated. The incision in the interspace (typically the fifth or sixth) is carried posteriorly, but the latissimus dorsi usually does not require incision. At times, the costal cartilage above or below the incision is transected.

The pericardium is opened anterior to the phrenic nerve. A purse-string suture is placed just off, and usually just lateral and superior to, the LV apex. The purse string is threaded into a Rummel tourniquet or similar device. A similar purse-string suture is placed around the tip of the left atrial appendage. With both the assistant and surgeon grasping their own side of the appendage with a sturdy thumb (tissue) forceps, an incision is made just off its tip. The incision must be of a size to accommodate the surgeon’s right index finger snugly. While bleeding is controlled by opposing the thumb forceps, blood is allowed to escape for two or three brief periods so that small clots may emerge. The surgeon’s right index finger is then insinuated through the appendage into the left atrium and passed directly to the mitral valve. After the valve is evaluated, pressure is applied with the exploring finger against the anterolateral commissure. Occasionally, this maneuver opens a pliable but severely stenotic valve widely and essentially completely, with no further action needed. In most cases, however, a Tubbs dilator is required and is inserted through a small stab wound in the center of the LV apical purse string (Fig. 11-6, A).

An assistant gently secures the Rummel tourniquet that has engaged the apical purse-string suture. Guided by the intraatrial finger and with the setscrew on the dilator...
positioned so that the maximal opening is 2.5 cm, the dilator is passed through the valve. The dilator blades are opened moderately for a few seconds to ensure that each dilating blade is against a leaflet and not a commissure (see Fig. 11-3, B). This and each successive dilatation last only 5 to 6 seconds, and the heart is allowed to recover completely between dilatations. Successive dilatations are then performed, first with the maximum opening set at 2.5 cm and then at about 2.9, 3.3, 3.7, and finally 4.0 cm. In small patients, the maximum dilator setting should be 3.3 to 3.5 cm. If important regurgitation develops after a dilatation, no larger settings should be attempted. Again, after the heart has recovered, the index finger is withdrawn as an assistant places a side-biting clamp across the lips of the incision in the appendage. At times, two Allis-Adair forceps close the incision well, and the clamp is not necessary. The purse string around the entrance of the Tubbs dilator is loosened slightly and then secured as the dilator is removed. No effort is made to tighten the purse string so that all bleeding stops, lest the purse string cut through the ventricular muscle. Digital control suffices for residual bleeding. Several full-thickness interrupted stitches are placed in the stab wound, and the purse-string suture is removed from the tourniquet and tied snugly but not tightly. The incision in the atrial appendage is closed with a few inter-

Figure 11-6 Closed mitral commissurotomy. A, Tubbs dilator (valvulotome). Note setscrew on handle and small size of closed tip. B, Dilator is advanced into mitral valve orifice against right index finger. Blades are opened against leaflets, not against commissures. Key: LV, Left ventricle. (From Ellis.15)
A catheter is placed posterolaterally in the left pleural space, hemostasis is secured, and the incision is closed in layers.

Open Mitral Commissurotomy

After the usual preparations and median sternotomy, pericardial stay sutures are placed and a left atrial catheter inserted (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Using intraoperative TEE, chamber size is evaluated and mitral valve pathology confirmed, including degree of valve narrowing and any regurgitant jets. Often, subvalvar stenosis can be identified. Important tricuspid regurgitation or stenosis is noted.

The aortic cannula is inserted and venous cannulation accomplished with a single venous cannula, or bicaval cannulation may be used when the left atrium is small and exposure difficult. CPB is established and perfusate temperature lowered to 18°C to 20°C. A stab wound (part of the later left atriotomy) is made at the base of the right superior pulmonary vein for initial left atrial venting. A cardioplectic needle or aortic root catheter is placed in the ascending aorta, and a retrograde coronary sinus cardioplectic cannula may be introduced as well (see “Technique of Retrograde Infusion” in Chapter 3). The aorta is clamped, cold cardioplectic solution infused, and perfusate temperature stabilized at 28°C to 32°C. The left atrium is opened vertically from the right side (Fig. 11-7, A). This may be done after developing the interatrial groove in cases of minimal left atrial enlargement, or the incision may be started medially on the right superior pulmonary vein without dissecting the groove. Superiorly, the incision is extended beneath the superior vena cava after the right pulmonary artery is dissected away from the superior aspect of the left atrium. Inferiorly, the incision may be extended by cutting behind the freed vena caval—right atrial junction. Rarely, when exposure remains poor because of the small size of the left atrium, the superior vena cava is transected on the atrial side of the cannulation site and the incision carried farther to the superior aspect of the left atrium.

A Cooley left atrial retractor or Deaver retractor is inserted (Fig. 11-7, B). An intracardiac sump sucker placed through the incision is positioned in the orifice of one of the left pulmonary veins to keep the operative field dry.

The mitral valve is examined to determine its suitability for commissurotomy, and judgment is made as to whether the leaflets will be sufficiently pliable after commissurotomy to open adequately at a low left atrial pressure. Determination is straightforward when the leaflets are pliable and noncalcified and there is little or no coalescence of chordae. However, mitral commissurotomy can often yield reasonably good results when the valve is less ideal, and even when it is partially calcified.

Thus, if some reasonable degree of mobility remains in the central portion of the anterior leaflet, persistent attempts should be made to open the valve widely by commissurotomy. If commissurotomy is chosen, one stay suture can be placed in the midportion of the free edge of the anterior leaflet and another placed similarly in the posterior leaflet. Retraction on these sutures puts tension on the leaflets and their commissures. With a sharp-pointed scalpel (#11 blade), a stab incision is made in the fused anterolateral commissure next to the anulus (see Fig. 11-7, B). The incision is extended with the scalpel toward the valve orifice, in the groove of the commissural fusion. A 3- to 4-mm incision reveals the fan of underlying chordae, making it easy to stay in the middle of the commissural tissue over the center of the fan. The incision is then carried into the valve orifice. Alternatively, a blunt-ended, long-handled hook is placed beneath each leaflet, and by trial and error these hooks are positioned exactly in the spot that provides the best exposure for division of each commissure. With the scalpel, an incision is made at the anterolateral commissure beginning at the valve orifice and extended toward the anulus. The surgeon takes care to follow the true line of the commissure, which extends more anteriorly than might be thought. With either method, when fused chordae are present beneath the commissure, they can usually be separated with the knife or scissors. When appropriate, the incision is carried down into the center of the papillary muscles, dividing them into anterior and posterior halves (Fig. 11-7, C).

The posteromedial commissure is usually less well defined and fused for a shorter distance than the anterolateral commissure. Using one of the techniques just described, this commissural leaflet tissue is incised. Chordae are often more fused beneath this commissure, and their separation by sharp dissection may be needed together with longitudinal division of the papillary muscle. If the chordae are fused together to form a fanlike fibrous sheet beneath either leaflet at one or both commissures, this sheet is fenestrated by removing a wedge of tissue from its center using a sharp-pointed scalpel. Localized but bulky calcium deposits are removed from the leaflets with bone-nibbling forceps.

A firm plastic catheter with multiple side holes (ideally a 24F chest drainage tube) is placed through the valve into the LV and tied to the left atrial vent snare to secure it. Catheter placement frustrates the valve, and the side holes lying in the left atrium are an additional safeguard to prevent ejection by the LV into the aorta until de-airing is complete. The left atrium is closed with continuous 3-0 polypropylene suture, but with the loops left loose where the catheter exits through the left atrial incision. The left atrial vent is removed during this procedure to allow the left side of the heart to fill with blood. If return to the left atrium is inadequate, right atrial pressure is raised by returning blood to the patient (see “De-Airing the Heart” in Section III of Chapter 2). With the patient’s head down, the aortic clamp is released while suction is applied to the aortic vent needle. The heart is defibrillated if necessary, and the ventricle is allowed to eject into the left atrium and pericardium via the transmitral catheter until all air is clearly eliminated.

Alternatively, after completion of the commissurotomy, the left atrium is completely closed before beginning aortic root reperfusion and later removing the aortic clamp. Closure with 3-0 polypropylene suture is started at the superior angle, carried partway down, and held. With another suture, closure is begun at the inferior angle and carried superiorly until the other suture is reached. The closure must be done accurately because it is difficult to see the angles later. The sump sucker is removed, and the left atrium is filled with saline solution just before the suture line is completed. A small stab wound is made through a purse string in the ascending aorta and a small curved clamp placed through the hole to allow egress of blood and air from the LV before removing the aortic clamp. The venous line is partially clamped, and while the lungs are inflated, air is evacuated from the ascending aorta stab hole. Suction is placed on the aortic root catheter in the ascending aorta, the aortic clamp is released, and rewarming
Chapter 11 Mitral Valve Disease with or without Tricuspid Valve Disease

Figure 11-7 Open mitral commissurotomy. 

A, Exposure is through a median sternotomy. Left atrium is opened from right side in front of right pulmonary veins. 

B, Cooley left atrial retractor is positioned. With traction on stay sutures in each leaflet, valve is well exposed for commissurotomy. An incision is made from valve orifice into posteromedial commissure; line to be incised is located by staying in leaflet tissue overlying center of underlying nest of chordae to posterior papillary muscle (see text for details). Note that correctly placed incision curves anteriorly. As incision is made, chordae beneath commissure are separated. Incision is carried vertically down into the papillary muscles to attain a larger orifice. Key: IVC, Inferior vena cava; SVC, superior vena cava.
is begun (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

If the period of global myocardial ischemia has exceeded 30 minutes, the technique of controlled aortic root or retrograde perfusion may be used (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). These maneuvers may aid in evacuating air from the coronary arteries. If careful observation reveals LV distention, a 13-gauge needle is inserted into the RV and across the septum into the LV. After good cardiac action has returned, the usual de-airing procedures are followed (see “De-Airing the Heart” in Chapter 2).

As rewarming progresses, two right atrial and two RV myocardial wires are placed. Before decannulation, examination by TEE should confirm no more than trivial or mild mitral regurgitation.

Repair of Mitral Regurgitation

Repair rather than replacement is the procedure of choice for treating mitral regurgitation, and current trends favor this approach. The proportion of patients undergoing repair for isolated mitral regurgitation rose from 51% in 2000 to 69% in 2007, as recorded in the Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database. However, not all cases are successfully managed in this fashion. Thus, at operation it must be determined whether repair will likely provide an acceptable result. This determination is aided appreciably by prebypass TEE. The magnitude and direction of the regurgitant jet can be assessed and the site of leaflet dysfunction accurately predicted. The abnormal valve physiology can often be characterized as restrictive, dilated, or prolapsing. These determinations allow informed decisions as to appropriate repair techniques. Repair can most confidently be performed when chordae are ruptured in a limited portion of the posterior leaflet and the anterior leaflet is essentially normal, or when there is simply prolapse of the posterior leaflet. Regurgitation from ruptured chordae to the anterior leaflet can be successfully repaired in most cases. Rheumatic mitral regurgitation can usually be repaired when distortion of the valve leaflets is minimal, as can certain cases of combined stenosis and regurgitation when commissurotomy precedes the repair. Nonrheumatic, noncalcific, almost pure mitral regurgitation in the adult, nearly always due to myxomatous degeneration, can usually be repaired. Regurgitation caused by infective endocarditis, with resultant chordal rupture or a perforated cusp, is repairable at times.

When regurgitation is associated with mitral valve prolapse, myxomatous degeneration, or chordal rupture, Carpentier’s techniques have proven reproducible and durable. Carpentier and Kumar (of Duran’s group) and their colleagues clarified the pathologic anatomy of the mitral valve. Their observations are fundamental considerations for a repair. As observed by echocardiography or at operation, the disease process of the mitral apparatus may be classified as restrictive, normal with annular dilatation, or degenerative (leaflet prolapse) (Fig. 11-8).

Thus, with the mitral valve exposed as usual and using saline distention, areas of prolapse and regurgitation are identified. With forceps and blunt hooks (crochet hooks), each element of the valve apparatus (anulus, leaflets, chordae, papillary muscle) is examined for pathologic changes. In particular, the normal primary chordae are distinguished from the abnormal stretched or ruptured chordae to the offending prolapsed portion. A rectangular excision of the prolapsed sector of the posterior leaflet is done (Fig. 11-9, A). This can involve 15% to 25% of the posterior leaflet. Further mobilization of the remaining leaflet may be accomplished by resecting some adjacent secondary and tertiary chordae. The resulting gap is bridged by a compacting (compression) suture at the base of the resected leaflet, beginning in atrial tissue just below the annulus. Alternatively, with a sliding plasty, adjacent normal portions of the posterior leaflet are incised at their bases and moved centrally to obliterate the gap (Fig. 11-9, B and C).

If a sliding plasty has been used, reconstruction is performed by suturing the mobilized leaflet to the posterior anulus and then reapproximating the cut edges of the leaflets with interrupted nonabsorbable sutures. Other techniques for closing the gap between the resected leaflets have been described, including the folding plasty technique. Usually an anuloplasty ring is then sutured into place to both support the repair and narrow the anulus (Fig. 11-9, D and E). Proper sizing of the anuloplasty ring (whether flexible or fixed) is essential to maintain competence and avoid postoperative LV outflow tract narrowing. Basically, the ring must recreate the normal anteroposterior depth of the anulus, which typically is the anteroposterior length of the splayed anterior leaflet. Thus, the size of the anterior leaflet rather than the intercommissural distance should be used to select the appropriate ring size. However, there is no uniform agreement about the technique or even the need to precisely measure anterior leaflet dimensions for ring selection. Brown and colleagues from the Mayo Clinic reported reproducibly good outcomes using a standard 63-mm posterior band in adult patients, without specific measurements.

Anterior leaflet prolapse repair (sector A₂) is more difficult and less often successful than posterior leaflet repair. A triangular wedge of the involved leaflet is resected, the leaflet is reconstructed, and a ring is placed (Fig. 11-10). To preserve available anterior leaflet for proper coaptation, the triangular resection should extend no more than one third of the distance between the free edge of the anterior leaflet and the mitral anulus. Often the repair involves other techniques described by Duran, Carpentier, Antunes, and Orszulak and their colleagues. These maneuvers are technically demanding and not as reliable as those applied to the posterior leaflet. Techniques include chordal shortening, chordal
Repair of mitral regurgitation caused by degenerative disease, with common form of ruptured chordae to posteromedial aspect of posterior leaflet ($P_2$).

A. After pathologic condition of valve is determined by careful inspection, the flail or prolapsing portion is isolated for excision. Projected incisions at base of posterior leaflet are also shown for closure of quadrangular gap by sliding plasty. Rectangular segment of leaflet tissue is excised back to annulus with lines of excision straight, not convex and outward.

B. After quadrangular resection, repair is accomplished in two phases. Anulus is narrowed at base of leaflet resection using a compression suture with or without pledgets, either figure-of-eight or horizontal mattress, with bites on ventricular and atrial aspects of annulus, to reapproximate the two sides of posterior leaflet.

C. Remaining segments of posterior leaflet are moved toward one another (sliding plasty) and reapproximated to base of leaflet. Leaflet repair is completed using fine interrupted, figure-of-eight, or continuous sutures.
Figure 11-9, cont’d  D, Carpentier-Edwards or similar anuloplasty ring is inserted. Size of ring is determined by height (depth) of anterior leaflet and by anterior intercommissural distance. Also, anterior leaflet is displayed using a crochet hook, and the two notches of sizer are approximated to anterolateral and posteromedial commissures. E, Anuloplasty ring is inserted using interrupted horizontal mattress sutures to create a purse-string effect at base of posterior leaflet, but using exactly matching intervals at base of anterior leaflet. Purse-string effect is attained both between the two arms of the suture and between each mattress suture. F, Completed ring insertion both narrows anulus and bolsters posterior repair. Only 10 to 12 double-armed mattress sutures are necessary to secure the ring.

Figure 11-10  Repair of mitral regurgitation from occasional isolated prolapse of anterior mitral leaflet or flail anterior leaflet from ruptured chordae. Valvuloplasty involves triangular resection, shown here for A, with repair of the leaflet using interrupted fine sutures (B), complemented by insertion of an anuloplasty ring (C). The triangular excision should not extend more than one third of the distance from the free edge to the anulus.
Dreyfus and colleagues have described an extensive experience with papillary muscle repositioning for anterior leaflet prolapse. The anterior head of the anterolateral papillary muscle is repositioned for A1/A2 prolapse, and the anterior head of the posteromedial papillary is repositioned for A2/A3 prolapse (Fig. 11-13).}

Alfieri and colleagues have described a simple technique that may be useful for anterior leaflet prolapse (Fig. 11-14). When the prolapse is near the commissure, the anterior and posterior leaflets are approximated “edge to edge” with one or two mattress sutures or, alternatively, with a figure-of-eight braided polyester suture. When the prolapse is in the central portion of the valve, one or two edge-to-edge leaflet-approximating sutures create a double-orifice mitral valve that functions adequately. Because mitral stenosis is a possible complication of this technique, it should probably be applied mainly in degenerative mitral valve disease. The resultant orifices should be at least 2 cm in diameter.

Figure 11-11 Repair of mitral regurgitation due to ruptured chordae to the anterior leaflet by chordal transfer. A, Area of anterior leaflet made flail secondary to ruptured chordae is resected. B, A small facing portion of normal posterior leaflet with its intact chordae is removed as a rectangular flap. C, Flap of posterior leaflet is flipped over to close defect in anterior leaflet, anchoring anterior leaflet with intact chordae. Base of flipped posterior leaflet segment is sutured to deepest aspect of anterior leaflet defect using fine polypropylene sutures. D, Quadrangular defect left in posterior leaflet is closed and the repair supported with an annuloplasty ring. (See Fig. 11-9, D and E.)
Use of 5-0 polytetrafluoroethylene (PTFE) sutures to create artificial chordae tendineae has largely supplanted chordal shortening or flip-over techniques as additions to classic mitral repair. Shown here is anterior prolapse with ruptured chordae to A. Offending primary chordae are resected, and occasionally, secondary chordae are freed. C-D, Double-armed 5-0 PTFE suture is passed in a figure-of-eight fashion, or buttressed with a pledget, through papillary muscle about 1 cm from its tip. Both arms of suture are then passed through leading edge of prolapsed leaflet, usually taking several over-and-over bites or anchoring suture over a pledget. E, Temporary guy-line stitch is placed through prolapsed leaflet area and through nonprolapsed apposing posterior leaflet. Tension applied to this guy suture determines appropriate height of anterior leaflet and length of artificial PTFE chord. PTFE suture is tied while maintaining tension on guy suture. Several such sutures are typically used.
Carpentier’s method, including an annuloplasty ring) has been the technique employed in most cases (see Fig. 11-9). When anuloplasty is necessary in young children with years of growth ahead, an anuloplasty ring is not used. Instead, an asymmetric measured anuloplasty is done by the technique described by Reed and colleagues\textsuperscript{R14,R16} (Fig. 11-15). This operation, as with most repairs of mitral regurgitation, is based on the fact that the central portion of the anterior mitral leaflet is usually pliable and of good quality. Its leading edge forms the line of closure for the repaired valve, both in the Reed repair and after insertion of a Carpentier ring.

Determining competence of the repaired valve while the left atrium remains open is imprecise. Yacoub’s maneuver involves perfusing warm blood into the aortic root proximal to the clamp through the cardioplegic needle or aortic root catheter so that function of the repaired valve can be inspected with the heart beating.\textsuperscript{Y1} A simpler method involves injecting saline under pressure through the valve into the LV. The distended leaflets and their opposing surfaces are examined, and areas of leakage, if present, are identified. The entire line of closure of the leaflets should be parallel to the mural part of the annulus—that is, to the hinge line of the posterior leaflet (or to this portion of the annuloplasty ring).\textsuperscript{C5} If all this is satisfactory, the left atrium is closed, de-airing is performed as described under Open Mitral Commissurotomy, and CPB is discontinued. At this point, competence of the valve is assessed by TEE. If more than mild regurgitation is present, CPB is resumed,\textsuperscript{M12} and the mitral valve is either re-repaired or replaced. In one institution, intraoperative TEE identified 26 of 309 patients (8%) undergoing repair for mitral regurgitation who had immediate failure of the procedure and required further repair or replacement at the same operation. Used in this manner, intraoperative TEE can limit the number of those who require late reoperation for failed repair.\textsuperscript{M8}

Repair of Mitral Regurgitation Associated with Submitral Left Ventricular Aneurysms

When there is bileaflet prolapse without anterior chordal pathology, often posterior leaflet resection and ring annuloplasty alone serve to correct the regurgitation, providing a durable repair without an additional procedure directed at the anterior leaflet.\textsuperscript{G14}

When repair rather than replacement is done for rheumatic mitral regurgitation in adults, annuloplasty (generally using CPB and myocardial management are as described for other mitral valve operations. The left atrium is opened from the right side. The aneurysmal sac is entered through an incision in the floor of the left atrium, parallel to and about 20 mm posterior to the hinge line of the posterior leaflet. The usually narrow pathway or “neck” between the LV and aneurysm is then easily visualized.\textsuperscript{A18} This pathway can be closed with interrupted pledgeted mattress sutures, bringing.
them anteriorly through the hinge line of the posterior leaflet. The opening from the left atrium into the aneurysm is then closed, draining the now-evacuated and exteriorized aneurysmal sac through its free wall into the pleural space if desired. Reparative operations can be performed for residual mitral regurgitation if indicated.

**Mitral Valve Replacement**

*Classic Procedure*

Mitral valve replacement begins with exposure of the mitral valve as described for mitral commissurotomy, using one or two valve hooks to display the leaflets. To excise the valve, an incision is begun with the knife in the center of the anterior mitral leaflet at approximately the 12-o’clock position about 2 mm from the anulus, because at that point the leaflet tissue is typically pliable and free of disease (Fig. 11-16). The incision is carried from this point leftward and rightward, either with the knife or scissors, and on to the commissural leaflet tissue at the anterolateral and posteromedial commissures. The incisions through the commissural leaflet tissue are kept next to the anulus so that the anterior and posterior leaflets stay together. The underlying papillary muscle and fused chordae are cut just in front of the incision for better exposure.

Classically, the excision is continued to the posterior leaflet from both sides. Ordinarily the posterior leaflet and its chordae are left in place when they are thin and pliable. Thus only the anterior leaflet is fully excised (but see “Chordal Sparing Procedure” later in this section). If this is not possible because of extensive disease, the secondary chordae that tether the posterior leaflet to the underlying ventricular myocardium are cut. When subanular calcification is present and can be excised without disturbing the anulus or the myocardium, it is removed. Otherwise, calcification is left in situ because overzealous efforts may damage the circumflex coronary artery or precipitate postrepair ventricular rupture.

The mechanical prosthesis or bioprosthesis can be sewn into place with interrupted simple sutures, but preferably with horizontal mattress sutures using pledgets on the atrial side, or with a continuous size 0 polypropylene suture (Figs. 11-17 and 11-18). All methods are associated with an extremely low
prevalence of periprosthetic leakage\textsuperscript{317} (see “Periprosthetic Leakage” under Modes of Death later in this section). A technique employing interrupted pledged mattress sutures with the pledgets on the ventricular side may be chosen when heavy calcification remains in some areas of the anulus or, rarely, when exposure is particularly difficult. With this technique, all sutures are placed in the heart first and then passed through the valve sewing ring. The prosthesis can then be lowered into position and the sutures tied. Protruding suture ends can damage the leaflets of bioprostheses.

After completing the valve insertion, a catheter is passed through the valve into the LV to act as a frustrator. The steps for exiting from the left side of the heart and de-airing are as described for mitral stenosis.

Chordal Sparing Procedure

Information based on experimental observation and clinical experience indicates that retention (rather than resection) of the mitral tensor apparatus at mitral valve replacement results in better LV function postoperatively\textsuperscript{1,12,25,30,31,32,325,316} (see “Cardiac Performance” later in this section). To insert a prosthesis while retaining both the anterior and posterior chordal attachments, the anterior leaflet may be split centrally and folded laterally and the posterior leaflet left as is. Alternatively, both the intact anterior and intact posterior leaflets can be folded toward their bases, then a prosthesis inserted (Fig. 11-19). These maneuvers (including folding the anterior leaflet) do not result in LV outflow tract obstruction or prosthetic obstruction when done for mitral regurgitation.\textsuperscript{116}

SPECIAL FEATURES OF POSTOPERATIVE CARE

In both the operating room and intensive care unit, patients may display a large \( v \) wave in the left atrial pressure pulse. This is \textit{not} a reliable indicator of mitral valve regurgitation, because the height of the \( v \) wave is related primarily to the level of mean left atrial pressure\textsuperscript{113} and in patients who have just undergone mitral valve repair or replacement, mean left atrial pressure is usually elevated. TEE can settle this issue.

Care of patients after mitral valve procedures is as described in Chapter 5. Ventricular unloading is an important aspect of the postoperative maintenance of optimal cardiac output in patients operated on for mitral regurgitation. Restoring mitral competence increases load-resisting shortening.\textsuperscript{34} Thus, by removing a parallel low-resistance circuit, myocardial oxygen requirement increases along with impairment of myocardial contractile reserve. Nitroglycerin, nitroprusside, and phosphodiesterase inhibitors are useful for decreasing afterload and improving cardiac performance.

Patients undergoing mitral valve replacement, including those receiving bioprostheses and often those undergoing commissurotomy or repair of mitral regurgitation, are begun on anticoagulant therapy using warfarin the evening of postoperative day 1 or 2 (day of surgery is postoperative day 0). For adults with a normal prothrombin time (PT), the initial dose is generally 7.5 to 15 mg, followed by daily doses in the hospital guided by daily PT measurements. The goal is prothrombin activity 20% to 30% of normal or PT twice the control value. This is best monitored and regulated using the international normalized ratio (INR) terminology. The INR allows standardizing the determination of PTs by accounting for differences among commercial thromboplas tin reagents.\textsuperscript{322} Optimal INR for patients after mitral valve replacement is 2.5 to 3.5.

When a mechanical valve has been inserted, this program is continued indefinitely, and the patient is educated about its extreme importance. Warfarin appears to be associated with a greater risk of excessive anticoagulation (hemorrhage) than reduced anticoagulation (thromboembolism and thrombosis). Thus, an appropriate recommendation is an INR of about 2.5 to 3.5.\textsuperscript{2,3,120,14} (See Special Situations and Controversies for additional details on long-term anticoagulation.)
Figure 11-17 Mitral valve replacement: continuous suture technique. A, One end of a double-armed size 0 polypropylene suture buttressed with a felt pledget is passed through mitral anulus just posterior to anterolateral commissure. Suture is then passed through prosthetic sewing ring, and valve without holder is lowered into place. Using about four throws, suture line is carried to the left, anteriorly passing stitches from anulus to sewing ring and taking deep bites, but avoiding noncoronary cusp of aortic valve. Suture is held midway across distance to posteromedial commissure. B, Other end of the suture, having been placed through mitral anulus as a mattress, is placed into prosthetic sewing ring and continued from anulus to sewing ring with four or five throws. It is helpful to move prosthesis in and out of anulus to accommodate needle passage. Suture is held. A second double-armed pledgeted suture is begun as a horizontal mattress just posterior to posteromedial commissure. Its ends are carried with four or five throws in each direction, first anteriorly and then posteriorly, to meet and tie with previously held ends. Knots then lie behind leaflet guards of the St. Jude Medical prosthesis depicted here.

When a bioprosthesis is inserted or anuloplasty or valvotomy performed, anticoagulation is continued for 2 to 3 months. Lower INR values (1.5-2.0) are acceptable during this period. Patients who undergo mitral valve repair and have paroxysmal or persistent atrial fibrillation should continue long-term anticoagulation with warfarin. Long-term treatment with low-dose aspirin (75-100 mg/day) is probably advisable for patients who remain in sinus rhythm after mitral valve repair. Patients who have undergone mitral valve repair or replacement should receive anti-endocarditis prophylactic antibiotics for medical procedures as indicated.

Evaluation of mitral valve repair or replacement by 2D and Doppler echocardiography should be routinely performed before hospital discharge or at first follow-up clinic visit. Assessment of right and left ventricular systolic function and identification of any residual mitral regurgitation will help guide afterload reduction therapy.
Figure 11-18  Mitral valve replacement: interrupted suture technique. A, Double-armed size 0 polyester sutures are generally placed with pledgets on atrial aspect of anulus. It is convenient to place one arm of a mattress suture just behind posteromedial commissure, reserving other end for placement later and holding suture for exposure. B, Posterior suture line proceeds counterclockwise beginning at anterolateral commissure. Sutures are placed from atrial side to ventricular side of anulus and may either be held or placed in prosthetic sewing ring. C, Anterior suture line usually proceeds clockwise from anterolateral commissure to posteromedial commissure. Along whole circumference, suture bites encompass base of residual leaflet. Clockwise from anterolateral commissure are the aortic cusps, conduction system, atrioventricular septum, coronary sinus, and circumflex coronary artery, which are at risk when bites are taken too deeply. With all sutures in place and on tension, valve is lowered into place and sutures tied, with about 12 mattress sutures used. Before tying, device struts are inspected to ensure that no suture is looped around a strut or caught within the device.
Figure 11-19 Mitral valve replacement: chordal sparing procedure. A, When it is appropriate to preserve anterior (and posterior) tensor apparatus, midportion of anterior leaflet is removed as a trapezoid or rectangle. Lateral and medial aspects of anterior leaflet remain and retain their chordal attachments. B, Residual portions of leaflet are folded back to be sutured to anulus. Leaving anterior leaflet totally intact may risk left ventricular outflow tract obstruction or, in the case of replacement for mitral stenosis, residual left ventricular inflow obstruction. Prosthesis is sutured into place using previously described interrupted (C and D) or continuous (E and F) suture technique. In either case, sutures surround retained leaflets, adding strength and purchase to the repair.
RESULTS

Mitral Commissurotomy

Survival

In an earlier era, mortality after closed commissurotomy was high. In the current era, hospital mortality after either closed or open commissurotomy approaches zero, and late survival is similar in risk-adjusted comparisons. A difference exists only in prevalence of postcommissurotomy mitral regurgitation (see “Mitral Regurgitation” in text that follows).

In many institutions, percutaneous catheter valvotomy has almost completely replaced surgical commissurotomy for isolated mitral stenosis. Procedure mortality approaches zero, and risk of complications (bleeding, severe regurgitation) requiring urgent operation is low.

Intermediate-term survival is good in those with favorable immediate hemodynamic results (Fig. 11-20).

Mitral commissurotomy is not curative with either open or closed (or balloon) commissurotomy, with survival progressively diverging from that of the general population. However, few late deaths result directly from the effects of recurrent or residual mitral stenosis or regurgitation. Rather, they result from thromboembolism or early or later sequelae of reoperation and mitral valve replacement.

Incremental Risk Factors for Premature Death

Few deaths occur early after mitral commissurotomy, and no risk factors are associated with these. Risk factors associated with later deaths include elevated Rp before commissurotomy, which directly affects survival rather than leading to reintervention, but its effect is moderate (Fig. 11-22 and Table 11-2). The aforementioned morphologic risk factors lead to recurrent symptoms and reintervention, usually valve replacement, and affect survival in this manner. Although not evident in a risk factor analysis using only preoperative variables, development of important mitral regurgitation after commissurotomy and occurrence of a thromboembolic event both adversely affect survival.

Mitral Regurgitation

Mitral regurgitation is a risk of mitral commissurotomy by any technique, but occurs in only 2% to 5% of patients who...
undergo open commissurotomy and in about 10% of patients who undergo closed commissurotomy. Rarely does the newly developed regurgitation require immediate operation, but it may lead to reoperation within a few months. Mild postcommissurotomy mitral regurgitation has little effect on survival or need for mitral valve replacement, but important postcommissurotomy regurgitation adversely affects both (Fig. 11-23).

Prevalence of new important mitral regurgitation is about 10% after percutaneous balloon mitral commissurotomy.

Cardiac Performance

Increase in calculated mitral valve area (or orifice size) produced by commissurotomy varies greatly and depends not only on the surgical opening but also on leaflet pliability and extent of subvalvar obstruction from fused chordae. Feigenbaum and colleagues found that closed mitral commissurotomy, usually with a transventricular dilator, increased mitral valve area by an average of 1.3 to 2.6 cm², with postoperative mitral valve areas ranging from 0.7 to 5.8 cm². Nakano and colleagues achieved valve areas of 2.52 ± 0.19 cm² in patients with pliable valves and minimal subvalvar disease, as well as good but smaller orifices in patients with extensive subvalvar diseases. Ben Farhat and colleagues reported an equivalent increase of mitral valve area (0.9-2.2 cm²) for open commissurotomy and percutaneous balloon valvotomy that was greater than for closed commissurotomy (0.9-1.6 cm²).

Younger patients tend to have a better functional result and experience greater increases in calculated valve area than older patients, perhaps because younger patients tend to have more pliable valves. The same general results are achieved by both open and closed commissurotomy and percutaneous balloon mitral valvotomy (Fig. 11-24). Enlargement after percutaneous balloon valvotomy results primarily from splitting of fused commissures.

Somewhat better orifices can be obtained by open than closed commissurotomy. Nakano and colleagues achieved valve areas of 2.52 ± 0.19 cm² in patients with pliable valves and minimal subvalvar disease, as well as good but smaller orifices in patients with extensive subvalvar diseases. Ben Farhat and colleagues reported an equivalent increase of mitral valve area (0.9-2.2 cm²) for open commissurotomy and percutaneous balloon valvotomy that was greater than for closed commissurotomy (0.9-1.6 cm²). The superior
hemodynamic results continued over a 7-year follow-up period (see Fig. 11-24).

A secondary effect of increased orifice size is lowering of left atrial pressure, although it frequently remains above normal. On average, left atrial pressure at rest is about 12 mm Hg after valvotomy, increasing to about 17 mm Hg on exercise. LV end-diastolic pressure often is modestly higher after commissurotomy. 

Cardiac output is usually increased by operation, and the amount of increase at rest and exercise correlates well with the increase in calculated valve area. RP usually falls immediately, especially in young patients, as verified by Block and Palacios during percutaneous balloon commissurotomy. 

Pulmonary artery pressure usually falls, which correlates well with the decrease in left atrial pressure and RP.

**Thromboembolism**

Successful mitral commissurotomy may reduce the likelihood of thromboembolism, although accurate comparisons are not available. About 90% of patients are free of a thromboembolic event 8 to 10 years after open commissurotomy. The linearized rate of thromboembolism has been reported at 1% to 2% per patient-year. This statistic is not very useful, however, because the hazard function for a first or subsequent thromboembolic event is not constant (Fig. 11-25). Atrial fibrillation, older age, and a history of thromboembolism preoperatively are reported risk factors for postcommisurotomy thromboembolism. Also, a postcommisurotomy thromboembolic event predisposes the patient to further events (Table 11-3). The type of surgical commissurotomy, open or closed, has not been shown to be a risk factor.

**Functional Status**

Successful open or closed mitral commissurotomy, in properly selected patients, results in dramatic relief of symptoms. More than 90% of patients are in NYHA functional class I or II during the first 1 or 2 postoperative years. Lack of permanent favorable results from mitral commissurotomy is evident in the gradual decline in functional status. Redevelopment of symptoms results from gradual loss of leaflet pliability as well as progression of subvalvar pathology and increase of valvar calcification. Although recurrence of rheumatic fever may accelerate this pathology, progression seems to occur even without further rheumatic episodes. Thus, NYHA functional class correlates well with estimated area of the mitral orifice late postoperatively; the mean value...
Partial text:

### Table 11-3 Incremental Risk Factors for New Postcommissurotomy Thromboembolic Event after Mitral Commissurotomy

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Hazard Phase</th>
<th>Early</th>
<th>Late</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Older) Age at commissurotomy (years)</td>
<td></td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>History of thromboembolism before commissurotomy</td>
<td></td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>(Greater) Number of previous postcommissurotomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>thromboembolic episodes (0, 1, 2)</td>
<td></td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>Morphologic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Greater) Leaflet calcification (grade 0-5)</td>
<td></td>
<td>•</td>
<td></td>
</tr>
<tr>
<td>Pliable leaflet</td>
<td></td>
<td>•</td>
<td></td>
</tr>
</tbody>
</table>

Data from Hickey and colleagues. Database is same as in Table 11-2. Variables entered into the analysis, ordinal logistic coefficients, and P values are provided in the original article.

Thromboembolism was considered to be a modulated renewal process (event), and thus the first, second, or third events (total of 44) are included.

Figure 11-25 Depiction of all postcommissurotomy thromboembolic events, not only the first episode. Format is as in Fig. 11-21. A, Cumulative event function for all thromboembolism. B, Hazard function for any thromboembolic event after mitral commissurotomy. (From Hickey and colleagues.)

Figure 11-26 Comparison of preoperative and postoperative New York Heart Association functional status in 123 patients surviving an average of 48 months after open mitral valvotomy. Key: Class IIa, Breathlessness with unusually strenuous activity; class IIb, breathlessness with ordinary activity. (From Smith and colleagues.)

Figure 11-27 Declining percentage of patients in New York Heart Association functional class I after open or closed commissurotomy. Changes across time of functional classes II and III are also shown. The longer the time since commissurotomy, the greater the percentage of patients undergoing mitral valve replacement. (From Hickey and colleagues.)

is 2.0 cm² in class I patients, 1.7 in class II, and 1.6 in class III. Immobility of valve leaflets and obstructive subvalvar agglutination of chordae are the main risk factors for a poor early functional result. Calcification of a portion of the leaflet(s) does not preclude a satisfactory result.

Despite excellent early and intermediate results in the current era, durability of results is limited. Scarring from the rheumatic process in the valve seems to progress gradually. Eventually, although not until 20 years postoperatively in some patients, most patients lose their good functional status and return with restenosis or new-onset regurgitation (Fig. 11-27). Absence of leaflet pliability in the presence of valvar calcification is a risk factor for the rate of decline in functional...
status after all types of commissurotomy. Type of surgical commissurotomy (open or closed) has not been shown to be a risk factor\textsuperscript{110} (Table 11-4).

**Reintervention**

Most patients undergoing mitral commissurotomy by any technique will require another procedure at some time, generally mitral valve replacement because of gradual loss of leaflet pliability, progression of subvalvar pathology, and increase of valvar calcification\textsuperscript{29,35,36,61,82} (see Fig. 11-27). About 20% of patients undergoing surgical commissurotomy require valve replacement within 10 years, and about half require it by 20 years (Fig. 11-28).

The same variables that cause survival to vary probably cause prevalence of postcommissurotomy mitral valve replacement to vary (Table 11-5). Again, type of surgical commissurotomy (open or closed) has not been demonstrated to be a risk factor for subsequent mitral valve replacement.\textsuperscript{111} Morphology of the mitral valve powerfully affects the time-related prevalence of mitral valve replacement after surgical commissurotomy (Fig. 11-29) as well as after percutaneous balloon valvotomy.\textsuperscript{81} At 7 years, freedom from restenosis was 93% for the open and balloon procedures vs. 63% after closed commissurotomy.

**Percutaneous Balloon Valvotomy**

Early hemodynamic, functional, and anatomic improvement after percutaneous mitral valvotomy is, as noted earlier, nearly equivalent to results following open surgical commissurotomy.\textsuperscript{316} Long-term outcomes are not available. There is a progressive decrease in valve area that closely parallels that seen historically and in concurrent studies for surgical approaches. Degree of deterioration can be predicted by variables related to preoperative functional class and morphologic features of the mitral valve.\textsuperscript{1118} (Table 11-6 and Fig. 11-30). Thus, long-term survival and need for reintervention after the catheter approach should be similar to results after the open surgical approach.

**Redo Mitral Commisurotomy**

Survival after a second mitral commissurotomy is surprisingly good in view of the more advanced valvar pathology usually present at reoperation. Peper and colleagues report 5-, 10-, and 15-year survival of 96%, 83%, and 63%, respectively, after repeat open commissurotomy. Also, 16 (31%) of 52 hospital survivors underwent still another mitral operation, usually a replacement, an average of 8.2 years later.\textsuperscript{76}

**Repair of Mitral Regurgitation**

In general, early, intermediate, and long-term results of repair of mitral valve regurgitation have been good.\textsuperscript{1113,84}

### Table 11-4 Incremental Risk Factors for Poor Functional Status after Mitral Commissurotomy\textsuperscript{a}

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Older) Age at commissurotomy</td>
<td>.03</td>
</tr>
<tr>
<td>(Higher) Precommissurotomy NYHA class</td>
<td>.0001</td>
</tr>
<tr>
<td>Morphologic</td>
<td></td>
</tr>
<tr>
<td>(Greater) Valve calcification (grades 0-5)</td>
<td>.0003</td>
</tr>
<tr>
<td>(Greater) Leaflet immobility (grades 0-5)</td>
<td>.002</td>
</tr>
<tr>
<td>(Longer) Follow-up interval</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Data from Hickey and colleagues.\textsuperscript{111} Variables entered into the analysis, ordinal logistic coefficients, and P values are provided in the original article.\textsuperscript{UAB group, 1967-1988; n = 339; deaths = 65. Key: NYHA, New York Heart Association.}

### Table 11-5 Incremental Risk Factors for Mitral Valve Replacement after Mitral Commissurotomy

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Late Hazard Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphologic</td>
<td>1</td>
</tr>
<tr>
<td>(Smaller) Preoperative mitral valve area</td>
<td>1</td>
</tr>
<tr>
<td>(Greater) Leaflet immobility (grades 0-5)</td>
<td>1</td>
</tr>
<tr>
<td>Leaflet calcification</td>
<td>1</td>
</tr>
<tr>
<td>(Greater) Postrepair (OR) mitral valve regurgitation (grades 0-5)</td>
<td>1</td>
</tr>
</tbody>
</table>

Data from Hickey and colleagues.\textsuperscript{111}

Key: OR, Operating room.
Survival

Early (Hospital) Death Hospital mortality after repair of isolated nonischemic mitral regurgitation is very low in the current era. Hospital mortality of 1% for isolated elective nonischemic mitral valve repair was reported in the STS Adult Cardiac Surgery Database in 2009.53

Time-Related Survival Time-related survival, including hospital deaths, of patients with mitral regurgitation undergoing repair with or without other cardiac procedures has been better than that of patients undergoing replacement. Most groups have reported similar findings, with 4- or 5-year survival after repair varying from 74% to 94%.10,30,32,23,14,15,16,30 Ten-year survival of one group of patients undergoing repair with or without other procedures was 59%.54

Variability in survival among reports and improved survival after repair compared with replacement are related in part to the differing prevalence of risk factors for death.57,63 Mayo Clinic surgeons reported surgical mortality of 2.6% for repair and 10% for replacement (P = .002).64 Late survival (in surgical survivors) at 10 years was 69% ± 6.0% vs. 58% ± 5.0% (P = .02), and late survival after valve repair did not differ from expected survival (Fig. 11-31). Again, the two groups differed mainly in degree of preoperative heart failure.65 A multicenter European study reported a 30-day mortality of 0.7% and a superior risk-adjusted 5-year survival with repair versus replacement (92% vs. 80%, P < .001).66 To address comparison of repair versus replacement, Gillinov and colleagues used propensity-score matching (see “Clinical Studies with Nonrandomly Assigned Treatment” in Chapter 6) and found that repair conferred a survival advantage in most (89%) patients that became evident after about 2 years.

Modes of Death
Modes of death early and late after mitral valve repair are similar to those after mitral valve replacement.54 The most common mode is cardiac failure.

Incremental Risk Factors for Premature Death
Incremental risk factors for premature death after repair of mitral regurgitation are the same as those after replacement (Table 11-7). In the UAB experience, neither procedure was a risk factor vis-à-vis the other. Akins and Dujardin and their colleagues, however, indicate that mitral valve replacement is a risk factor for late mortality compared with mitral repair in a univariable analysis, but not by multivariable analysis.10,23 In most studies, this reflects choice of replacement for those
patients who are older or in a more advanced NYHA functional class. However, Gillinov and colleagues found by both multivariable analysis and propensity adjustment that replacement was a risk factor.\textsuperscript{16,16}

**Residual or Recurrent Mitral Regurgitation**

Many patients have no residual mitral regurgitation after repair.\textsuperscript{4,7,29} Alvarez and colleagues reported that only 4.5% of 155 repair patients experienced repair failure within 6 months.\textsuperscript{15} In a group of more than 1000 patients analyzed for late failure, only 30 repair patients needed late reoperation (freedom from reoperation at 10 years 93%; CL 91%-94%).\textsuperscript{13} Recurrent regurgitation in these and other series is caused by either progression of disease or inadequate operation, including suture dehiscence.\textsuperscript{13} In most patients, residual regurgitation is present immediately after repair rather than developing later.\textsuperscript{13} Although reoperation may underestimate the prevalence of late regurgitation, various groups report freedom from reoperation of 80% to 96% at 10- to 15-year follow-up, suggesting satisfactory durability of repair.\textsuperscript{12,13,3,10,13,31,32}

A clear relationship has not been established between technique of repair and prevalence of residual regurgitation. However, repair is clearly more effective for patients with degenerative (myxomatous) disease than for those with restrictive (rheumatic) disease.\textsuperscript{12,17} (Fig. 11-32). The best results may be in patients with ruptured chordae to the posterior leaflet,\textsuperscript{5,16,29} although Orszulak and colleagues have found almost equally good results when the ruptured chordae belong to the anterior leaflet.\textsuperscript{3,27,33} For complex repairs and those involving the anterior leaflet, chordal replacement is superior to chordal shortening.\textsuperscript{17,39} Historically, surgical repair of posterior leaflet prolapse has been more durable than repair of anterior leaflet prolapse, but results of the latter have improved in the current era.\textsuperscript{3,30} Lawrie and colleagues reported a contemporary experience in which outcomes were equally

### Table 11-7 Incremental Risk Factors for Premature Death after Valve Repair or Replacement for Mitral Regurgitation\textsuperscript{a}

<table>
<thead>
<tr>
<th>Risk Factor\textsuperscript{b}</th>
<th>Hazard Phase</th>
<th>Early and Decreasing</th>
<th>Constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Older) Age</td>
<td>•</td>
<td>•</td>
<td>•</td>
</tr>
<tr>
<td>African American</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphologic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papillary muscle ischemic disease</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Greater) LV enlargement (grades 1-6)</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous CABG</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Higher) LVEDP</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Higher) NYHA functional class (I-V)</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV resection for aneurysm</td>
<td>•</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Patients with or without associated cardiac procedures are included in this study (UAB group, 1975 to July 1983; \( n = 490 \); deaths = 158). See original article for equations, \( P \) values, and coefficients.

\textsuperscript{b}Mitral replacement as a risk factor has a \( P \) value of .14 (early phase only).

Key: CABG, Coronary artery bypass grafting; LV, left ventricular; LVEDP, left ventricular end-diastolic pressure; NYHA, New York Heart Association.
good for artificial chord replacement in anterior leaflet prolapse as in posterior leaflet prolapsed. In patients with isolated posterior leaflet prolapse, chordal replacement plus anuloplasty ring appears to provide midterm valve competence equivalent to that of traditional quadrangular resection plus ring. Others have extended leaflet resection to the severely prolapsing anterior leaflet with good midterm valve function. G8, S6 Gazoni and colleagues emphasize, however, that a triangular resection technique should be used, and the height of the resected leaflet segment should not exceed one third of the distance from the anulus to the free edge of the anterior leaflet.

**Cardiac Performance**

LV performance responds to mitral valve repair in the same general manner as it does to mitral valve replacement. Some regression of LV hypertrophy occurs, with decreased heart size, LV volume, and muscle mass. Preoperative LV systolic function is more or less preserved, although EF is often moderately decreased. However, some studies document LV performance to be better after mitral valve repair than after replacement. B30, C35 Corin and colleagues found that systolic and diastolic function returned to normal in mitral repair patients, but that global and regional systolic function as well as diastolic function were depressed in replacement patients. This difference is probably attributable to preservation of the tensor apparatus in the repaired valve (Fig. 11-33) but may also reflect earlier intervention in patients undergoing repair vs. replacement.

An important issue is the potential reversal of preexisting LV dysfunction following mitral valve repair (also see discussion of mitral valve repair in Chapter 20). Among patients with preserved EF preoperatively, large regurgitant volume (>80 mL by quantitative Doppler and proximal isovelocity surface area method) is predictive of LV dysfunction (EF < 50%) following mitral valve repair.

**Thromboembolism**

Patients undergoing mitral valve repair are generally free of late thromboembolic complications, even though they rarely receive anticoagulants. Duran and colleagues found 93% of patients free of thromboembolism within the first 4.5 years after repair, a prevalence similar to that for xenograft replacement in their experience.

**Left Ventricular Outflow Obstruction**

In about 5% to 10% of patients with mitral regurgitation associated with mitral valve prolapse, abnormal systolic anterior motion (SAM) of the mitral valve develops immediately after mitral anuloplasty with a Carpentier ring. Related to this, gradients of 60 mmHg across the LV outflow tract have been measured. This complication appears to be
limited to patients with myxomatous degeneration\textsuperscript{18,20,99} and excessive redundancy of the anterior and posterior leaflets, although presence of a small hyperdynamic LV and excessive ventricular hypertrophy may also contribute. SAM is now believed to be the result of anterior displacement of leaflet coaptation.\textsuperscript{15} LV outflow tract obstruction has not been observed in patients undergoing suture (rather than ring) mitral anuloplasty.\textsuperscript{95} Cosgrove and colleagues have shown that simple removal of the rigid anuloplasty ring abolished the obstruction while retaining competence of the mitral valve.\textsuperscript{37} Substitution of a larger ring, flexible ring, or half-ring or addition of a posterior leaflet sliding plasty may also eliminate SAM. Grossi and colleagues noted a prevalence of 6.4\% (CI 5.2\%-7.8\%) in their series of valve repair. All patients were treated medically, with resolution of gradients in all patients and resolution of SAM in half of patients within a year.\textsuperscript{30}

**Functional Status**

Functional status of most patients is excellent after repair or replacement of a regurgitant mitral valve, with greater than 90\% of surviving patients in NYHA class I or II.\textsuperscript{38,39,34}

**Reoperation**

Freedom from reoperation late after mitral valve repair is generally 85\% to 95\% at 10 years,\textsuperscript{16,20,47,81,83,84,14,15} similar to that after mitral valve replacement.\textsuperscript{27} Prevalence of reoperation is greater for anterior leaflet repair than for posterior leaflet repair.\textsuperscript{2,14}

Factors that may increase risk of reoperation late after repair include rheumatic disease (as opposed to degenerative disease; see Fig. 11-32), advanced degenerative changes involving the anterior leaflet, and residual regurgitation at completion of the initial procedure. When patients with 1+ or 2+ (of possible 4+) early postoperative regurgitation were compared with those with “echo-perfect” results (no regurgitation), Fix and colleagues found 83\% freedom from reoperation in the former group vs. 96\% in the latter group at late follow-up ($P = .07$).\textsuperscript{34} Type of repair appears to have no effect on prevalence of reoperation.\textsuperscript{29,29} Reed, Chauvaud, and Ohno and their colleagues showed mitral repair to be as successful in children as in adults\textsuperscript{20,22,24} (Fig. 11-34).

![Figure 11-34](image)

**Figure 11-34** Freedom from reoperation after mitral valve repair in children younger than age 12 years. Vertical bars represent one standard error. (From Chauvaud and colleagues.\textsuperscript{19})

The hazard function of reoperation after repair of mitral regurgitation is low, constant, and different from that of replacement (Fig. 11-35). Mitral valve repair does not have the peaking early hazard phase for reoperation, which in mitral replacement is related to periprosthetic leakage and prosthetic valve endocarditis. Furthermore, at least until now, no rising late hazard phase for reoperation after repair has been demonstrated, indicating the durability of this approach. In fact, in a 20-year experience reported by the Mayo Clinic, the absolute prevalence of reoperation in the current era was 5\% ± 2\% for posterior leaflet repair and 10\% ± 2\% for anterior leaflet repair at 10 years.\textsuperscript{27} A more recent analysis from the Mayo Clinic\textsuperscript{36} examined reoperations after mitral valve repair over 35 years. New pathology was the cause for reoperation in about 55\% of patients, and failure of mitral repair in most of the remainder. Mitral valve re-repair was possible in 44\% of patients.

**Infective Endocarditis**

Infective endocarditis is rare after repair of mitral regurgitation.\textsuperscript{41} No cases were found in the UAB experience, with a follow-up of 21 to 120 months.\textsuperscript{34} This complication is more common when the affected valve is replaced rather than repaired.\textsuperscript{44}

**Mitrval Valve Replacement**

**Survival**

**Early (Hospital) Death** Hospital mortality after primary isolated mitral valve replacement for nonischemic valve disease with preserved LV function is generally less than 2\% among patients without serious comorbidities in the current era.\textsuperscript{12} A hospital mortality of 5.7\% for isolated mitral valve replacement for any etiology, primary and reoperation, was reported from the STS Adult Cardiac Surgery Database during the years 2002 to 2006.\textsuperscript{11} Medicare sources indicated a hospital mortality of 14\% for isolated mitral valve replacement among patients older than age 65.\textsuperscript{65} Mortality after mitral valve replacement with tricuspid surgery is similar or slightly higher.\textsuperscript{12} When mitral valve replacement has been preceded by mitral valve repair, hospital mortality is not affected appreciably.
Time-Related Survival Considering both isolated mitral valve replacement and replacement done concomitantly with other procedures, 1-, 5-, and 10-year survival in an earlier era was 82%, 68%, and 55%, respectively. The hazard function had a rapidly declining early phase, but also a constant phase extending as long as patients had been followed (Fig. 11-36). Time-related survival has been higher in patients undergoing primary isolated mitral valve replacement than in those having replacement combined with other cardiac procedures (Fig. 11-37). Survivals similar to those reported here, including some 15-year survivals of 35% to 50%, have been reported by other groups.810,821,825,836-838,847 Both early and late survival after primary mitral replacement are considerably improved over that obtained in earlier eras.821,810,813 Improvement is related to better myocardial management,83 reduction in technical problems such as atrioventricular rupture and air embolization, and improved mechanical and bioprosthetic valve replacement devices.

Survival both early and late after reoperation is less than that after original valve replacement (Fig. 11-38). This is related not only to technical aspects of reoperation but also to the fact that prosthetic valve endocarditis is often the indication for reoperation, and reoperative patients as a group tend to have greater functional disability than those undergoing their first valve replacement.826

Mitral valve replacement in children and adolescents has low early mortality, and time-related survival is probably equal to or superior to that of adults. However, mitral replacement in the first year of life may carry a higher risk; 9 of 25 patients died (36%; CL 25%-48%) in the experience of Kadoba and colleagues.83 Seven of the deaths were in patients with atrioventricular (AV) septal defects. Recent experience with improved repair of the left AV valve in AV septal defects, better myocardial management, and supraannular placement of the prosthesis have reduced early risk in infants considerably (see Results in Chapter 34). Time-related morbidity is attributable to reoperation associated with bioprosthetic tissue degeneration and acquired prosthetic stenosis associated with somatic growth.

Modes of Death
Most early deaths are attributable to cardiac failure, usually acute and within a few days of operation. Subacute cardiac failure may be the mode of death in the hospital or within 1...
to 2 months after hospital discharge. It is characterized by stable but low cardiac output and consequent widespread subsystem failure, often including cool (rarely frankly ischemic) extremities, abdominal distention, and occasionally ischemic bowel, gastrointestinal bleeding, jaundice, poor renal function, and mental confusion. Infection may occur as a terminal event.

**Incremental Risk Factors for Premature Death**

Some of the incremental risk factors for death that existed during the earliest eras of mitral valve replacement have been neutralized by improvements in surgical technique, myocardial management (see Chapter 3), and perioperative care (see Chapters 4 and 5). Among specific improvements is sparing of the tensor apparatus, as demonstrated particularly by the Stanford group (see “Cardiac Performance” later in this section). Surprisingly, large size of the left atrium is a risk factor for poor outcome that approaches the risk imposed by LV enlargement. Presumably, marked LV enlargement connotes reduced ventricular contractility (see “Mitral Regurgitation” under Natural History earlier in this section), and this may actually be responsible for increased risk.

**Marked Left Ventricular Enlargement** LV enlargement is a risk factor for death early after repair (see Table 11-8). Presumably, marked LV enlargement connotes reduced ventricular contractility (see “Mitral Regurgitation” under Natural History earlier in this section), and this may actually be responsible for increased risk.

**Previous CABG**

<table>
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<td>Important TV disease</td>
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<td>Concomitant LV resection in ischemic MVD</td>
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<td>Global myocardial ischemic time using cardioplegia</td>
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</table>

*Based in part on patients with or without concomitant procedures from a UAB study, 1975 to July 1983; n = 819; deaths = 222.

**Ischemic Mitral Regurgitation** Ischemic etiology is a greater risk factor for death late after mitral valve replacement than nonischemic etiology.

**Advanced Functional Disability** Expressed as NYHA functional class, advanced disability is an important risk factor for death in the early phase of hazard.

**Global Myocardial Ischemic Time** Prolonged global myocardial ischemic time using cold cardioplegia is an incremental risk factor for death in the early phase after operation. This can be seen from predicted 30-day mortality of 6% or less when global myocardial ischemic time is 120 minutes or shorter (Fig. 11-39). Almost all mitral valve operations, including those with concomitant coronary artery bypass grafting (CABG) and tricuspid anuloplasty, can be accomplished within that time.

<table>
<thead>
<tr>
<th>Device</th>
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| No device currently in use has been clearly shown to be a risk factor for premature death after mitral valve replacement. Earlier, the “high profile” of caged-ball valves was alleged to be an incremental risk factor because of its supposed obstructive effect and detrimental effect on LV function. This may have been true, in view of the superior early results from 1970 to 1973 using a stent-mounted aortic allograft valve, suggesting that a nonobstructive device with a central orifice flow pattern is optimal. Also, at least in the experience of Cohn and colleagues, survival after mitral valve replacement with a bioprosthesis of any type was higher than after replacement with a prosthetic disc valve, perhaps related

### Table 11-8 Incremental Risk Factors for Death after Primary Mitral Valve Replacement

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**Marked Left Ventricular Enlargement** LV enlargement is a risk factor for death early after repair (see Table 11-8). Presumably, marked LV enlargement connotes reduced ventricular contractility (see “Mitral Regurgitation” under Natural History earlier in this section), and this may actually be responsible for increased risk.

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**Incremental Risks of Concomitant Tricuspid Anuloplasty and CABG** are discussed separately under “Results” in Sections II and III.

### Devices

No device currently in use has been clearly shown to be a risk factor for premature death after mitral valve replacement. Earlier, the “high profile” of caged-ball valves was alleged to be an incremental risk factor because of its supposed obstructive effect and detrimental effect on LV function. This may have been true, in view of the superior early results from 1970 to 1973 using a stent-mounted aortic allograft valve, suggesting that a nonobstructive device with a central orifice flow pattern is optimal. Also, at least in the experience of Cohn and colleagues, survival after mitral valve replacement with a bioprosthesis of any type was higher than after replacement with a prosthetic disc valve, perhaps related. Undergoing mitral valve replacement for mitral regurgitation. Overall reported operative mortality in this age group in the United States exceeds 14%, and is notably higher (>20%) in low-volume centers.

### Nonischemic Mitral Regurgitation

In contrast to mitral stenosis, nonischemic mitral regurgitation is probably a risk factor for death (see Table 11-8), but not to the extent that might be predicted from the sudden increase in LV afterload imposed when the regurgitant mitral valve is made competent. This is probably because a number of the other sudden hemodynamic changes (e.g., reduction in LV stroke work) are favorable.
to fewer thromboembolic events and only infrequent anticoagulation in the former group\textsuperscript{228} (see “Mechanical Mitral Valve Replacement Devices” and “Bioprosthetic Mitral Valve Replacement Devices” later in this section).

Previous closed or open mitral valve repair or percutaneous balloon valvotomy cannot be considered incremental risk factors.

**Cardiac Performance**

Left AV valve function usually is greatly improved, but a transvalvar end-diastolic gradient is present in most patients following mitral valve replacement.\textsuperscript{519,515} Magnitude of the gradient depends on patient size and physical activity (e.g., cardiac output at rest and during exercise), size of device inserted, and its type.\textsuperscript{823} Gradients are small when devices larger than 29 mm can be used, but they vary according to the device and are typically present with 29-mm, 27-mm, and 25-mm sizes (Table 11-9). Zero-pressure fixation techniques may improve the performance of porcine bioprostheses by making the leaflets more pliable.\textsuperscript{842}

Response of LV performance to valve replacement in patients with mitral stenosis who have impaired function preoperatively has not been determined, but the abnormalities of compliance (which this type of impairment usually induces) probably remain.

Sudden ablation of mitral regurgitation by mitral valve replacement triggers a particularly complex LV response (see “Mitral Regurgitation” under Natural History earlier in this section).\textsuperscript{514,515,585} If the LV is normal, as usually occurs in acute experimental or clinical regurgitation, sudden correction of regurgitation immediately increases forward flow (cardiac output) despite increased afterload.\textsuperscript{531} After valve replacement for chronic mitral regurgitation, however, EF is lower, at least transiently, than preoperatively in most patients.\textsuperscript{85,510} When preoperative LV enlargement is only mild or moderate (with an end-diastolic dimension of 7 cm or less and an end-systolic dimension of 5 cm or less by echocardiography),\textsuperscript{510} reduced EF after valve replacement generally remains within the normal range.

In patients with a more than moderately enlarged LV at operation (with an echocardiographically determined end-diastolic dimension > 7 cm or an end-systolic dimension > 5 cm), a condition accompanied by decreased LV contractility and increased myocardial degenerative changes,\textsuperscript{511} EF is greatly reduced 2 weeks after valve replacement and at times deteriorates still further during the later postoperative period.

 Patients undergoing effective repair have generally better ejection indices postoperatively than similarly matched candidates after valve replacement. Tischler and colleagues reported reduction of rest and exercise EFs in 10 mitral replacement subjects, but no change in repair patients.\textsuperscript{75} Repair patients had a higher stroke volume and EF at rest and exercise, associated with lower end-systolic wall stress.

LV enlargement regresses after operation, with both end-diastolic and end-systolic dimensions returning toward normal.\textsuperscript{510} LV contractility is probably normal or near normal preoperatively and remains so after operation.\textsuperscript{510,516} In many patients, however, LV size is reduced early postoperatively (end-diastolic volume is less, and end-systolic volume is about the same), but increases late postoperatively (6-12 months after operation).\textsuperscript{510} LV wall hypertrophy does not regress.\textsuperscript{510} In such patients, the preoperative LV structural and contractile abnormalities not only show no regression after valve replacement but in fact progress and account for many recurrences of symptoms 2 to 5 years postoperatively and for many deaths 2 to 10 years postoperatively.

These findings apply to conventional mitral valve replacement in which the tensor apparatus (chordae tendineae) of the native valve is excised or transected (see “Chordal Sparing” under Technique of Operation earlier in this section). Experiments by Miller and colleagues have demonstrated that chordal division results in deterioration of LV systolic function in both isovolumic and ejecting heart preparations.\textsuperscript{115-117} These observations were extended to animals with surgically induced mitral regurgitation.\textsuperscript{75} Mitral valve replacement was performed with all chordae tendineae intact; LV systolic function was then assessed and subsequently remeasured after division of the chordae. End-systolic pressure volume (E\textsubscript{syst}V) and end-systolic stress volume (M\textsubscript{syst}) relationships decreased by 46% and 36% when the chordae were divided (P = .001 and .0001, respectively), indicating deterioration in LV energetics and mechanical efficiency (Fig. 11-40).

Miller termed the effect of an intact tensor apparatus on optimal global ventricular function “valvular-ventricular interaction.”\textsuperscript{515} Deterioration of function after division of the chordae resulted from an exacerbated mismatch of ventricular-arterial coupling with increased load-resisting shortening. In fact, chordal sparing was first suggested by Lillehei in 1964,\textsuperscript{112} then later disputed by some.\textsuperscript{85} However, David and colleagues in 1983 and later Daenen, Miki, Goor, and Hennein and their colleagues produced clinical results suggesting that chordal sparing during mitral valve replacement improved hospital survival and global LV function,\textsuperscript{51,D9,G2,G1,H1,M23} Carabello’s group again documented preservation of systolic ejection performance in mitral valve replacement with intact tensor apparatus compared with otherwise similar mitral valve replacement patients without chordal preservation.\textsuperscript{527} Preservation resulted in postoperative decrease in diastolic volume, reduced end-systolic stress, and no reduction of ejection indices. In analogous experiments in dogs, these investigators found individual myocyte contractile function normal when global contractile indices

![Figure 11-39](image-url) Nomogram representing probability of death within 30 days of mitral valve replacement, with or without concomitant cardiac procedures, in patients with mitral stenosis, according to length of global myocardial ischemic (aortic clamp) time when cold cardioplegia is used. (From Ferrazzi and colleagues.)
Table 11-9  Hemodynamic Conditions after Insertion of Currently Available Mitral Valve Replacement Devices

<table>
<thead>
<tr>
<th>Devices and Standard Values</th>
<th>Mean Diastolic LA-LV Gradient (mmHg)</th>
<th>Effective Orifice Area (cm²)</th>
<th>Effective Orifice Area Index (cm² · m⁻²)</th>
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**Standard Values**

- Normal: ±0, 4-6, 3
- Severe stenosis: >12, <1, <0.6
- Desired Postoperative Value: <10, <15, >1.5, >0.9

Key: LA-LV, Left atrium to left ventricle.

Among long-term survival and ventricular function are not yet known, it is apparent that some form of chordal continuity is desirable in mitral valve replacement for regurgitation.

**Pulmonary Vascular Resistance**

When severe pulmonary hypertension is present preoperatively, it is usually the combined result of simple back pressure...
Table 11-10 Thromboembolism after Mitral Valve Replacement According to Replacement Device

<table>
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<tr>
<th>Replacement Device</th>
<th>Freedom from First Event (%)</th>
<th>Linearized Rate of First Event (%/patient-year)</th>
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<tr>
<td>Starr-Edwards</td>
<td>73-78</td>
<td>54-57</td>
<td>C25, M24</td>
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<td>St. Jude Medical</td>
<td>88-96</td>
<td>1.5-1.75</td>
<td>C44, K16</td>
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<td>93</td>
<td>0.9-7.6</td>
<td>C36, D16, E1, E2, M22, R2</td>
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<td>Bjork-Shiley Monostrut</td>
<td>95 (3 y)</td>
<td>2.6-3.8</td>
<td>T4</td>
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<tr>
<td>Carpentier-Edwards</td>
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<td>80</td>
<td>C23</td>
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<tr>
<td>Medtronic-Hancock</td>
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<td>H12</td>
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<td>CarboMedics</td>
<td>94</td>
<td>1.0-2.5</td>
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</table>

*Rate 9.5% when multiple events included.
*In patients 51 to 65 years of age at insertion.

*Thromboembolism*

Table 11-10 shows the incidence of thromboembolism reported for selected mechanical and bioprosthetic valves (Fig. 11-41). In general, the incidence is somewhat less with bioprostheses. The incidence and importance of thromboembolism and anticoagulant-related hemorrhage are sufficient to have unfavorable effects on the life expectancy of patients with mechanical valves.

Adequacy of warfarin therapy appears to be the most important determinant of the rate of thromboembolism in patients with mechanical valves in the mitral position. With bioprosthesis, warfarin therapy for 3 months or aspirin indefinitely appear to be as effective as long-term warfarin therapy.

*Acute Thrombotic Occlusion*

Acute thrombotic occlusion of a mitral prosthesis occurs more often with a mechanical device (3 per 100 patient-years) than with a bioprosthesis (1.9 per 100 patient-years) (see “Mechanical Mitral Valve Replacement Devices” later in this section).

The problem in using linearized rates is well exemplified in the case of acute thrombotic occlusion. Linearized rates assume a constant hazard function (see “General Comments” under Time-Related Events in Chapter 6). However, at least in the case of the Bjork-Shiley tilting-disc valve, the hazard function for this event had a single peaking phase that returned to a low level by 4 years after operation. In addition to the scientific importance of this finding, the shape of
the hazard function and a limited clinical experience supports the use of thrombectomy (through both the left atrium and aorta) rather than valve replacement.

Acute thrombotic occlusion occurs primarily but not exclusively in patients receiving suboptimal anticoagulant therapy. A possible risk factor is female gender. Patients with this catastrophic complication usually become symptomatic only 1 to 3 days before admission to the hospital and present principally with extreme dyspnea and orthopnea. The patient may have noticed a decrease in intensity of prosthetic valve sounds about the time symptoms began. Many experience chest pain, and signs of shock usually appear. Although regurgitation is often present, an apical systolic murmur is rarely heard. A fluoroscopic finding of limited disc movement supports this procedure. 

Cardiac catheterization usually gives conclusive evidence of mitral obstruction, but such patients are usually too ill to withstand this procedure. Surgical thrombectomy often achieves a good result. Thrombolyis has been used with mixed results (see previous text and “Thrombosis” under Results in Chapter 14).

Complications of Long-Term Anticoagulation
Complications of long-term anticoagulation with warfarin or warfarin-like compounds appear to be independent of type of prosthesis. Certainly the quality of the surveillance program for patients receiving long-term anticoagulation affects both freedom from anticoagulant-related hemorrhage and prevalence of thromboembolic complications. Percentage freedom from first anticoagulant-related hemorrhage at 5, 10, and 15 years is about 87%, 79%, and 71%, respectively. Linearized rate of important hemorrhage is generally estimated to average 2.3 to 3.4 per 100 patient-years in patients with mechanical prostheses who are taking warfarin.

Figure 11-41 Summary of linearized rate of thromboembolism for mechanical mitral valve prostheses from reports published from 1989 to 2000, each containing at least 400 patient-years of follow-up. Vertical axis is linearized rate in units of percent per year (equivalent to events per 100 patient-years). Each symbol represents one series; height of symbol represents point estimate of event rate, and vertical bars show 95% confidence intervals. Series are grouped on the horizontal axis by valve model, shown below the axis by a two-letter abbreviation. Lower horizontal dashed line indicates the U.S. Food and Drug Administration’s Objective Performance Criteria (OPC). For approval of a new valve, the upper confidence limit should be less than twice the OPC (upper dashed line). Circles indicate that only late events were used to calculate the rates; diamonds indicate that both early and late events were used calculated to calculate the rates; diamonds indicate that both early and late events were used calculated to calculate the rates; diamonds indicate that both early and late events were used calculated to calculate the rates; diamonds indicate that both early and late events were used.

Prophylactic Valve Endocarditis
Prophylactic valve endocarditis is an uncommon but serious complication that results in the death of more than half of affected patients. Endocarditis strongly predisposes the patient to periprosthetic leakage. When it appears within 3 to 6 months of operation, prosthetic valve endocarditis is probably related to events in the operating room. When it develops later, it probably results from a new bacteremia (infective endocarditis is covered in detail in Chapter 15). When mitral prosthetic infection becomes evident within 6 months of implantation, prosthetic leakage is likely to occur, and the risk of death is high. Intensive antibiotic treatment followed by early prosthetic replacement in most patients is indicated. The organism and its antibiotic sensitivity should be identified and specific therapy used. In the unusual circumstance of excellent response to antibiotics, no evidence of peripheral embolization, and no evidence of peri-prosthetic leakage, reoperation may be deferred. The patient is followed closely under hospital conditions that permit immediate reoperation in the event any of these complications occur. When mitral prosthetic infection becomes apparent for the first time more than 6 months postoperatively, the same management protocols apply. More of these patients respond well to intensive medical treatment alone than those with infections occurring in the first 6 months after operation.

Periprosthetic Leakage
At UAB in an era when various suture techniques were used (1975 to July 1979), 13 of 452 (2.9%; CI 2.1%-3.9%) patients required reoperation for periprosthetic leakage. Currently, the incidence in uninfected patients approaches zero

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1Prophylactic valve endocarditis and its abbreviation PVE are familiar, standard, and historical designations for infective endocarditis on any heart valve substitute. The rationale for a more appropriate term, replacement device endocarditis, is presented in Chapter 12.
when suture techniques described in this chapter are used. Preoperative infective endocarditis increases risk of prosthesis dehiscence with periprosthetic leakage. Anular calcification also increases risk.

Chronic Hemolysis
Well-functioning bioprosthetic and mechanical prostheses used in the current era rarely produce more than mild chronic hemolysis unless periprosthetic leakage is present. With periprosthetic leakage, hemolysis may be severe with any device; red cell trauma and fragmentation may be extreme under these circumstances. A mechanical prosthesis of small size relative to body size and hemodynamics may result in severe hemolysis.

Functional Status
Symptoms are reduced and functional capacity increased in most patients. However, prevalence of an excellent functional status after replacement is related to preoperative functional class. Only about half of patients with severe preoperative chronic functional disability return to NYHA functional class I. This finding suggests that many patients with mitral valve disease and advanced chronic disability have a secondary irreversible ventricular myopathy. Infrequently, a patient may display striking symptomatic improvement for 2 to 5 years, after which important symptoms and disability gradually reappear despite good function of the prosthetic device. This sequence is believed to result from progression of a secondary cardiomyopathy that was present before operation or occasionally from progression of other valve lesions.

Reoperation
Reoperation, usually for periprosthetic leakage with or without infectious endocarditis or for bioprosthetic degeneration, has been required within 5 years of the original operation in about 5% of patients. Prevalence, and particularly the hazard function for reoperation, are different for mechanical and bioprosthetic devices; only bioprostheses exhibit degeneration and a late-rising hazard function (Fig. 11-42). Risk of death after reoperation, both early and intermediate term

![Image](https://via.placeholder.com/150)

**Figure 11-42** Hazard function for reoperation for mechanical prostheses and bioprostheses, determined by separate analyses. Hazard function for mechanical prostheses has an early peaking phase and a constant phase. Hazard function for bioprostheses has an early peaking phase and a second, late rising phase. (From Blackstone and Kirklin.)

Summary
Although not free of complications in all patients, mitral valve replacement provides a considerably better prognosis than could be expected according to natural history. About 70% of patients are alive and without complications for at least 5 years after valve replacement.

INDICATIONS FOR OPERATION, SELECTION OF TECHNIQUE, AND CHOICE OF DEVICE

Mitral Stenosis
Patients with mitral stenosis and at least NYHA class II symptoms of heart failure should be considered for medical, interventional, or surgical therapy based on clinical, echocardiographic, and catheterization considerations. Useful algorithms for NYHA class II patients (Fig. 11-43) and class III and IV patients (Fig. 11-44) have been developed by the ACC/AHA. When an opening snap is prominent, when calcification cannot be demonstrated fluoroscopically, and when echocardiography demonstrates pliable leaflets and little or no subvalvar narrowing, good results from surgical mitral commissurotomy can usually be obtained. Under these circumstances, even mild symptoms (NYHA functional class II) in the presence of severe mitral stenosis are an indication for intervention (see Fig. 11-43). Percutaneous balloon mitral commissurotomy is often chosen, although surgical commissurotomy is a reasonable alternative. Particularly in young women, one acute episode of important paroxysmal nocturnal dyspnea or pulmonary edema in the presence of at least moderate mitral stenosis is an indication for intervention. It is particularly indicated before onset of atrial fibrillation. Intervention is also advisable when there is an important increase in Rp, even in the absence of symptoms. Asymptomatic patients with recurrent episodes of arterial emboli while receiving adequate anticoagulation are advised to undergo intervention if commissurotomy is a strong possibility; in this setting and in the presence of demonstrated thrombi in the left atrium, open surgical commissurotomy is advisable.

When mitral valve replacement seems likely (because of absence of an opening snap, immobile leaflets, heavy mitral valve calcification, severe subvalvar disease, or associated mitral regurgitation), a more symptomatic state is demanded as the indication for operation because of the added long-term imponderables introduced by the device inserted; these would be more severe chronic symptoms (NYHA functional class III or higher) or several acute episodes of symptoms of pulmonary venous hypertension.

Advanced disability, associated tricuspid valve disease, and associated coronary artery disease are not contraindications to operation, nor is severe pulmonary hypertension.

Mitral Regurgitation
At operation, mitral valve repair rather than replacement is chosen whenever possible: in 50% to 70% of all patients and in up to 90% of patients with mitral valve prolapse. Repair avoids the potential complications of long-term
Mitral Regurgitation

Management strategy for patients with mitral stenosis and mild symptoms. Mitral valve area (MVA) measurements may vary, and mean transmitral gradient, pulmonary artery wedge pressure (PAWP), and pulmonary artery systolic pressure (PASP) should also be taken into consideration. There is controversy regarding whether patients with severe mitral stenosis (MVA < 1 cm²) and severe pulmonary hypertension (PASP > 60 to 80 mmHg) should undergo percutaneous mitral balloon valvotomy (PMBV) or mitral valve replacement (MVR) to prevent right ventricular failure. Key: CXR, Chest radiograph, ECG, electrocardiogram; echo, echocardiography; LA, left atrial; MR, mitral regurgitation; MVG, mean mitral valve pressure gradient; NYHA, New York Heart Association; PAP, pulmonary artery pressure; 2D, two-dimensional. (From Bonow and colleagues.31)

Figure 11-43 Management strategy for patients with mitral regurgitation and gradually deteriorating LV function and/or may have only mild symptoms associated with long-term outcome. A strong predictor of valve reparability, operative mortality, and long-term survival and freedom from cardiovascular complications is a cardiographic anatomic and physiologic classification is a strong predictor of valve reparability, operative mortality, and long-term outcome.

Patients with mitral regurgitation may remain asymptomatic or may have only mild symptoms associated with long-standing disease and gradually deteriorating LV function because of the mitigating effect of regurgitant mitral flow on LV systolic function, reflected in EF. Thus, whereas the diagnosis and symptoms of mitral stenosis generally provide sufficient evidence for decision making, special attention must also be paid to the status of the LV in mitral regurgitation. A decline in LV contractility, assessed by end-systolic pressure-volume relationships or a similar method, portends a state of irreversibility and may be used to advise operation in relatively asymptomatic patients. Additionally, operation in most of these asymptomatic patients is well advised if repair is probable, because it has been well documented that postoperative LV systolic and diastolic LV function are preserved after mitral valve reconstruction.33,51

Reference has been made to more sophisticated methods of assessing the functional state of the LV in patients with mitral regurgitation (see “Mitral Regurgitation” under Natural History). Zile, Schuler, and their colleagues identified groups of patients with elevated end-diastolic dimensions, elevated systolic dimensions, and low-normal LVEF in whom symptoms were not relieved, heart failure was persistent, or high mortality followed operation.510,21 If LV end-systolic dimension exceeded 26 mm · m⁻² body surface area (BSA) and fractional shortening was less than 31%, consistent deterioration of LV function occurred postoperatively.21 Based on these findings, Ross has suggested operating on patients with few or no symptoms if LVEF is less than 55%, fractional shortening is less than 30%, and end-systolic diameter approaches 50 mm (26 mm · m⁻² BSA).225 These
failure to increase EF with exercise is an indication for surgical intervention if severe mitral regurgitation is present and repair appears likely. The role of left atrial enlargement in decision making is uncertain. More than moderate left atrial dilatation likely has a deleterious effect after valve repair or replacement and therefore favors operation.

The recommendation for early operation (assuming mitral valve repair is highly likely) in the asymptomatic patient with severe mitral regurgitation secondary to degenerative disease and normal LV function is supported by data from a European multicenter study (see also “Natural History of Mitral Regurgitation” earlier in this section). Early operation (within 1 year of diagnosis) resulted in an important reduction in subsequent heart failure and combined heart failure/cardiovascular mortality (Fig. 11-45).

The updated 2006 ACC/AHA guidelines also recommend that mitral valve repair be considered in asymptomatic patients with severe mitral regurgitation and preserved LV size and function in the presence of new-onset atrial fibrillation or pulmonary artery systolic pressure greater than 50 mmHg at rest or greater than 60 with exercise.

The adverse natural history of severe mitral regurgitation secondary to mitral valve prolapse with flail leaflet supports this condition as an isolated indication for operation, even in asymptomatic patients. The decision to recommend

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Figure 11-44 Management strategy for patients with mitral stenosis and moderate to severe symptoms. Mitral valve area (MVA) measurements may vary, and mean transmitral gradient, pulmonary artery wedge pressure (PAWP), and pulmonary artery systolic pressure (PASP) should also be taken into consideration. There is controversy regarding which patients with less favorable valve morphology should undergo percutaneous mitral balloon valvotomy (PMBV) rather than mitral valve surgery. Key: CXR, Chest radiograph, ECG, electrocardiography; echo, echocardiography; LA, left atrial; MR, mitral regurgitation; MVM, mean mitral valve pressure gradient; MVR, mitral valve replacement, NYHA, New York Heart Association; 2D, two-dimensional. (From Bonow and colleagues.)

Recommendations were reaffirmed in the ACC/AHA Practice Guidelines for the Management of Patients with Valvular Heart Disease, which recommends operation for asymptomatic severe mitral regurgitation in patients with LVEF less than 60% and LV end-systolic dimension greater than 40 mm. Further evidence of contractile dysfunction in the presence of severe mitral regurgitation and normal EF was reported by Ahmed and colleagues, who noted evidence of myofibrillar degeneration on LV biopsy and persistence of wall stress/volume index abnormalities following mitral valve repair.

The magnitude of regurgitant volume may also refine the timing of intervention. Yamano and colleagues noted a strong correlation between large regurgitant volume and the likelihood of postoperative LV dysfunction (see “Cardiac Performance” under Results of Mitral Valve Repair in the Results section). Thus, if mitral valve pathology is such that successful repair is highly likely, operation is probably advisable if mitral regurgitant volume exceeds 80 mL before the onset of other established criteria for operation. Based on natural history studies, Enriquez-Sarano and colleagues from the Mayo Clinic recommended consideration for mitral repair in asymptomatic patients with an effective regurgitant orifice (by echocardiography) exceeding 40 mm².

Diminished response of EF with exercise also has been found to predict postoperative LV dysfunction. Thus, failure to increase EF with exercise is an indication for surgical intervention if severe mitral regurgitation is present and repair appears likely.

The role of left atrial enlargement in decision making is uncertain. More than moderate left atrial dilatation likely has a deleterious effect after valve repair or replacement and therefore favors operation.

The recommendation for early operation (assuming mitral valve repair is highly likely) in the asymptomatic patient with severe mitral regurgitation secondary to degenerative disease and normal LV function is supported by data from a European multicenter study (see also “Natural History of Mitral Regurgitation” earlier in this section). Early operation (within 1 year of diagnosis) resulted in an important reduction in subsequent heart failure and combined heart failure/cardiovascular mortality (Fig. 11-45).

The updated 2006 ACC/AHA guidelines also recommend that mitral valve repair be considered in asymptomatic patients with severe mitral regurgitation and preserved LV size and function in the presence of new-onset atrial fibrillation or pulmonary artery systolic pressure greater than 50 mmHg at rest or greater than 60 with exercise.

The adverse natural history of severe mitral regurgitation secondary to mitral valve prolapse with flail leaflet supports this condition as an isolated indication for operation, even in asymptomatic patients. The decision to recommend
operation in the subset of patients with mild or no symptoms is predicated on the assumption that a successful valve repair with mild or less postoperative mitral regurgitation can be accomplished with a likelihood of 90% or higher. Therefore, asymptomatic patients with severe mitral regurgitation and a floppy valve (prolapse as opposed to ischemic or restrictive functional anatomy) are excellent candidates for early operation, because operative mortality is low (<2%), reparability high (90%), and long-term survival good.\textsuperscript{11,12,13} In the case of chronic severe mitral regurgitation, the 2006 ACC/AHA guidelines present an algorithm for decision making that includes mitral valve repair for asymptomatic patients with preserved LV size and function (Fig. 11-46).

At the other end of the functional spectrum, advanced disability with NYHA functional class IV heart failure is not a contraindication to operation, although it is recognized that secondary LV myopathy associated with, and in part responsible for, this state has a deleterious effect on early and late results of operation. The 2006 ACC/AHA guidelines recommend that mitral valve repair be considered for patients with chronic severe mitral regurgitation secondary to severe LV dysfunction (EF < 30%) in the setting of NYHA functional class III or IV symptoms despite optimal therapy for heart failure, including biventricular pacing.\textsuperscript{13,14} If a stage of irreversibility can be securely identified by preoperative studies, valve surgery may be ineffective and cardiac replacement indicated.

Elderly patients with mitral regurgitation require special consideration because operative mortality is increased and late survival benefit reduced for patients older than about age 75 years, especially those with concomitant coronary artery disease\textsuperscript{5,15,20} (see “Older Age” under Incremental Risk Factors for Premature Death in the Results section). The increased operative risk is worth accepting in elderly patients with important symptoms that limit their quality of life. Otherwise, medical therapy is advisable.

Nonischemic Chordal Rupture

The decision about operation is more difficult in patients with mitral regurgitation from nonischemic chordal rupture of recent onset. If the symptoms of pulmonary venous hypertension are brought promptly under control by medical management, as often occurs, operation may be deferred and the patient reevaluated at frequent intervals (see Natural History earlier in this section). Thereafter, the criteria used in chronic mitral regurgitation apply. If the pansystolic murmur radiates into the aortic area and neck, however, and if echocardiographic evidence shows that the ruptured chordae belong to the posterior leaflet, indications for operation should be liberalized because a durable reparative operation can be done at low risk.

Infective Endocarditis

Mitral regurgitation may develop acutely as a result of infective endocarditis. If symptoms are initially mild or moderate and are brought under good control together with the infection, continuing in-hospital medical treatment is indicated. Surveillance must be close, however, because of possible rapid progression in severity of regurgitation. If this is suspected, operation is urgently indicated before hemodynamic deterioration occurs. Acute pulmonary edema, paroxysmal nocturnal dyspnea, or rising blood urea nitrogen or creatinine levels are indications for urgent operation. Systemic embolization during treatment or persistent active infection despite intense antibiotic treatment also indicate the need for operation (see Chapter 15).

Mixed Mitral Stenosis and Regurgitation

Patients with a mixture of important stenosis and mitral regurgitation usually have a clinical picture similar to that of patients with pure mitral stenosis. Valve replacement is usually required, and indications for operation are the same as in mitral stenosis.

Selection of Technique for Repair of Mitral Regurgitation

Anular dilatation is a central feature of degenerative mitral regurgitation, and therefore reduction anuloplasty is a standard component of most repairs. However, particularly in an era when percutaneous techniques for mitral valve repair (which do not include reduction anuloplasty) are being introduced, it is useful to consider situations in which reduction anuloplasty might not be needed. Maisano and colleagues used the concept of anular-to-leaflet mismatch to identify anular dilatation. The ratio of the septolateral (SL) dimension (distance between midpoint of the anterior mitral leaflet at the anulus to midpoint of the posterior leaflet at the anulus, measured during systole via TTE) to the anterior leaflet height (ALH) was used to define anular-to-leaflet mismatch. A ratio of SL/ALH greater than 1.4 corresponded to patients whose mitral anulus was reduced more than 20% by

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<tr>
<td>Heart failure (HF/CVD)</td>
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Figure 11-45 Time-dependent analysis in asymptomatic patients with severe mitral regurgitation and normal ventricular function (n = 102) (after adjusting for age) shows favorable associations between prompt surgery (vs. no or delayed surgery) and heart failure and the combined endpoint heart failure/cardiovascular death (only cardiovascular death failed to reach statistical significance). Mitral valve repair in asymptomatic patients with normal ventricular function seems to prevent cardiac morbidity. Prompt surgery was defined as an operation performed less than 12 months after echocardiography (delayed surgery was longer than 12 months). Point estimates of hazard ratios are graphically depicted as circles, with their 95% CI (lines). Key: HR, Hazard ratio; MV, mitral valve. (From Grigioni and colleagues).\textsuperscript{26}
the anuloplasty procedure, which was termed “reductive.” “Nonreductive” anuloplasties (SL/ALH < 1.4) occurred in less than 20% of patients. Although good results have been reported following mitral valve repair without ring anuloplasty, the general consensus would favor placing a reductive partial or complete anuloplasty ring in patients with an enlarged anulus. By inference, less than 20% of patients with degenerative mitral valve disease would be expected to receive maximal benefit from techniques (including current percutaneous strategies) that do not include an anuloplasty ring. This inference is supported by a propensity-matched analysis by Gillinov and colleagues that demonstrated an accelerated return of mitral regurgitation when mitral valve repair was performed without an anuloplasty band or ring.

Coexisting Mild Aortic Stenosis
A number of patients treated by percutaneous or surgical valvotomy for mitral stenosis have mild aortic involvement at the time of the procedure. Most do not progress to severe disease even after long follow-up, and aortic valve replacement is rarely needed. Thus, at initial mitral operation, prophylactic aortic valve replacement is not indicated.

Choice of Device for Valve Replacement
Some surgeons routinely use one device or another for mitral valve replacement, but the valve of choice varies widely. Rabago and Cooley and others have reviewed a number of factors involved in the choice of device. Two of the most important considerations are durability and requirement for permanent anticoagulation.

Currently available xenograft bioprostheses degenerate more rapidly in young patients who would otherwise be good surgical candidates for tissue valves. Advanced age and atrial fibrillation increase the probability of thromboembolism even in patients with bioprostheses. Also, Warnes and colleagues reported that bioprostheses degenerate more rapidly in the mitral position than in the aortic position. Bioprostheses are in a state of evolution; continuing improvements will probably lead to increased durability.

Prosthetic mechanical valves are also evolving, but there is no evidence that a device that does not require lifelong anticoagulation will soon be available. Hemodynamic characteristics and performance of the mitral valve prosthesis may also influence choices, particularly in very young patients.

For patients undergoing mitral valve replacement, the basic decision is whether to use a mechanical valve or a...
bioprosthetic valve. In patients older than about 60 years, survival may be better with a bioprosthetic valve because of thromboembolic and anticoagulant-related problems associated with mechanical valves. Also, reoperation 7 to 15 years later may be preferable to lifelong anticoagulant (warfarin) therapy. In patients younger than age 60, survival may be better with a mechanical valve because of the more rapid degeneration of bioprostheses in the young, despite need for lifelong anticoagulation. Infrequently, a bioprosthesis is used in young women, with anticipated replacement after successful childbearing (see “Complications of Long-Term Anticoagulation” later in this section).

The newest approach to mitral valve substitute devices is use of a cryopreserved stentless allograft. Early reports suggest good hemodynamic performance and adequate freedom from thromboembolism (in the absence of anticoagulation). The important issue is durability. There are also scattered reports describing placement of a pulmonary valve autograft in the mitral position. The valve is implanted as a cylinder ("top hat") using two suture lines augmented with an atrial cuff.

Mechanical Mitral Valve Replacement Devices

The design of mechanical valve prostheses has evolved over the last 5 decades. A discussion of modern mechanical valves is complicated by two factors: (1) changing availability of specific valves because of continuing introduction and withdrawal of new models and (2) variability in prevalence of use in different countries, in part because of differing regulatory requirements. Here we discuss mechanical valves currently available and in use in at least several countries.

The major types of mechanical heart valves available are ball and cage (rarely used now), tilting disc, and bileaflet valves. Disc valves contain struts attached to the valve orifice (together called the valve housing) that guide and retain the occluder disc. Tilting disc valves contain a disc generally constructed from graphite with a coating of pyrolytic carbon. The valve opening is separated into two areas designated the major and minor orifices.

Bileaflet valves have variable design features, but all contain two leaflets that swing apart during opening, providing three separate flow areas. The leaflets are guided by a hinge or pivot mechanism that acts to retain the leaflets and defines their opening angle. Nearly all valves are rotatable following implantation to address potential impingement on leaflet closure by surrounding tissues.

Current mechanical valve design has focused on excellent hemodynamics, lifetime durability, and maximal resistance to thromboembolism. Transvalvar gradients are determined by orifice diameter, occluder characteristics, the opening angle, and leaflet or occluder orientation to the plane of the mitral orifice. A wide opening angle generally improves the effective orifice area and decreases the diastolic pressure gradient. Dynamic regurgitation is a feature of all mechanical prosthetic valves and is increased with larger effective orifice size and time needed for leaflet or disc closure. A small regurgitant volume is beneficial because it minimizes stasis and decreases platelet aggregation.

The Starr-Edwards (S-E) mitral ball-valve prosthesis (model 6120; Fig. 11-47), no longer available in the United States, was introduced in its current design in 1965. The occluder is a barium-impregnated silicone elastomer ball in a cobalt-chromium alloy cage. The sewing ring has a silicone rubber insert under seamless PTFE or polyester cloth.

Diastolic gradients across S-E prosthetic mitral valves in vivo are slightly greater, and effective orifice area slightly less, than for other available mechanical valves. No firm evidence indicates that projection of the valve cage into the LV is functionally disadvantageous, except when the ventricle is unusually small.

Thromboembolism is probably more common with the S-E valve than with other valves and more common after mitral valve replacement than after aortic valve replacement (see Table 11-10 and Fig. 11-41). The linearized rate of valve thrombosis in the mitral position is very low, about 0.2% per patient-year.

Mechanical failures in the current S-E silicone elastomer ball-valve prosthesis in the mitral position have not been reported. The valve is provided in sizes 5M (34 mm), 4M (32 mm), 3M (30 mm), 2M (28 mm), 1M (26 mm), 0M (22 mm), and 00M (20 mm).

The Björk-Shiley Monostrut valve (Fig. 11-48), introduced in April 1982, is commonly used in Europe but is not approved by the U.S. Food and Drug Administration (FDA).
for use in the United States. Earlier versions of the valve are no longer available. Its orifice ring and integral struts are constructed from a cobalt-chromium alloy as a single piece. The pyrolytic carbon convexo-concave disc opens to 70 degrees. Hemodynamics are good (see Table 11-9). Available information suggests that in the mitral position, the valve has a relatively low rate of thromboembolism (see Table 11-10 and Fig. 11-41). Daenen and colleagues found that freedom from thromboembolism was 86% ± 4% at 6 years. It is provided in odd-numbered external diameter sizes from 17 to 33 mm.

The Omniscience tilting-disc valve (Fig. 11-49) is an FDA-approved valve introduced in 1978 and distributed worldwide. It is a second-generation device based on modifications of the Lillehei-Kaster pivoting-disc valve. The pivoting occluder device consists of a free-floating convexo-concave disc of pyrolytic carbon within a one-piece titanium housing. The disc opens to 80 degrees. Hemodynamic performance is similar to that of other tilting-disc valves.

Thromboembolic complications have been the subject of considerable controversy. Several investigators have found linearized rates of thromboembolism to be higher with the Omniscience valve than with other mechanical prostheses, but others have found the rate to be low. The linearized rate of valve thrombosis was 3.1% ± 1.1% per patient-year, higher (P = .01) than for Medtronic-Hall and Bjork-Shiley tilting-disc valves. Scotten and colleagues found a smaller regurgitant volume with the Omniscience valve than with other mechanical prostheses, producing approximately 10% regurgitation. The original SJM was not rotatable, but the newer Masters Series allows rotation to an “anatomic” or “anti-anatomic” position of the leaflets. The sewing cuff on the mitral prosthesis has a supra-orifice area. The favorable hemodynamics in the smaller sizes is an advantage in small children. Regurgitant flow may be greater than optimal, particularly at low heart rates. Between 88% and 96% of patients with device placement in the mitral position are free from a thromboembolic event at 5 years after operation (Fig. 11-51; see Table 11-10). Linearized rate of the first thromboembolic event is about 1.5% to 1.75% per patient-year. Up to 75% of thromboembolic episodes occur when anticoagulation is inadequate (INR < 2.5). Thrombosis is uncommon. Incidence is approximately 0.1% per patient-year and is usually associated with inadequate anticoagulation. Mechanical failure is uncommon. The SJM
This solid pyrolytic carbon valve has a unique pivot design in which the pivot areas are entirely within the orifice ring, and the valve leaflets hinge on convex pivot guides on the ring. This differs from other mechanical valves that have cavities in the hinge area. The open pivot design feature is intended to decrease blood stasis and thrombus formation near the hinge points. The valve design minimizes overall valve height and generates a larger orifice area. Valve noise is reportedly reduced by this design.

The mitral prosthesis is available in sizes 27 to 33 mm. The On-X mechanical valve (Fig. 11-54), approved by the FDA in 2002, is a pure pyrolytic carbon leaflet valve prosthesis with a bileaflet design similar to other bileaflet prosthetic valves. The pure pyrolytic carbon structure is stronger than the silicon-alloyed pyrolytic carbon used in other mechanical prostheses. The On-X valve contains a flared inlet that produces a higher volume of flow with increased washing to minimize flow stagnation. The leaflets open 90 degrees, with "soft landing" leaflets designed to reduce blood element stress. The On-X mitral prosthesis comes in sizes 23 to 33 mm. It is available with an intra- and supra-anular sewing ring.

**Bioprosthetic Mitral Valve Replacement Devices**

A number of stent-mounted bioprosthetic devices are in clinical use for mitral valve replacement, including those with leaflets made of xenograft aortic valves, bovine or equine pericardium, and allograft aortic valves, fascia lata, and dura mater. Commercially available stented bioprosthetic mitral valves contain either porcine aortic valve leaflets or leaflets constructed from pericardium. These stented valves are designed to mimic flow characteristics of the in situ aortic valve. Pericardial prostheses have been greatly modified since the original Ionescu-Shiley valve, which demonstrated poor durability, manifested frequently by leaflet tearing. Bioprosthetic valves are preserved with glutaraldehyde, which cross-links collagen fibers and reduces normal turnover of extracellular matrix tissues. Glutaraldehyde fixation of porcine valves is achieved at high (60-80 mm Hg), low (<3 mm Hg), or zero pressure conditions. Lower fixation pressures in newer-generation porcine valves may reduce the tendency for calcification. Current pericardial valves include glutaraldehyde fixation at low pressure and mounting of the pericardium completely within the stent, producing less leaflet abrasion and potentially greater durability.

The major advantage of bioprosthetic mitral valves is their resistance to thromboembolism, which is sufficiently
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characteristics have been only partially evaluated, but the information available indicates that its performance is good.

The Carpentier-Edwards mitral porcine bioprosthesis is composed of porcine (xenograft) aortic valves preserved in buffered glutaraldehyde and mounted on a flexible lightweight frame made of cobalt-chromium-nickel alloy. The glutaraldehyde fixation reduces antigenicity and increases tissue stability. The suturing ring consists of a soft silicone rubber insert covered by porous seamless PTFE. An additional treatment removes phospholipids from the valve tissue. The mitral prosthesis (model 6625) is available in sizes 25 through 35 mm.

The Carpentier-Edwards Duraflex low-pressure porcine mitral valve prosthesis (model 6625LP; Fig. 11-56) employs low-pressure fixation techniques designed to preserve the natural flexibility of valve leaflets. It has a reported freedom from structural valve deterioration of 96% at 14 years for patients aged 70 and older. This model is available in sizes 27 to 35 mm. An extended sewing ring for the Duraflex valve is available in the same sizes (model 6625-ESR-LP).

The St. Jude Medical Biocor stented porcine heterograft (Fig. 11-57) incorporates three separate porcine leaflets with low-pressure fixation. Actuarial freedom from reoperation due to structural valve degeneration has been reported at 96% at 14 years for patients aged 70 and older. This prosthesis is characterized by low stent posts in the mitral position. The St. Jude Epic stented porcine valve carries the same design as the Biocor valve, with the addition of a proprietary anticalcification treatment designed to increase valve durability. To
Fig. 11-58 Carpentier-Edwards PERIMOUNT Plus mitral valve prosthesis. (Courtesy Edwards Lifesciences, Irvine, Calif.)

date, there are no long-term data available on the effect of this anticalcification treatment on valve durability in humans.

The Carpentier-Edwards PERIMOUNT mitral pericardial valve (Fig. 11-58) is a glutaraldehyde-fixed stent-mounted valve introduced into clinical use in 1984 and approved by the FDA in 2000. It has a similar profile and configuration to the Carpentier-Edwards aortic pericardial device. Hemodynamic performance is comparable with other mitral bioprostheses. Ten-year freedom from thromboembolism was 93% ± 3.0% in the series reported by Poirier and colleagues.113 Freedom from structural valve deterioration at 10 years was 81% ± 7.0%, although no failures were noted in patients aged 70 years or older. The newer Magna mitral valve adds a nonreversible fixation process to reduce residual glutaraldehyde and phospholipids that contribute to periocardial leaflet calcification. In addition, the Magna Mitral bioprosthesis is designed with an asymmetric sewing cuff to maximize annular conformity.

SPECIAL SITUATIONS AND CONTROVERSIES

Alternative Surgical Approaches to Mitral Valve

Right Thoracotomy

Right thoracotomy was employed by Lillehei and colleagues in their first open operations for mitral valve disease and continues to be used by some surgeons.146 With this approach, the incision is through the left atrium just behind the interatrial groove, as in the median sternotomy approach. The chief disadvantages of right thoracotomy are the limited field provided by the anterolateral inter-space approach (with the patient positioned obliquely) and relative inaccessibility of the ascending aorta, both for cannulation and infusion of cardiopulmonary solution. The arterial cannula may have to be positioned in the external iliac (or femoral) artery. A particular advantage of this approach may be in reoperations after median sternotomy. With this approach, the mitral valve after commissurotomy or repair is easier. Closure of this incision is made in the roof of the left atrium as far as from the aortic root origin as possible (Fig. 11-59, C). The mitral valve is found to be very accessible; often, only stay sutures are required for retraction. Because of this, studying the competence of the valve after commissurotomy or repair is easier. Closure of this incision must be accurate, catching all layers (including the endocardium) with each stitch. Hemostasis should be secure before discontinuing CPB.

The superior approach is also useful when a short, limited upper sternotomy is used. A single-stage venous cannula is inserted through the right atrial appendage, and distal ascending aortic cannulation is used in combination with antegrade cardioplegia. Exposure is adequate.

Approach Across Atrial Septum

Approach through the right atrium and across the atrial septum can be used but may be unsatisfactory. Exposure is limited, and retraction is impeded by concern about injury to the AV node. Exposure can be improved by extending the incision onto the roof of the right atrium (Fig. 11-59, B). A variation of this approach is that of Guiraudon and colleagues (Fig. 11-60). Incision is begun high on the right atrial free wall and is extended caudally on the interatrial septum. It is completed by extending the septal incision to the superior aspect (roof) of the left atrium. Exposure is excellent, although closure is somewhat tedious. It is useful for patients with deep chests and those with small left atria.

Good results have also been reported with a “minitrans-septal” incision in the atrial septum extending from the inferomedial edge of the fossa ovalis up toward the medial base of the superior vena cava without incising the superior surface of the left or right atrium.110

Limited-Access Mitral Valve Strategies

Over the last 15 years, a gradually increasing number of cardiac surgical centers have gained experience with limited access approaches to the mitral valve, either with direct vision or video-assisted techniques (most recently with robotic technology). Successful repair of mitral regurgitation resulting from degenerative disease of the posterior leaflet, anterior leaflet, or both has been reported with a variety of these techniques. A single-stage venous cannula adds a nonreversible fixation process to reduce residual glutaraldehyde and phospholipids that contribute to periocardial leaflet calcification. In addition, the Magna Mitral bioprosthesis is designed with an asymmetric sewing cuff to maximize annular conformity.

Approach Through Superior Left Atrial Wall

Occasionally in large patients with small left atria, exposure is not optimal with the approach described earlier under Technique of Operation. The “superior approach” through the most superior aspect of the left atrium, where it appears in the transverse sinus, is an attractive alternative (Fig. 11-59). The superior vena cava is mobilized and retracted laterally, and the aorta is retracted to the left (after clamping it and injecting cardioplegic solution, because retraction may make the aortic valve regurgitant). A transverse incision is made in the roof of the left atrium as far as from the aortic root origin as possible (Fig. 11-59, C). The mitral valve is found to be very accessible; often, only stay sutures are required for retraction. Because of this, studying the competence of the valve after commissurotomy or repair is easier. Closure of this incision must be accurate, catching all layers (including the endocardium) with each stitch. Hemostasis should be secure before discontinuing CPB.

The superior approach is also useful when a short, limited upper sternotomy is used. A single-stage venous cannula is inserted through the right atrial appendage, and distal ascending aortic cannulation is used in combination with antegrade cardioplegia. Exposure is adequate.
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the internal jugular vein with positioning by TEE, but this requires anesthesiologist expertise and is less reliable for routine use. A left atrial incision in the right interatrial groove anterior to the entrance of the right pulmonary veins provides exposure of the mitral valve. De-airing is facilitated by flooding the surgical field with CO₂, placing a urinary catheter or vent across the mitral valve during initial de-airing, and venting the ascending aorta through the antegrade cardioplegia catheter.

Under certain circumstances, mitral valve surgery on the beating heart at near normothermia has been advocated. As long as the necessary precautions for preventing ejection of air into the aorta are understood and followed, this technique can be an important option in the presence of prior CABG, severe LV dysfunction, or extensive arteriosclerotic disease of the ascending aorta.

Figure 11-59  Three incisions for exposing mitral valve. A, Classic approach involves retracting lateral right atrial wall. Groove between posterior right atrium (RA) and left atrium (LA) is developed, and inferior aspect of left atrium is freed from pericardium behind inferior cavoatrial junction. Incision extends cephalad behind superior vena cava (SVC) and caudad to the left under the inferior vena cava. B, Modification of DuBost transseptal approach. Vertical incision is made in lateral wall of right atrium. Interatrial septum is incised through the fossa ovalis, extending laterally to patient’s right to meet the right atrial incision and continuing to ventral aspect of right superior pulmonary vein. Atrial septal component must not extend inferiorly or medially, which could put the tricuspid anulus, atrioventricular septum, or bundle of His at risk. C, “Superior approach” involves retracting superior vena cava laterally and aorta to the left. Roof of left atrium is opened with incision directed leftward and posteriorly, leaving an adequate rim of atrial tissue anteriorly so as not to infringe on the mitral anulus.
In the evolution of limited-access approaches to the mitral valve, current surgical philosophies are divided between a greater emphasis on techniques for direct visualization using more standard surgical techniques and instrumentation, and video-assisted endoscopic or robotic approaches. Whether the enhanced visualization using thoracoscopic and robotic techniques provides sufficient benefit to justify the more expensive technology will await further long-term studies.

Mitral Valve Repair versus Replacement for Degenerative Disease in the Elderly

When successful reconstruction is feasible, repair is advisable for degenerative disease in the elderly to avoid risk of prosthesis-related complications. However, a propensity-matching analysis by Gillinov and colleagues demonstrated similar survival and freedom from reoperation in elderly patients undergoing mitral replacement or repair. Thus, in patients older than about age 70, mitral valve replacement with a bioprosthetic valve is an acceptable alternative to repair when the pathologic anatomy is suboptimal for repair (posterior anular calcification, marked prolapse of both anterior and posterior leaflets, valvar calcification).

Mitral Valve Replacement with Allograft

Acar and colleagues revitalized interest in mitral valve replacement with a mitral allograft using new techniques for fixation of the papillary muscles (side-by-side fine monofilament suture) and employing an anuloplasty ring in all cases (Fig. 11-61). Use of an allograft in the mitral position has a potential advantage in the setting of endocarditis.
Figure 11-61 Mitral valve replacement with mitral allograft using papillary muscle fixation and anuloplasty. 

A, Mitral valve is exposed in usual manner, and leaflets are completely resected at their bases. Chordae are excised at their papillary muscle origin. Muscular trabeculations attaching papillary muscles to free wall of left ventricle are divided. B, Cryopreserved mitral allograft, thawed and trimmed, is positioned for insertion. Interrupted 5-0 monofilament sutures (10-12) secure donor papillary muscle to recipient papillary muscle in side-by-side fashion. Donor papillary muscle is placed on mural (outside) aspect of recipient papillary muscle.

because of its known resistance to recurrent infection (see Chapter 15). Early enthusiasm for this technique was also, in the past, related to the possibility of better durability in younger patients than bioprosthetic valves.

An 8-year analysis of allograft mitral valve replacement (complete in 65 patients and partial in 39) by Ali, Acar, and colleagues underscored the important risk of early reoperation for valve dysfunction related to restriction of leaflet movement secondary to deep implantation of papillary muscles or an undersized allograft. Based on recommendations from Acar and colleagues, selection of allograft size was based on matching the height of the anterior leaflet. However,
Figure 11-61, cont’d C. Using continuous 4-0 polypropylene suture, donor anulus is sewn to bases of resected recipient leaflets beginning at left fibrous trigone and working clockwise anteriorly to right fibrous trigone, then in a counterclockwise direction posteriorly. A supporting annuloplasty ring is added.

Mitral valve replacement with a pulmonary autograft has been reported in a small number of patients, with good valve function at a mean follow-up of 6 years.\textsuperscript{K20}

### Surgical Plication of Giant Left Atrium

Massive enlargement of the left atrium can develop in patients with long-standing severe mitral regurgitation.\textsuperscript{P4} Surgical reduction has been recommended since the early days of cardiac surgery but has not been generally adopted.\textsuperscript{K6} Kawazoe and colleagues have used a special plication procedure designed to reduce bronchial compression and improve LV performance; their experience suggests effective results.\textsuperscript{K8} The procedure is probably indicated only when left atrial enlargement is causing severe compression of the left main bronchus.

### Left Ventricular Rupture Complicating Mitral Valve Replacement

Massive intrapericardial hemorrhage may occur shortly after discontinuing CPB or in the intensive care unit a few hours later. This complication is usually from LV rupture in or near the AV groove posteriorly. Nearly all patients die when the rupture occurs postoperatively, but some may be saved when it occurs while the chest is open.\textsuperscript{B23} LV rupture with hemorrhage is more likely to occur in women and in patients with small LVs.

There are several causes of LV rupture, but the surgeon must always assume that it is preventable. The most common contributing factors are (1) undue traction on the anulus during excision of the mitral valve or insertion of the prosthesis, (2) tearing of the anulus by sutures already placed when the heart is manually tilted up after the mitral prosthesis is in place, and (3) penetration of stitches into the left AV groove posteriorly.\textsuperscript{B21} These are particularly
dangerous problems because the surgeon is usually unaware of producing them during the operation, which may otherwise have been a technically simple procedure. In the initial report on this problem, Roberts and Morrow indicated that LV rupture can also result from (1) perforation of the LV wall as papillary muscle is excised and (2) perforation of the AV groove as a calcific deposit is being removed. stav1

Because of potential LV rupture, the surgeon must be very gentle in all maneuvers during mitral valve replacement. The heart should not be tipped up for air evacuation or ligation of the left atrial appendage or for routine inspection of the back of it after the prosthesis has been inserted. Excising only the chordae tendineae rather than the whole papillary muscle, and simply leaving in place deeply embedded calcific deposits in the anulus and placing sutures around them or only on their atrial side, should eliminate these causes of LV rupture. Alternatively, a chordal-sparing mitral valve replacement can be performed.

LV rupture can occur in the midportion of the posterior wall rather than in the region of the AV valve anulus. stav1 stav10

Whether the mechanism of this type of rupture is different is not certain, but LV trauma can be caused by penetration of a pillar of a stent-mounted valve.

Once massive hemorrhage has occurred, CPB must be reinitiated as quickly as possible while the hemorrhage is controlled digitally to the extent possible. A premature attempt to suture it will surely end in death, and even with proper management, the risk of death is great. After establishing CPB, clamping the aorta, and administering cardioplegic solution, the left atrium is reopened and the valve removed. An appropriately shaped piece of pericardium is fashioned and positioned as an onlay patch on the inside of the heart over the presumed or identified area of rupture, using multiple large, felt-pledgeted sutures. Even though every attempt is made to avoid the proximal circumflex artery, it may be compromised by these sutures, so the area of the circumflex artery must be carefully inspected before reinserting the valve.

If it is compromised, a saphenous vein bypass graft to a large marginal branch should be placed. The valve is then reinserted and the remainder of the procedure completed as usual. Great care must be taken with myocardial management throughout this procedure.

A small or moderate-sized hematoma is present in the left AV groove in 10% to 30% of all patients immediately after mitral valve replacement. If bleeding is not occurring, the patient’s condition remains good, and the hematoma does not increase in size, it should be left untreated and unsuspected, with nothing further done. The hematoma rarely results in LV rupture, but false aneurysms occasionally develop in this area.

Management of Antibiotic Prophylaxis with Prosthetic Valves

Prophylactic antibiotics against infective endocarditis are required for all patients with prosthetic heart valves. The details for specific situations are discussed in Chapter 15.

Management of Anticoagulation with Prosthetic Valves

The risk of thromboembolism is greater for prosthetic valves in the mitral position than in the aortic position (see Chapter 12 for recommendations about anticoagulation with aortic prosthetic valves). Long-term warfarin therapy is required for all patients with mechanical valves. In the mitral position, an INR of 2.5 to 3.5 is recommended. stav1 stav11 In patients with a mitral bioprosthetic valve, aspirin is recommended at 81 mg daily. Among patients with a bioprosthetic mitral valve and risk factors of atrial fibrillation, prior thromboembolism, LV dysfunction, or hypercoagulable conditions, warfarin (in addition to aspirin) is indicated to keep the INR at 2.0 to 3.0. stav11 When warfarin is indicated for mechanical or bioprosthetic valves and the patient cannot take warfarin, aspirin is indicated at a dose of 81 to 325 mg daily.

Among patients who experience a thromboembolic event while on recommended antithrombotic therapy, a more intensive regimen of warfarin or aspirin is advisable. stav1 stav1 If the warfarin INR is 2.0 to 3.0, it should be increased to 2.5 to 3.5; if the latter was used, it should be increased to 3.5 to 4.5 unless bleeding issues contraindicate this level of anticoagulation. If aspirin is used in the late regimen, it should be increased from 81 to 325 mg daily, or if the 325 mg daily is maintenance, addition of clopidogrel 75 mg daily should be considered.

When patients experience excessive anticoagulation (INR > 5), risk of hemorrhage is greatly increased. In the absence of bleeding, simply withholding warfarin until the INR is again therapeutic is usually sufficient. If more aggressive reversal is desirable, oral vitamin K (phytonadione) should be administered with caution because overcorrection may lead to a hypercoagulable state. Low-dose oral (1-2.5 mg) or intravenous (1 mg) vitamin K appears generally safe in this situation. stav4 stav13 In emergency situations, administration of fresh frozen plasma is preferable to high-dose vitamin K.

When patients with a mechanical mitral prosthesis require interruption of warfarin therapy for noncardiac surgery, invasive procedures, or dental work, warfarin is discontinued, and either intravenous heparin or low-molecular-weight heparin injections (twice daily) should be administered when the INR falls below 2.0. stav1 These agents should be stopped 4 to 6 hours before the procedure, resumed following the procedure when bleeding stability is appropriate, and continued thereafter until the INR with warfarin resumption reaches 2.0. Low-molecular-weight heparin is attractive because it may be administered on an outpatient basis.

Treatment of Valve Thrombosis

Thrombosis of a mechanical mitral prosthesis is uncommon but devastating, usually affecting patients who are inadequately anticoagulated. Thrombosis may be subacute or may present as an urgent event characterized by low cardiac output and pulmonary venous hypertension, and occasionally is preceded by thromboembolism. Although auscultation and cardiac fluoroscopy were appropriate elements for diagnosis in the past, echocardiography is by far the most reliable diagnostic study.

Optimal therapy is controversial. In general, surgical therapy is preferred for valve thrombosis, particularly for left-sided prostheses. In some patients, simple thrombectomy is appropriate. In most patients, however, thrombotic material may be adherent and often extends to the relatively inaccessible ventricular aspect of the prosthesis. Occasionally, thrombotic material is indistinguishable from the vegetations of
endocarditis. Thus, removal and replacement of the device is preferred. Mortality in these situations is 10% to 20%. Fibrinolytic therapy with urokinase, streptokinase, or recombinant tissue plasminogen activator has been successful, but the important risk of internal bleeding must be weighed against surgical intervention. Fibrinolytic therapy carries a major increased risk of active internal bleeding, recent trauma, history of hemorrhagic stroke, large or mobile thrombi, and recent surgery. In addition, lysis may be incomplete, with the potential for associated systemic embolization. Fibrinolytic therapy is perhaps most effective for valves in the tricuspid position, but is also effective in some cases of acute mitral prosthetic thrombosis. The 2006 ACC/AHA practice guidelines support consideration of fibrinolytic therapy as first line for patients with thrombosed right-sided prosthetic valves with NYHA class III/IV symptoms, thrombosed left-sided prosthetic valves, NYHA class I/II symptoms and a small clot burden, and thrombosed left-sided prosthetic valves with NYHA class III/IV symptoms if the risk of emergent surgical intervention is considered excessive. In the presence of excessive pannus formation, fibrinolytic therapy is ineffective.

Section II Mitral Valve Surgery with Coexisting Tricuspid Valve Disease

MORPHOLOGY

Slightly under half of patients undergoing mitral valve surgery exhibit some evidence of tricuspid regurgitation, which may be organic (rheumatic) in origin or, more frequently, functional. The importance of distinguishing between functional and organic tricuspid regurgitation in patients with mitral valve disease was illustrated by Duran and colleagues. When they ignored functional tricuspid regurgitation present at mitral valve surgery, tricuspid regurgitation was absent late postoperatively in all eight patients with low pulmonary vascular resistance (Rp) postoperatively, but was present in all nine patients with high Rp late postoperatively (P < .0001). Untreated functional tricuspid regurgitation disappeared in eight (47%; CL 32%-62%) of 17 patients undergoing mitral valve surgery. In contrast, ignored organic tricuspid regurgitation disappeared in none (0%; CL 9%-13%) of 14 patients undergoing mitral valve surgery (P = .005).

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Tricuspid regurgitation is apt to coexist when mitral regurgitation is rheumatic in origin and long-standing and when important symptoms have been present for more than about 6 years. In the absence of actual rheumatic involvement of the tricuspid valve, this finding is probably related to low RVEF (<30%), found in many patients with long-standing mitral regurgitation. Clinical features and diagnostic criteria of other forms of tricuspid regurgitation are discussed in Chapter 14.

NATURAL HISTORY

Patients with functional tricuspid regurgitation secondary to mitral valve disease who do not undergo repair of regurgitation at mitral valve surgery have a variable course late postoperatively (see also Chapter 14). Although Braunwald and others in an earlier era recommended against concomitant mitral valve and tricuspid valve surgery, the appearance of important late tricuspid regurgitation subsequently became apparent. Data from many sources have confirmed the deleterious late effects of failure to address severe tricuspid regurgitation at the time of surgery for the primary mitral valve lesion. Probably depending in part on the surgeon’s reason for not repairing the tricuspid valve at the original mitral valve operation, 6% (CL 4%-9%) to 35% (CL 23%-49%) have moderate or severe regurgitation late postoperatively. In most patients, tricuspid regurgitation is a persistent form of the preoperative condition, but some patients have a newly developed or worsening postoperative form despite surgically improved mitral valve function.

Clinically severe tricuspid regurgitation is present in one quarter to one third of patients undergoing surgery for rheumatic mitral valve disease. The presence and severity of tricuspid regurgitation late after mitral valve surgery is at least in part a function of the morphology (rheumatic vs. functional) of the tricuspid regurgitation and the type and severity of the mitral disease. By echocardiographic studies, evidence of at least moderate tricuspid regurgitation in patients with rheumatic mitral valve disease exceeds 60%. Moderate or severe tricuspid regurgitation is reported in more than 70% of patients 3 years after surgical repair of ischemic mitral regurgitation, but prevalence of late severe tricuspid regurgitation of less than 20% is reported following mitral valve repair with an added tricuspid anuloplasty. Late severe tricuspid regurgitation is less common after surgery for degenerative mitral valve disease, with a prevalence of less than 20% by 4 years.

Usually, late tricuspid regurgitation is secondary to anular dilatation (see Chapter 14). Although the probability of late progressive worsening of tricuspid regurgitation is unknown, Matsuyama and colleagues reported that among patients with grade 2 tricuspid regurgitation before mitral valve surgery who did not have tricuspid anuloplasty at time of that surgery, 37% developed late moderate to severe tricuspid regurgitation.

When pulmonary hypertension secondary to severe mitral stenosis is associated with moderate or severe tricuspid regurgitation, the regurgitation usually regresses after mitral valve surgery. Although pulmonary arteriolar medial hypertrophy can cause permanent major pulmonary hypertension, reactive pulmonary vasoconstriction usually regresses and pulmonary artery pressure progressively falls in the weeks or months following successful mitral valve surgery. Perhaps predictably, patients with severe preoperative tricuspid regurgitation associated with marked pulmonary hypertension have less late tricuspid regurgitation after successful mitral valve surgery than patients with severe preoperative tricuspid regurgitation and mild or moderate pulmonary hypertension.

Other predictors of improvement in tricuspid regurgitation after mitral valve surgery without tricuspid anuloplasty include younger age, functional (as opposed to organic) tricuspid regurgitation, and absence of atrial fibrillation.
Incremental risk factors for persisting or worsening tricuspid regurgitation after mitral valve repair or replacement without surgery on the tricuspid valve include:

- Persistent or recurrent mitral disease predisposes the patient to continuing or increasing tricuspid regurgitation. The more severe the un repaired tricuspid regurgitation, the more likely it is to persist or increase late after mitral valve surgery. Thus, tricuspid regurgitation judged mild at operation rarely persists or progresses after adequate mitral valve surgery, whereas moderate or severe regurgitation may progress.\(^{8,9}\)
- When there is no remaining left-sided stenosis or regurgitation, progression is most frequently related to persistent pulmonary hypertension or worsening secondary RV dysfunction. Long-standing and perhaps irreversible RV enlargement secondary to mitral or pulmonary vascular disease predisposes the patient to persistent tricuspid regurgitation. Such situations likely interfere with systolic shortening of the tricuspid anulus. Thus, tricuspid regurgitation that does not disappear promptly with intensive decongestive treatment preoperatively and is therefore fixed rather than variable is more likely to persist late postoperatively if not repaired.\(^{59}\)
- Organic (rheumatic) tricuspid regurgitation, usually associated with some stenosis, is more likely to persist than functional regurgitation.

De Bonis and colleagues\(^{312}\) identified RV dilatation, preoperative RV dysfunction, higher tricuspid regurgitation grade at discharge, and pulmonary hypertension as strong predictors of late significant tricuspid regurgitation. Presence of atrial fibrillation at the first operation and rheumatic etiology are also risk factors for late tricuspid regurgitation.\(^{527}\) A dilated tricuspid anulus (≥3.5 cm in adults) is also predictive of important tricuspid regurgitation, irrespective of level of regurgitation at operation.\(^{517}\) In fact, tricuspid anular dilatation is probably the most important factor in development of late tricuspid regurgitation.\(^{534}\) Normal dimensions of the tricuspid valve are discussed in Chapters 1 and 14.

Presence of tricuspid regurgitation late after mitral valve surgery is clearly associated with poor long-term survival and reduced functional capacity.\(^{519}\) Whether the reduced survival is caused by the tricuspid regurgitation itself or the pathogenic factors that produce late regurgitation (see Morphology earlier in this section) is unknown, but it is likely a combination of both. Among patients with moderate or severe tricuspid regurgitation late after mitral valve surgery, pulmonary artery systolic pressure greater than 40 mmHg, depressed LV function (EF < 50%), depressed RV function, and RV dilatation are predictive of reduced survival.\(^{517}\) In the setting of balloon valvuloplasty for rheumatic mitral stenosis, increasing severity of tricuspid regurgitation at time of the procedure is associated with a progressive decrement in midterm survival.\(^{519}\) (Fig. 11-63).

**RESULTS**

Assessing the results of repair of functional tricuspid regurgitation in patients undergoing mitral valve surgery is difficult because of insufficient information regarding the outcome had the patient’s tricuspid regurgitation been left untreated. The effect of tricuspid anuloplasty in preventing late tricuspid regurgitation was examined by Song and colleagues\(^{526,527}\) in a large cohort of patients with mitral stenosis and severe tricuspid regurgitation who underwent either balloon valvotomy or mitral and tricuspid valve surgery. At 7 years, 98% of patients in the surgery group had less than grade 2+ tricuspid regurgitation compared with 46% in the balloon valvotomy group. Furthermore, event-free survival was superior in the surgical group.

It has been reported that tricuspid anuloplasty is performed in 10% to 20% of patients undergoing mitral valve replacement. Less than 1% of these patients undergo subsequent tricuspid valve replacement.\(^{519,533,534,535}\) The early benefit likely relates to associated comorbidities or severity of the rheumatic process (making the valve unsuitable for repair), but the late disadvantages of valve replacement are clear (see Chapter 14).

Intermediate-term survival is lower in patients undergoing concomitant mitral valve replacement and tricuspid anuloplasty than in those undergoing isolated mitral valve replacement (see Fig. 11-37). When multivariable analysis accounts for other differences between patients undergoing mitral valve replacement alone and those undergoing concomitant tricuspid valve repair, important tricuspid regurgitation treated by anuloplasty is not a strong risk factor for death early after operation, but it is later after repair (see Table 11-8). These relationships are also reflected in the higher hazard function for death 3 or more months after operation for those undergoing mitral valve replacement plus tricuspid anuloplasty. The inference is that despite tricuspid valve repair, the RV dysfunction usually associated with important preoperative tricuspid regurgitation persists in some patients and is a risk factor for death after mitral valve surgery. Nonetheless, survival is probably better than if

**TECHNIQUE OF OPERATION**

Techniques of concomitant tricuspid valve surgery are discussed in detail under Technique of Operation in Chapter 14.
the tricuspid regurgitation had been left untreated, although this has not been proven.

The functional result in patients surviving at least intermediate term after mitral valve replacement plus tricuspid valve repair is good. However, the prevalence of return to an excellent clinical status (NYHA functional class I or II) is less than when only mitral valve replacement is deemed necessary. This finding again suggests that in general, patients requiring concomitant tricuspid anuloplasty have a more advanced cardiac condition than those requiring only mitral valve replacement. The tendency for gradual progression of tricuspid regurgitation even after prosthetic ring anuloplasty underscores the importance of other RV factors in determining late tricuspid regurgitation.11

When patients undergo tricuspid anuloplasty or replacement late after mitral valve surgery, perioperative mortality is high, often exceeding 20%22 (particularly with rheumatic heart disease), late survival is poor, and functional capacity is frequently unchanged.22,23,88 Poor late outcomes undoubtedly reflect the adverse effect of long-standing poor RV function.

INDICATIONS FOR OPERATION

When surgery is planned for mitral valve disease, tricuspid repair should be considered if important tricuspid regurgitation is present at the time of the mitral surgery.24,25,88 However, there remains uncertainty in estimating the presence and magnitude of tricuspid regurgitation both preoperatively and intraoperatively. Fournier, Carpentier, and Duran and their colleagues have emphasized that digital estimation at operation, with a finger through the right atrial appendage, is unreliable.28,29 In the current era, evaluating tricuspid regurgitation during anesthesia induction as well as before and after CPB is most reliably accomplished with TEE. The value of anuloplasty is less certain in patients whose tricuspid regurgitation is less than severe. Consensus is emerging that patients with tricuspid anular dilation (>2 to 5 cm · m⁻² or 3.5 cm in the average adult) should undergo tricuspid anuloplasty whether or not important regurgitation is present.24,25

Further details regarding indications for operation and current ACC/AHA guidelines are found under Indications for Operation in Chapter 14.

Tricuspid anuloplasty is generally not indicated when the tricuspid anulus is not dilated and (1) tricuspid regurgitation is variable preoperatively and is absent during periods of good medical control of heart failure, (2) organic tricuspid disease is excluded based on digital or echocardiographic examination of the valve at operation, (3) a good repair or replacement can be done for the mitral disease, and (4) Rp is low. If regurgitation is more severe (moderate or severe by intraoperative TEE) and has been important and constant, anuloplasty is indicated.29,30 Because the left-sided disease is usually long-standing and the possibility of irreversible left and right ventricular dysfunction high, a procedure directed at the tricuspid valve may decrease postoperative morbidity and avoid a second operation.

If tricuspid regurgitation has been left unrectified, if right atrial pressure is the same or higher than left atrial pressure immediately after CPB, and if tricuspid regurgitation is assessed as moderate or severe by TEE (grade 3 or more), tricuspid anuloplasty is indicated provided that temporary acute RV dysfunction (usually from right coronary air embolization) can be excluded. This exclusion can be made by resuming CPB; a vasoconstrictor is then given to ensure normal arterial blood pressure (see Chapter 4), the heart is “unloaded,” and CPB is continued for 5 to 10 minutes.

Organic (rheumatic) tricuspid disease virtually always requires intervention, either repair or replacement at the time of mitral valve surgery.

Indications for isolated tricuspid repair late after mitral valve surgery are more problematic (see discussion in Chapter 14).

Section III Mitral Valve Surgery with Coexisting Ischemic Heart Disease

MORPHOLOGY

In recent years, about 15% to 20% of patients undergoing mitral valve replacement for nonischemic mitral valve disease have undergone concomitant CABG.

NATURAL HISTORY

Reliable assessment of the results of isolated mitral valve surgery (without CABG) in patients with coexisting coronary artery disease is not available. Studies by Czer and Chaffin and their colleagues, however, suggest that survival is less satisfactory in these situations when operation is restricted to the mitral valve.24,25

TECHNIQUE OF OPERATION

Primary considerations in CABG accompanying mitral valve replacement or repair are (1) planning the operation to limit duration of CPB and global myocardial ischemia (aortic clamping) and (2) reducing the need to tilt the heart up after the valve is inserted or repaired (see “Left Ventricular Rupture Complicating Mitral Valve Replacement” in Section 1). Two methods can be recommended.

In one method, operation is begun by performing the distal anastomoses of vein grafts and in situ internal thoracic artery (see “Internal Thoracic Artery” under Technique of Operation in Chapter 7). After administering an additional dose of cardioplegia, the left atrium is opened from the right side and the mitral valve procedure performed. The left atrium is closed. After aspiration of air from the ascending aorta and with strong suction on the aortic needle vent, the aortic clamp is removed and rewarming begun. Venous and arterial grafts are routed as usual, and the venous grafts are anastomosed to the openings in the exteriorized portion of the aorta. After the side-biting clamp is removed, the usual de-airing procedures are performed (see “De-Airing the Heart” in Section III of Chapter 2). Operation is then completed in the usual manner. To avoid ventricular rupture, unless urgently indicated, the heart should nor be tipped up for inspection of the posterior anastomoses. Alternatively, the proximal anastomoses are made with the aortic clamp still in place. Operation proceeds as in isolated CABG, using the technique of initially hyperkalemic controlled aortic root
reperfusion (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).

In the second method, proximal anastomoses are made directly after initiating CPB. Cardioplegic solution is then administered, and distal anastomoses are performed as usual. Care is taken to ensure that the vein graft coursing to the right of the right atrium is slightly more redundant than usual to avoid damage from retraction during the mitral procedure. Particular care is taken to ensure the anastomoses are hemostatic, again to avoid the potentially dangerous maneuver of tilting up the heart after the mitral valve prosthesis is inserted. After infusing another dose of cardioplegic solution, small bulldog clamps are placed very proximally on each vein graft (they must be removed later, a minute or so after release of the aortic clamp) to prevent air that enters the aortic root during mitral replacement from entering the vein graft. Thereafter, the left atrium is opened and mitral valve repair or replacement carried out as usual. After the left atrium is closed, controlled aortic root reperfusion is begun, and the operation proceeds as in an isolated mitral valve procedure.

In both methods, TEE is useful to assess the adequacy of air removal from the cardiac chambers.

**RESULTS**

**Early (Hospital) Death**

Hospital mortality of patients undergoing mitral valve replacement and concomitant CABG is higher than that of patients undergoing isolated mitral valve replacement, with or without concomitant tricuspid valve anuloplasty. In an analysis by Gillinov and colleagues at the Cleveland Clinic, factors associated multivariably with greater likelihood of repair included isolated posterior chordal rupture ($P < .0001$), more recent date of operation ($P < .0001$), and younger age ($P = .0003$). Factors associated with a greater likelihood of replacement were bileaflet prolapse ($P < .0001$), retracted leaflet from abnormal chordal mesh ($P = .01$), and previous cardiac surgery ($P = .008$).

**Time-Related Survival**

Intermediate-term survival is less satisfactory, and the hazard function for death in the constant phase is greater in patients undergoing mitral valve surgery and concomitant CABG than in those undergoing mitral surgery without concomitant CABG and thus presumably without coexisting ischemic heart disease (see Fig. 11-37). This finding is partly explained by coexistence of two diseases, but also partly by older age at operation of patients with the two existing diseases, and the longer global myocardial ischemic time when the two procedures are performed concomitantly. In the study by Gillinov and colleagues, for the mitral repair group, survival was 79% and 59% at 5 and 10 years, and for the mitral replacement group, it was 70% and 37%, respectively (Fig. 11-64, A). The unadjusted survival curves diverged at about 4 years because of earlier divergence ($< 2$ years) of the late-rising phase of hazard (Fig. 11-64, B), with patients undergoing mitral valve replacement having a marked increase in mortality risk compared with those undergoing repair.

**Incremental Risk Factors for Death**

Because patient characteristics differed between those undergoing mitral repair vs. replacement, a propensity score was used by Gillinov and colleagues to adjust the multivariable risk factor analysis for these differences (see “Clinical Studies with Nonrandomly Assigned Treatment” in Section I of Chapter 6). After using the propensity score to adjust for dissimilarities in patient characteristics, replacement was identified as a risk factor for death in the late hazard phase, beginning about 2 years after surgery.

**Functional Status**

Prevalence of good functional status (NYHA functional class I or II) among patients surviving at least the intermediate term after mitral valve replacement and concomitant CABG is as high as after isolated mitral valve replacement. This finding is probably related to coexisting coronary artery disease in this group of patients generally being moderate and well treated by CABG.

---

1 At UAB, age of patients undergoing isolated mitral valve replacement was $52 \pm 14$ [SD] years vs. $61 \pm 8.2$ years in those with both diseases, $P < .0001$. 

2 Prevalence of good functional status (NYHA functional class I or II) among patients surviving at least the intermediate term after mitral valve replacement and concomitant CABG is as high as after isolated mitral valve replacement. This finding is probably related to coexisting coronary artery disease in this group of patients generally being moderate and well treated by CABG.
INDICATIONS FOR OPERATION AND SELECTION OF TECHNIQUE

Chapter 10 discusses the special topic of ischemic mitral regurgitation.

Proper surgical procedure for patients with coronary artery disease who require mitral surgery for nonischemic mitral valve disease has been debated in the past. However, ignoring coronary artery disease increases the risk of death.\textsuperscript{12} In view of this finding and good results achieved in treating both diseases, important coronary artery disease should be treated surgically at the time of mitral repair or replacement.

Selection of Technique

Whether a patient should undergo repair or replacement of the mitral valve depends on the feasibility of repair and possible survival benefit if repair is done. The probability of valve calcification, for example, increases beyond about age 60. As noted previously, important valve calcification strongly favors replacement over repair. Although their analysis includes patients undergoing operation between 1973 and 1999, and therefore likely not directly applicable in the current era, Gillinov and colleagues developed an algorithm to assist in decisions regarding mitral valve repair or replacement for degenerative disease and concomitant CABG.\textsuperscript{13,14}

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DEFINITION
This chapter describes the surgical aspects of aortic valve disease, excluding congenital aortic stenosis in infants and children (see Chapter 47) and aortic regurgitation with either ventricular septal defect (see Chapter 35) or sinus of Valsalva aneurysm (see Chapter 36).

HISTORICAL NOTE
In 1947, Smithy and Parker at the University of South Carolina in Charleston first reported an experimental study of aortic valveotomy. During the early 1950s, Bailey and colleagues in Philadelphia used closed methods—either a dilator introduced transventricularly or a digital approach through a “poncho” sewn onto the ascending aorta—in clinical attempts to relieve severe aortic stenosis. Modest success in some patients was obtained by them and by Ellis and Kirklin. In 1951, Hufnagel in Washington, D.C., developed a ball valve prosthesis for rapid insertion into the descending thoracic aorta. (From his work with Gross in developing the coarctation operation, Hufnagel was well aware of the risk of paraplegia with aortic clamping and therefore emphasized the rapidity of insertion of his device; see Chapter 24.) The prosthesis could be inserted quickly because of two multipoint fixation rings, each placed around the aorta and over the end of the prosthesis lying within the aorta. Hufnagel and Harvey, Ellis and Kirklin, and others obtained fairly good palliation of severe aortic regurgitation in some patients with this device. However, upper body signs of aortic regurgitation became severe. During the early 1950s, Bailey and Likoff developed and used a number of ingenious but unsuccessful closed methods of overcoming aortic regurgitation.

A more effective approach to surgical treatment of aortic valve disease in adults began with the advent of clinical cardiopulmonary bypass in 1954 and 1955 (see Chapter 2). At first, aortic valvotomy and removal of calcific deposits were all that could be done. Then Bahnson and colleagues and, independently, Hufnagel and Conrad developed a single-leaflet prosthesis that was commercialized. Generally, the leaflets were used to partially replace the aortic valve, but three leaflets could be used together for total aortic valve replacement. Probably the first single-unit prosthesis for total aortic valve replacement was the polytetrafluoroethylene (PTFE) sleeve prosthesis developed and first used by McGoon at the Mayo Clinic in 1961. Although this device was successful in terms of early results, competence was sometimes not achieved, leading to appreciable hospital mortality. Introduction of the ball valve prosthesis by Harken and colleagues and Starr and colleagues in 1960 and reported in 1963 established aortic valve surgery on a firm basis. Many types of prosthetic valves have subsequently appeared.

In 1956, Murray demonstrated that the aortic valve could be used as an allograft valve transplant in the descending thoracic aorta in patients with aortic regurgitation, and Kerwin and colleagues reported 6-year follow-up. The first orthotopic insertions of an allograft valve using the double-suture-line technique were performed in 1962 by Barratt-Boyes and separately by Ross using a single-suture-line technique described by Duran and Gunning. At first, cadaveric valves were collected aseptically and implanted within a few days or weeks, but for logistic reasons this technique was soon replaced by unsterile collection and sterilization by β-propiolactone, ethylene oxide, or irradiation. The allografts were then stored either in Hanks’ balanced salt solution at 4°C or frozen and dried. In 1968, because of high occurrence of cusp rupture with these techniques, antibiotic sterilization was introduced.

Cryopreservation rather than wet preservation was introduced in 1975 by O’Brien and colleagues. Yacoub and colleagues and Ross and colleagues expanded the use of allografts to include combined aortic valve and ascending aorta replacement.

In 1967, Ross and colleagues introduced the pulmonary autograft for aortic valve replacement, after Lower and colleagues had shown the feasibility of the procedure experimentally in 1960. Subsequently, the pulmonary valve and trunk were introduced as autograft composite conduits (cyinders) for replacing the aortic valve and ascending aorta.

Other biological valves were introduced. Senning in Zurich replaced the aortic valve clinically with individual cusps made of the patients’ fascia lata. Because of high late postoperative occurrence of infective endocarditis, however, this method was abandoned. Use of autologous fascia lata mounted on a frame was described by Ionescu and Ross but abandoned because of late dehiscence. Allograft dura mater valves, stent-mounted and preserved in glycerol, were used for aortic valve replacement by Zerbini and colleagues in Brazil. Bovine pericardium, glutaraldehyde treated and frame mounted, was introduced by Ionescu and colleagues at Leeds, England, in 1971.

In 1965, Binet and colleagues in Paris implanted porcine xenograft aortic valves, sterilized and preserved in a special formaldehyde solution, directly into the aortic root. The valves degenerated rapidly, most likely because of suboptimal tissue preservation. This led to abandoning direct xenograft valve implantation in favor of xenograft valves mounted on a stent frame. Stent-mounted bioprostheses are manufactured to provide a standard device that is easily implanted and provides reproducible results in the aortic position. Glutaraldehyde-preserved stent-mounted porcine valves were introduced by Carpentier and colleagues in Paris in 1967.

David and colleagues revived the concept of direct insertion of nonstented porcine xenografts into the aortic root. This valve was manufactured on a limited trial basis by Hancock Laboratory and by St. Jude Medical as the Toronto SPV (stentless porcine valve).

In April 2002, Professor Alan Cribier at the University of Rouen, France, performed the first percutaneous aortic valve replacement for aortic stenosis in a 62-year-old man who was not a candidate for surgery. Cribier used the antegrade transseptal approach through the femoral vein. The second percutaneous aortic valve insertion was in a 30-year-old man with severe aortic regurgitation who had no contraindication for surgery.

Beginning in 1979, Yacoub and colleagues developed the remodeling method of aortic valve-sparing root replacement for patients with aneurysms of the ascending aorta and root (including those associated with Marfan syndrome) and aortic dissection. In 1988, David and Feindel described an aortic valve-sparing operation (subsequently termed the reimplantation technique) for patients with aortic regurgitation and aneurysm of the ascending aorta in which the aortic valve is reimplanted within a polyester tubular graft.
**MORPHOLOGY**

**Aortic Valve Stenosis**

**Calcific Aortic Stenosis (Congenital)**

Calcific aortic stenosis implies stenosis secondary to heavy dystrophic calcification of a congenitally abnormal valve (Fig. 12-1, A and B). Calcification is rarely present before age 20; thereafter it is slowly progressive and results in important stenosis, most often in the fifth and sixth decades of life, earlier in unicommissural than bicuspid valves, and earlier in men than women. The calcification presents as a bulky califlower-like mass within the cusps, maximal at sites of commissural fusion or congenital buttress formation, often extending into the anulus (left ventricular [LV]-aortic junction) and adjacent aorta. Retrograde extension of calcification into the region beneath the right noncoronary cusp commissure adjacent to the membranous septum may lead to complete heart block. The valvar orifice is slitlike, often eccentrically located and oriented in a sagittal (most often) or transverse plane, and fixed, which often results in trivial or mild aortic regurgitation. (For description of critical congenital aortic stenosis, see Morphology in Chapter 47, Section I.)

**Bicuspid Aortic Valve**

Bicuspid aortic valve is considered the most common congenital heart anomaly, reported in 0.5% to 2% of the general population. The valve has two cusps of unequal size, the larger one containing a central raphe. The raphe results from commissural fusion (type 1). The most common pattern involves fusion of the right and left cusps and is associated with coarctation of the aorta. Rarely, the cusps are symmetric without residual commissure or raphe (type 0). Even less common is two raphes (type 2), usually with a well-developed commissure between the left and noncoronary sinuses.

Among patients with a bicuspid aortic valve, structural abnormalities exist at the cellular level that are independent of hemodynamic effects. The thoracic aorta typically shows reduced fibrillin-1, and increased matrix metalloproteinases are associated with smooth muscle cell detachment, matrix disruption, and cell death. The genetics of bicuspid aortic valve is complex and likely involves multiple pathways. Mutations in the signaling and transcriptional regulator NOTCH1 and in the ACTA2 gene (which encodes vascular smooth muscle cell B-actin) are linked with bicuspid aortic valve and familial thoracic aortic aneurysms. Numerous cardiac malformations are associated with bicuspid aortic valve: coarctation, Shone syndrome, William syndrome, Turner syndrome, and hypoplastic left heart syndrome. Abnormalities of the aorta (aortopathy) are the most frequent cardiac anomalies (with a male predominance of 3:1). Although ascending aortic dilatation is most common, aortic root and arch involvement are also frequent.

Controversy exists regarding the contribution of genetic mutations vs. flow characteristics in the genesis of the aortopathy. Using magnetic resonance imaging (MRI), Hope and colleagues demonstrated two distinct flow patterns specific to the two most common cusp fusion types and related these to location of thinning and dilatation of the ascending aorta. Asymmetric distribution of wall stress in patients with a bicuspid aortic valve (likely superimposed on genetically conferred aortic wall weakness) has been linked with asymmetric aortic smooth muscle cell apoptosis that could be flow mediated.

**Degenerative Aortic Stenosis**

Degenerative disease is often present in stenotic aortic valves of patients older than 65 years of age, and its prevalence increases with age. In a series of patients whose mean age was older than 70, prevalence of degenerative aortic valve stenosis exceeded 70%. The valve is tricuspid, without commissural fusion; the cusps are held in a closed position by deposits of diffuse nodular or eggshell calcification (Fig. 12-1, D). These deposits are not bulky and may also involve the sinuses of Valsalva and ascending aorta. Although degenerative (senile) aortic stenosis is presumed to be arteriosclerosis, Hoagland and colleagues found no correlation between aortic stenosis in adults over age 50 and systemic hypertension, elevated serum cholesterol, smoking, or diabetes. A more recent study of 5201 subjects older than 65, however, found that clinical factors associated with aortic sclerosis and stenosis are similar to risk factors for arteriosclerosis. Aortic valve sclerosis was present in 26% and aortic valve stenosis in 2% of the entire study cohort. In patients over age 75 the prevalence of aortic sclerosis was 37% and stenosis 2.6%. Smoking increased the risk by 35% and hypertension by 20%. Other factors associated with increased risk of aortic valve disease were high lipoproteins, elevated low-density cholesterol levels, and diabetes mellitus. Older age was directly associated...
with risk, with a twofold increase in risk for each 10-year increase in age.

Mitral annular calcification is common in elderly patients with calcific aortic stenosis. Presumably, both are degenerative in origin.

**Rheumatic Aortic Stenosis**

Rheumatic aortic stenosis is characterized primarily by diffuse, prominent fibrous cusp thickening of a tricuspid valve (Fig. 12-1, C), with fusion to a variable extent of one or two commissures (rarely all three). The orifice is approximately central and irregular in shape. Calcification other than a mild form is rarely present except in elderly patients, but is bulkiest at sites of commissural fusion. Rheumatic aortic stenosis is seldom if ever isolated, although at the patient’s first operation this may appear to be the case. In surgical series of apparently isolated aortic stenosis, prevalence of rheumatic etiology is low compared with that when patients with important mitral valve stenosis are included.

About half of patients with so-called rheumatic aortic stenosis fail to report a history of rheumatic fever, suggesting other unrecognized inflammatory processes as the cause. However, with the decline in incidence of rheumatic fever in the United States and other developed countries, rheumatic aortic stenosis decreased from a prevalence of 30% to 18% by the 1980s (and senile degenerative disease increased from 30% to 46%).

**Aortic Valve Regurgitation**

The terms aortic regurgitation, aortic incompetence, and aortic insufficiency are used interchangeably. Regurgitation is the preferred and most descriptive term. Morphologic characteristics of aortic regurgitation depend on etiology. These characteristics are not as easily categorized as in aortic stenosis.

**Relevant Aortic Root Anatomy**

Basic anatomy of the aortic root is detailed in Chapter 1. This section provides additional details about aortic root anatomy and relationships that are relevant to aortic root reconstruction and valve-sparing aortic root replacement (discussed later in this chapter). The aortic root is that part of the aorta bounded proximally by the bases of the aortic valve cusps and distally by the sinutubular junction. McAlpine conceptualizes a continuous membrane covering the ostium or opening of the LV (the aortoventricular membrane) that contains the anulus of the mitral valve and the aortic anulus and adjacent fibrous components. The left anterior fibrous trigone is a membrane between the left and right cusps and the ostium of the LV. The remaining structures related to the aortic root result from thickening of the aortoventricular membrane (at the aortoventricular membrane, and these are the right anterior fibrous trigone, the ventricular and atrial segments of the membranous septum, intervalvar trigone, right fibrous trigone, and fila coronary (the portion of the aortoventricular membrane between the ostium of the LV and the left atrial attachment, which comprises about 75% of the mitral anulus). The region where the aortic valve cusps are in fibrous continuity with the anterior leaflet of the mitral valve (aortomitral anulus) is thickened at each end to form a left and right fibrous trigone. The right fibrous trigone is in continuity with the membranous portion of the septum, and these two structures form the central fibrous body. The left anterior fibrous trigone, right anterior fibrous trigone, and intervalvar trigone are also termed intercusp triangles. The membranous septum is divided into the ventricular membranous septum and atrial membranous septum by attachment of the tricuspid valve septal leaflet to the aortoventricular membrane (Fig. 12-3). Attachment of the right ventricle (RV) to the aortoventricular membrane is in close relationship to the left and right anterior fibrous trigones (Fig. 12-4).

The aortic root forms the outflow tract from the LV and contains the aortic valve cusps, sinuses of Valsalva, and intercusp triangles (trigones). Morphology of the aortic valve cusps reflects their exposure to the mechanical stress of diastolic pressure. They have three distinct layers. The outflow surface is the fibrosa, comprising bundles and sheets of collagen aligned in the circumferential direction. The cusp has a coaptional portion (where the collagen bundles are discontinuous) and a noncoaptional surface or cusp belly (where the collagen bundles are continuous). The ventricular surface of the cusp is composed of the ventricularis, which is another fibrous layer. It is a mixture of both collagen and elastin (although the elastin is not as important as the collagen from a biomechanical standpoint). The fibers are arranged
PART III Acquired Valvar Heart Disease

The tissue in between the attachment of the aortic valve cusps to the aortic wall is the intercusp triangle, a layer composed of circularly oriented collagen fibers. The base of two of the intercusp triangles is LV muscle, and the intercusp triangle beneath the commissure of the left and right cusps is fibrous (left anterior fibrous trigone). Attachment of the base of the aortic root is approximately 55% fibrous and 45% muscular. The intercusp triangles are exposed to ventricular hemodynamics, and they may function in part to allow each of the sinuses to act independently.

An important surgical point regarding the ventricular-aortic junction is the site of attachment of prosthetic valves, which are largely circular structures. Prosthetic valves are actually attached to the anatomic ventricular-aortic junction and do not follow the cusp attachment, although this is usually regarded as the “anulus.”

Aortic Regurgitation Related to Aortic Root Pathology
A spectrum of aortic pathology may result in aortic regurgitation due to alterations in the geometry of the sinutubular junction, sinuses, and the ventricular-aortic junction. Ascending aortic aneurysms and aortic root disease may be distinct processes, or they may coexist as a blending of morphologic manifestations.

Many different pathologies may result in ascending aortic aneurysms (see Chapter 26). These include long-standing hypertension, arteriosclerosis, aneurysms associated with bicuspid aortic valves, and extreme forms of post-stenotic dilatation of a stenotic aortic valve. Ascending aortic aneurysms may also result from inflammatory processes causing aortitis, including rheumatoid arthritis, ankylosing spondylitis, and Reiter syndrome. Ascending aortic aneurysms and aortic root disease may arise from clearly defined genetic syndromes, including Marfan syndrome, Loeys-Dietz syndrome, Ehlers-Danlos syndrome, and filamin A mutations. Most patients with thoracic aorta disease and aortic dissections do not have a clearly defined genetic disorder, but many have an inherited predisposition to the process.

Marfan syndrome, one of the most common connective tissue disorders, is an autosomal dominant condition affecting about 1 in 3000 to 5000 people. Most patients with the typical Marfan phenotype have mutations involving the FBN1 gene that codes for fibrillin-1, an extracellular matrix protein.

Figure 12-3 Components of the ventriculoarterial membrane from within left ventricle, with aortic valve opened through the right aortic sinus. Key: L, Left noncoronary sinus; LA, left atrium; LAF, left anterior fibrous trigone; LF, left fibrous trigone; N, noncoronary sinus; R, right noncoronary sinus; RA, right atrium; RV, right ventricle; TV, tricuspid valve. (From McAlpine.)

Figure 12-4 Attachment of right ventricle and tricuspid valve anulus to the ventriculoarterial membrane. Right ventricular outflow tract has a very close relationship and fibrous attachment to the left anterior trigone (which is of particular importance to the operation of aortic valve-sparing root replacement). There is a further attachment of the posterolateral wall of the right ventricle together with the septal leaflet of the tricuspid valve to the ventriculoarterial membrane. The dashed line indicates demarcation between right and left ventricles. (From McAlpine.)

randomly, and therefore when the ventricularis is under load, the fibers realign in the direction of the applied load and only then resist further extension. The spongiosa layer between the fibrosa and ventricularis is composed principally of glycosaminoglycans, which are responsible for energy dissipation and lubrication of the movements between fibrosa and ventricularis. The biomechanical properties of the fibrosa and ventricularis allow radial extension of the cusp to form a large coaptational area.

The sinuses of Valsalva are the bulging portions of the aortic root from which the coronary arteries arise. They accommodate the open cusps of the aortic valve and generate vortices that are important for aortic cusp closure. The base of the aortic cusp attachment forms a coronet-like structure (Fig. 12-5).
glycoprotein that contributes to structural integrity of connective tissue. In a minority of cases, an FBN1 mutation is not found. Fibrillin-1 is an important component of both elastic and nonelastic connective tissue. In about 10% of Marfan phenotypes, mutations have been noted in transforming growth factor (TGF)-β receptor genes. Criteria for diagnosis of Marfan syndrome involve genetic studies, family history, and major and minor clinical manifestations. Because of the linkage between these genetic entities and phenotypes that overlap with typical Marfan syndromes, the clinical diagnosis requires specific combinations of criteria. Histologic features of the ascending aorta media in Marfan patients include fragmentation of elastic lamellae, loss of smooth muscle cells, fibrosis, and cystic medial necrosis (a misleading term coined to describe the lacunar appearance of medial degeneration when, in fact, cystic changes and necrosis are absent).

Other connective tissue disorders that predispose to aortic aneurysmal disease and dissection include Loeys-Dietz syndrome and the vascular type of Ehlers-Danlos syndrome. \(^{P1}\) Loeys-Dietz syndrome is an autosomal dominant aortic syndrome resulting from mutations in genes for the cytokine (TGF)-β receptor (TGFBR) type I or II. Arterial tortuosity and aneurysms, hypertelorism, and bifid uvula or cleft palate characterize the disease phenotype. Skeletal features are similar to those of Marfan syndrome. The aortic disease in this syndrome is particularly aggressive, and 98% of patients develop aortic root aneurysms that have a high propensity for dissection. \(^{L15,W11}\) Mean age of death with this syndrome is 26 years. \(^{L15}\) In children affected with Loeys-Dietz syndrome, prominent craniofacial features are associated with more severe aortic disease. Because these patients are prone to aneurysm development in other locations, yearly MRI or computed tomography (CT) is advisable from the pelvis to the brain.

The vascular form (type IV) of Ehlers-Danlos syndrome is a rare autosomal dominant disease caused by a defect in type III collagen, encoded by the COL3A1 gene. Prominent clinical features include easy bruising, thin skin, characteristic facial features, and tendency for rupture of arteries, uterus, or intestines. \(^{P1}\) The role of prophylactic aortic replacement surgery to prevent aortic rupture or dissection is less clear than for Marfan or Loeys-Dietz syndromes. Of importance, these patients typically have extreme tissue fragility, so if aortic aneurysms or aortic regurgitation require cardiac surgery, reinforcement of suture lines with felt pledgets or strips is recommended. \(^{S47}\)

Anuloaortic ectasia can produce aortic regurgitation of varying but sometimes severe degree even though the cusps are normal. \(^{S8}\) It is most often caused by cystic medial degeneration of the aorta and may be associated with Marfan syndrome. Even in the absence of Marfan syndrome, anuloaortic ectasia appears to be a genetic disease. \(^{S48}\) It begins in the sinuses of Valsalva; at this stage, regurgitation is usually not present. With time, the process extends to involve the proximal ascending aorta, producing a symmetric, pear-shaped aneurysmal enlargement. Regurgitation now appears and progresses because dilatation of the aortic wall at the sinutubular junction separates the commissures and tightens the free cusp edges, preventing coaptation during diastole. As dilatation of the aorta progresses, central aortic valve regurgitation increases. The LV-aortic junction usually does not increase in size, even in patients with large aneurysms associated with anuloaortic ectasia. Size of the aortic valve prosthesis used in these patients (if indicated) is generally similar to that used for replacement in patients with rheumatic or other disease. \(^{S26}\)

The aneurysmal process eventually involves the entire ascending aorta, but usually stops just before the level at which the brachiocephalic artery originates, although the remainder of the arch may show cystic medial degeneration. The aneurysms are thin walled with a smooth lining. Dissection may begin within the aneurysms, extending proximally and distally or remaining localized (although most acute aortic dissections occur in the absence of an aortic root aneurysm). In patients with Marfan syndrome, about 30% of those operated on for anuloaortic ectasia and aneurysm of the ascending aorta have an aortic dissection. It is limited to the ascending aorta in about half the patients and extends into the transverse and descending aorta in the rest. \(^{S15}\) Frequently, dissection is unexpectedly found at operation. With proximal extension of this dissection, the commissural attachment of the valve becomes separated from the outer aortic wall such that the valve prolapses centrally, and regurgitation may abruptly increase (see Chapter 25).

Arteriosclerotic and Syphilitic Ascending Aortic Aneurysms

Ascending aortic aneurysms also produce valvar regurgitation because of thickening of the free edges of the cusps that results from aortic dilatation. In syphilitic ascending aortic aneurysm, aortic regurgitation is exacerbated by a valvulitis that produces thickening and retraction of the cusp edge. Neither condition, however, is generally associated with aortic dissection.
Aortitis
In some patients with rheumatoid arthritis, ankylosing spondylitis,\textsuperscript{537} or Reiter disease, an aortitis occurs that may lead to aneurysmal dilatation of the ascending aorta and aortic valvar regurgitation.\textsuperscript{58} The aortitis is characterized by dense adventitial inflammatory fibrosis involving the sinuses of Valsalva and proximal aorta, especially adjacent to the commissures.\textsuperscript{667} The process may extend below the base of the aortic valve to form a characteristic subvalvar ridge and may involve the base of the anterior mitral leaflet or even the adjacent ventricular septum, causing conduction disturbances. Particularly in rheumatoid arthritis, the cusps may be thickened and shortened and show rheumatoid nodules histologically.\textsuperscript{R12}

Rheumatic Aortic Regurgitation
Rheumatic aortic regurgitation results from a different response of the valve to the rheumatic process than occurs when stenosis develops. Commisural fusion is minimal or absent, and the cusps are only slightly thickened. Minor calcification is present in about 10% of affected valves. The major pathologic process is cicatricial shortening of the cusps between their free edge and their anular attachment, with rolling of the free edge. As time passes, the aortic root widens in response to the regurgitation, further increasing central valvar regurgitation.

Native Valve Endocarditis
Native valve endocarditis, which may occur on a structurally normal valve or on congenitally or rheumatically deformed valves, is a common cause of aortic regurgitation. The regurgitation may result from a destroyed commissure and consequent cusp prolapse or from a perforation in the belly of the cusp. An infected pannus may appear below the cusps, or extensive destruction of the aortic root may occur, with a periaortic root abscess sometimes extending into the mitral anulus and anterior mitral leaflet. Mitral regurgitation may also develop because of perforation of the anterior leaflet by a “drop lesion” caused by the infected regurgitant stream from the diseased aortic valve.

Congenital Aortic Valve Disease
A congenitally bicuspid or unicuspid valve can produce regurgitation from prolapse of the free edge of a redundant cusp.\textsuperscript{513} In such patients, the regurgitation may be aggravatad by infective endocarditis or an improper valvotomy (see Chapter 47). Lack of support of the aortic anulus in association with ventricular septal defect may result in aortic valve prolapse and regurgitation (see Chapter 35).

Flappy Aortic Valve
Occasionally, aortic regurgitation may be caused by prolapse of redundant aortic cusps that are mildly thickened and myxomatous. The aortic root may be normal or dilated, usually with cystic medial necrosis, and mitral valve prolapse may also occur.\textsuperscript{B27,W16}

Iatrogenic Aortic Valve Disease
Aortic valve regurgitation may be caused by a number of physician-related interventions. Perforation of the aortic valve cusps may result from diagnostic or balloon dilatation catheters. Even with newer methods and lower doses of mediastinal irradiation, occasional cases of mediastinal fibrosis occur, with injury to the pericardium, cardiac valves, coronary arteries, and myocardium. Cardiac valve disease has also been associated with migraine medications (ergotamine, methysergide) and appetite suppressants (fenfluramine, with or without phentermine)\textsuperscript{233} (Fig. 12-6).

Other Types of Aortic Regurgitation
Other causes of aortic valve regurgitation include spontaneous cusp rupture,\textsuperscript{O1} rupture caused by severe closed-chest trauma,\textsuperscript{M16,R8} and severe long-standing systemic hypertension with aortic root dilatation. In patients with long-standing hypertension, regurgitation may result from typical myxoid degeneration of the valve.\textsuperscript{A6,12,712} Some instances of regurgitation are probably related to arthropathies with minimal joint involvement or to hypertension, psoriasis, giant cell aortitis,\textsuperscript{527} or Takayasus disease. Occasionally the etiology of regurgitation is not apparent.

Combined Aortic Stenosis and Regurgitation
The etiology and morphology of combined aortic stenosis and regurgitation are similar to those of aortic valve stenosis. In some cases, an episode of endocarditis produces regurgitation of a previously stenotic valve.

Changing Etiology and Morphology
A time-related change in etiology and morphology has been observed at operation in patients with aortic valve disease. Although the overall prevalence of bicuspid aortic valves in the general population has not changed over the past 50 years,\textsuperscript{8} its relative frequency in the surgical population has decreased (Table 12-1). In surgical patients at the Mayo Clinic the relative frequency of bicuspid aortic valves fell from 49% in 1965 to 36% in 1990.\textsuperscript{D1,S42} The relative frequency of patients with degenerative aortic valve disease increased greatly, however, and the prevalence of aortic stenosis doubled from 32% to 65%. Mean age at operation increased from 49 years in 1965 to 66 years in 1990 and continues to rise.\textsuperscript{D1,S99,P96,S41,S42}

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA
Aortic Stenosis
Patients with aortic stenosis are usually symptomatic when first seen. They may present without symptoms, however, having been referred because of a cardiac murmur. The classic triad of effort dyspnea, angina, and syncope is present in 70% of patients.\textsuperscript{E12} Understanding and recognizing the symptoms of aortic stenosis is particularly important because of the heavy reliance on symptoms in decisions regarding advisability of operation (see Indications for Operation, Selection of Technique, and Choice of Device later in this chapter).

Angina pectoris is present as the only symptom or is combined with others in 50% to 70% of patients.\textsuperscript{B20,E1} It is more common in patients with combined aortic stenosis and coronary artery disease than in those with isolated aortic stenosis.\textsuperscript{1,24} Angina in patients without coronary artery disease presumably results from an imbalance between coronary blood flow and oxygen demand in the hypertrophied LV. Angina appears to occur more frequently in patients with severe...
Figure 12-6  Iatrogenic aortic valve disease. Aortic valve regurgitation caused by physician intervention. A, Aortic valve affected by fenfluramine/phentermine (Fen/Phen). One cusp is contracted due to a fibrotic plaque. The other two cusps are normal. B, Echocardiogram of Fen/Phen iatrogenic aortic valve disease. A regurgitant jet indicates moderately severe aortic valve regurgitation before repair. Repair consisted of débridement of fibrotic plaques from the valve cusps and narrowing of the sinutubular junction by a prosthetic band. After repair, there is trivial aortic valve regurgitation.

Table 12-1  Time-Related Changes in Aortic Valve Morphology at Operation

<table>
<thead>
<tr>
<th>Morphology</th>
<th>AS (Pure)</th>
<th>AS/AR (Mixed)</th>
<th>AR (Pure)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatic (%)</td>
<td>49</td>
<td>36</td>
<td>20</td>
</tr>
<tr>
<td>Degenerative (%)</td>
<td>0</td>
<td>51</td>
<td>0</td>
</tr>
<tr>
<td>Dilatation ascending aorta (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Iatrogenic (%)</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Infective endocarditis (%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other (%)</td>
<td>18</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>Patients (%)</td>
<td>32</td>
<td>65</td>
<td>39</td>
</tr>
</tbody>
</table>

Data from William D. Edwards, MD, based on references D1, O9, P6, S41, S42 and surgical patients at the Mayo Clinic.

A few patients (10%) survive typical symptoms long enough for secondary RV failure to develop. These patients present with a clinical picture dominated by elevated right atrial and jugular venous pressure, hepatomegaly, cardiac cachexia, and rarely, tricuspid regurgitation. Patients often appear to have combined aortic stenosis and mitral regurgitation as well.

Diagnosis of important aortic stenosis can often be made by physical examination with reasonable certainty when, in addition to the presence of an aortic ejection murmur (usually best heard in the second right intercostal space beside the sternum and transmitted to the carotids, but also often at the apex and in the second left intercostal space), the arterial pulse is of small volume with a slow upstroke. Support for the diagnosis may be obtained from expiratory splitting of the second heart sound and from evidence of LV hypertrophy provided by the character of the apex beat and electrocardiogram (ECG). Usually the ECG provides evidence of LV hypertrophy, with or without inverted T waves in lead V6 (the so-called strain pattern). When chest radiography or fluoroscopy also shows calcification of the aortic valve and convexity along the upper part of the LV silhouette produced by LV hypertrophy, the diagnosis of calcific aortic stenosis becomes a near certainty.
Table 12-2 Classification of Severity of Aortic Valve Disease in Adults

<table>
<thead>
<tr>
<th>Aortic Stenosis</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jet velocity (m·s⁻¹)</td>
<td>&lt;3.0</td>
<td>3.0-4.0</td>
<td>&gt;4.0</td>
</tr>
<tr>
<td>Mean gradient (mmHg)⁶</td>
<td>&lt;25</td>
<td>25-40</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Valve area (cm²)</td>
<td>&gt;1.5</td>
<td>1.0-1.5</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Valve area index (cm²·m⁻²)</td>
<td>&lt;0.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Aortic Regurgitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualitative</td>
</tr>
<tr>
<td>Angiographic grade</td>
</tr>
<tr>
<td>Color Doppler jet width</td>
</tr>
<tr>
<td>Doppler vena contracta width (cm)</td>
</tr>
</tbody>
</table>

| Quantitative (Cath or Echo) | Mild | Moderate | Severe |
| Regurgitant volume (mL·beat⁻¹) | <30 | 30-59 | ≥60 |
| Regurgitant fraction (%) | <30 | 30-49 | ≥50 |
| Regurgitant orifice area (cm²) | <0.10 | 0.10-0.29 | ≥0.30 |

Data from Bonow and colleagues.⁶³⁰

¹Valve gradients are flow dependent and, when used as estimates of severity of valve stenosis, should be assessed with knowledge of cardiac output or forward flow across the valve.

Key: Cath, Cardiac catheterization; echo, echocardiogram; LVOT, left ventricular outflow tract.

At times, physical findings are less diagnostic. Systemic hypertension or, in older patients, inelasticity of aortic and arterial walls may alter the character of the arterial pulse wave and prevent development of a clinically recognizable slow upstroke or soft, weak pulse (pulsus parvus). Absence of the aortic component may prevent assessment of the respiratory behavior of the second heart sound, whereas in patients with right or left bundle branch block, splitting of this sound is of no value as a guide to the severity of aortic stenosis. In older patients especially, the character of the cardiac apex may be unreliable as a clinical guide to presence and degree of LV hypertrophy. The ECG also may fail to show the degree of LV hypertrophy associated with severe aortic stenosis and occasionally remains normal without showing evidence of LV involvement.

In these patients, judicious use of graded exercise testing may uncover a clinically silent state of LV dysfunction and functional aerobic impairment. Exercise has generally been considered dangerous in patients with severe aortic valve stenosis because of effort syncope. Experience has shown, however, that graded exercise testing is not a risky procedure in patients with aortic stenosis who are asymptomatic, but it is not advised in symptomatic patients. Impaired exercise tolerance (as by 6-minute walk testing), occurrence of symptoms, inadequate blood pressure increase (10 mmHg · 30 watts⁻¹ or less) or blood pressure drop (≥10 mmHg), bradycardia, arrhythmia, conduction disturbance, and ST-segment depression (≥0.2 mV) indicate impaired aerobic or LV function. This information may be helpful in deciding on operative intervention or, if continued observation is advised, recommendations concerning vocational, recreational, or sports participation. Finally, in the terminal stages of low-output heart failure, the murmur may be so faint that aortic stenosis is not suspected, particularly in adult patients in whom the heart sounds are distant either because of chest wall thickness or inelastic and voluminous lungs.

Doppler echocardiography is a reliable means of establishing the presence of aortic stenosis and is usually performed in patients suspected of having aortic valve disease. In most patients with aortic stenosis, the degree of obstruction to outflow, aortic valve peak and mean gradient, and valve area can be reliably determined. It is the main modality for serial evaluation. Maximal instantaneous gradient is obtained by applying the modified Bernoulli equation to peak aortic velocity; this may be 30% to 40% higher than gradient determined by cardiac catheterization (Table 12-2). Using continuous wave Doppler, the simplified Bernoulli equation can be applied to obtain the peak instantaneous gradient: Peak pressure gradient (mmHg) = 4 × peak velocity². The mean gradient across the aortic valve is obtained by planimetry of the continuous wave signal. Mean gradient is more useful clinically than instantaneous gradient. Mean pressure gradient is the arithmetic mean of the derived instantaneous gradients; it correlates well with mean pressure gradient obtained by cardiac catheterization. Aortic valve area may also be determined by echocardiography based on the continuity principle, which states that flow through a nonstenotic region of the heart should equal flow through a stenosis (assuming no regurgitation or shunt). Aortic valve area derived by cardiac catheterization is well correlated with this.

Hemodynamic data derived by Doppler echocardiography or cardiac catheterization can provide a grading of degree of stenosis (see Table 12-2). The aortic valve area must be reduced to about one fourth its normal size before important changes occur in the circulation. The normal adult aortic valve area is 3.0 to 4.0 cm². Thus, an area of less than 1.0 cm² is likely to produce clinical symptoms. The American College
of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines states that aortic valve stenosis is mild when aortic valve area is greater than 1.5 cm² (with transvalvar gradient < 25 mmHg), moderate when 1.0 to 1.5 cm², and severe when less than 1.0 cm² (see Table 12-2). Because pressure gradient is flow dependent, stenosis is considered severe when mean gradient is 40 mmHg or higher and cardiac output is normal. However, when cardiac output is low, severe aortic stenosis may be present with a lower transvalvar gradient.

These hemodynamic criteria are helpful, but therapeutic decisions related to operative intervention are largely based on presence or absence of symptoms.

In patients over age 40, coronary arteriography is also performed when operation is being considered, because coronary artery disease coexists in many of these patients whether or not angina is present. At the time of coronary arteriography, systolic pressure gradient across the aortic valve is measured. Cardiac output can be measured and the valve area calculated by the Gorlin equation.

Hematologic abnormalities associated with severe aortic stenosis include impairment of platelet function and decreased levels of von Willebrand factor, which correlate with severity of stenosis. Clinical bleeding is observed in about 20% of patients with severe aortic stenosis, most often epistaxis or ecchymoses. Coagulation abnormalities usually disappear after aortic valve placement.

Aortic Regurgitation

Patients with aortic regurgitation present more frequently without symptoms than do those with aortic stenosis, perhaps because of the more dramatic physical and radiographic findings and relatively long asymptomatic phase of regurgitation. In most patients, the dominant symptoms reflect pulmonary venous hypertension (dyspnea, orthopnea, paroxysmal nocturnal dyspnea, pulmonary edema). Angina pectoris is often part of the presenting complaint, but is the chief complaint in less than one fourth of patients and is more common in older patients. Coronary artery disease is present in about 20% of patients with angina pectoris. Syncope is rare.

In severe aortic regurgitation, the LV apex is usually displaced and overactive in character. The carotid and other pulses are jerky to palpation in moderate regurgitation and collapsing or “water-hammer” in severe regurgitation because of the wide pulse pressure and rapid rise and fall of the pulse wave. Blood pressure measured by Korotkoff sounds may reach 200 to 250 mmHg systolic and 50 to 0 mmHg diastolic. Normally, brachial or radial pulse pressure measured by an arterial needle is less than that measured by Korotkoff sounds, and central aortic pulse pressure is even less. These phenomena, including systolic amplification between central aortic and radial artery blood pressures, are related to standing waves created by the pulsatile ejection of an unusually large LV stroke volume into the aorta and remainder of the arterial tree. If cardiac output is low because of severe cardiac failure, these phenomena are minimal.

Auscultation in the aortic area reveals an early diastolic murmur that radiates toward the apex of the heart. Intensity of the murmur has been shown to correlate with degree of aortic valve regurgitation. Murmur grade 3 or greater predicts severe aortic regurgitation in 71% of patients, whereas murmur grade 1 or less predicts that aortic regurgitation is not severe in 100% of patients. Often a systolic click or ejection murmur is present as well. At the apex a mid-diastolic murmur is frequently caused by fluttering of the anterior mitral leaflet from a prominent regurgitant jet (Austin Flint murmur). This may be difficult to distinguish from the murmur of mitral stenosis, although in the latter an opening snap is often present. When mitral stenosis coexists, the ECG usually shows P mitrale and the left atrium is enlarged, although in severe and long-standing pure aortic regurgitation, the ECG may also show P mitrale. Two-dimensional echocardiography is useful in making the distinction between mitral stenosis and merely an Austin Flint murmur (Fig. 12-7). The chest radiograph confirms LV enlargement; the left atrium is usually normal or slightly enlarged. Radiographic evidence of pulmonary venous hypertension may or may not be present. Enlargement of the shadow of the ascending aorta to the right suggests an accompanying aneurysm of the ascending aorta, but an aneurysm can be present without this sign. The ECG shows evidence of LV
enlargement, often with the high-peaked T waves and prominent Q waves of LV volume overload. T-wave inversion and ST-segment depression are seldom present until the LV is extremely large.

Diagnosis of aortic valve regurgitation can usually be made on the clinical findings, but other abnormalities in the aortic root allowing a rapid aortic runoff (e.g., ruptured sinotubular junction, large patent ductus arteriosus with pulmonary valve regurgitation) cannot be entirely eliminated without special studies. Color flow Doppler echocardiography firmly establishes the diagnosis.

Doppler echocardiography can be used to quantify aortic valve regurgitation (see Table 12-2). Measurements are made of regurgitant volume (volume regurgitated per heart beat) and of regurgitant fraction (proportion of total ejection of the LV). These measurements are highly dependent on technical experience, with overestimation the rule at first. Size of the jet visualized by color Doppler echocardiography may not represent the degree of aortic regurgitation. It is possible to measure the vena contracta, which is the size of the regurgitant jet within the regurgitant aortic valve orifice. This measurement correlates well with effective regurgitant orifice size. The width of the vena contracta just below the flow convergence is measured using the parasternal long-axis view. The vena contracta of 7 mm or greater uniformly favors severe aortic valve regurgitation, whereas measurements of 5 mm or less correspond to less regurgitation. The degree of aortic regurgitation may also be quantified by cineangiography using an aortic root contrast injection in the right anterior oblique projection, but this method is difficult and often unreliable.

Coronary arteriography is indicated in patients over age 40.

Combined Aortic Stenosis and Regurgitation

Although many patients with severe aortic stenosis have mild regurgitation and a few patients with severe regurgitation have some stenosis, a small group of patients have virtually balanced lesions. Their symptoms are generally similar to those associated with aortic stenosis. This group may have a particularly unfavorable prognosis because there is both volume and pressure overload on the LV.

NATURAL HISTORY

Aortic Stenosis

The natural history of adults with aortic valve disease is incompletely known, although it is evident that severity of the stenosis gradually increases. Synthesis of four echocardiographic studies indicates that once moderate aortic stenosis is present (jet velocity by echocardiography > 3.0 m · s⁻¹), the average rate of progression in mean pressure gradient is about 7 mmHg · y⁻¹, an increase in jet velocity of 0.3 m · s⁻¹ · y⁻¹, and a decrease in valve area of 0.1 cm² · y⁻¹. Aortic stenosis appears to progress more rapidly in patients with degenerative disease than in those with congenital or rheumatic etiology. A complicating factor is that some degree of stenosis may have existed in childhood, often with associated regurgitation. The natural history in these patients may be more favorable than when the disease develops de novo and more rapidly later in life.

Medical therapy has generally been regarded as ineffective in preventing or retarding disease progression in aortic stenosis. Research over the past decade indicates that aortic valve disease of the elderly is not just a passive “wear-and-tear” process, but an active inflammatory process with histologic changes similar to arteriosclerosis. An evaluation of statin therapy (based on its efficacy in arteriosclerosis stabilization) in the Simvastatin Ezetimibe Aortic Stenosis (SEASten) and Scottish Aortic Stenosis and Lipid Lowering Trial, Impact on Regression (SALINE) prospective randomized trials failed to identify a favorable effect of statins on progression of aortic stenosis. Ongoing research efforts may clarify the potential role of these and other agents in ameliorating disease progression.

Survival

Grant reported that 35% of unoperated patients with usual symptoms of aortic stenosis are alive at 10 years. Wood stated that 46% of such patients were alive 1 to 7 years later. Frank and Ross reported that of 12 unoperated patients with severe aortic stenosis, only 18% were alive 5 years later. Based on their data, Ross and Braunwald concluded that average survival after onset of angina or syncope is 3 years and after onset of heart failure about 1.5 years. ACC/AHA guidelines suggest that after onset of symptoms, average survival is less than 2 to 3 years, with a high risk of sudden death. Thus, development of symptoms identifies a critical point in the natural history of aortic stenosis. O’Keefe and colleagues followed 50 symptomatic patients with severe aortic stenosis in whom operation was declined or deferred. Average age of these patients was 77 (60-89) years. Survival was 55%, 37%, and 25% at 1, 2, and 3 years, respectively, compared with a matched general population of 93%, 85%, and 77%. Death was from cardiac causes in all cases except one. Of 179 patients aged 83 ± 8.3 years deemed inoperable in the PARTNER IB cohort, 1-year survival was 49%.

Although it is impossible to rigorously assemble such disparate data, a likely survival curve for adult patients with severe, unoperated aortic stenosis is estimated in Fig. 12-8.

![Figure 12-8](image-url) Nonrigorously derived survival curves for patients with surgically untreated severe aortic stenosis (solid line) and severe aortic regurgitation (dashed line). Time zero is the time of developing an important hemodynamic effect. Survival of patients with aortic stenosis reported by Wood, Frank and Ross, and Grant is shown by filled circles.
Deaths within the first 1 or 2 years are likely to be sudden, presumably associated with ventricular fibrillation (15%-20% of all deaths in aortic stenosis are sudden\textsuperscript{[10]}), or, after a few hours or days of acute pulmonary edema, from sudden LV failure. Most unoperated patients die in the latter mode within about 5 years of diagnosis. Beyond 5 years of follow-up, some die of gradually worsening cardiac failure, with low cardiac output and gradually worsening symptoms of pulmonary venous hypertension. Moderate pulmonary artery hypertension develops in some patients who exhibit these findings; in a few, typical symptoms and signs of RV failure become prominent.

Asymptomatic patients with severe aortic stenosis usually develop symptoms within a few years of diagnosis. Otto and colleagues showed that about one fourth of initially asymptomatic patients with aortic valve stenosis had developed symptoms,\textsuperscript{[13]} half by 3 years and three fourths by 4 years. When the Doppler outflow velocities were initially 4.0 m · s\textsuperscript{-1} or greater, progression was more rapid, with three fourths of patients symptomatic by 2 years. Thus, even in initially asymptomatic patients with aortic stenosis, progression to symptoms may be rapid, and patients should be monitored closely for progressive disease. Sudden death is uncommon in asymptomatic patients with aortic stenosis, occurring in less than 1% per year.\textsuperscript{[550]} However, as noted by Freed and colleagues, failure to identify subtle symptoms of severe aortic stenosis is common, and the subsequent mortality without surgery may exceed 10% in the ensuing 1 to 1.5 years.\textsuperscript{[512]}

Left Ventricular Structure and Function
The LV hypertrophies progressively in the presence of important aortic stenosis, which usually develops over decades. The increase in wall thickness is usually enough to counter the high intraventricular systolic pressure and maintain normal ventricular volume.\textsuperscript{[41,56]} In this circumstance, LV wall stress (afterload) remains within normal range, and EF remains preserved (given the inverse relationship between systolic wall stress and EF).\textsuperscript{[236]} However, when the hypertrophic response is not adequate for progressively higher intracavitary pressures, the increased afterload can cause a decrease in EF, which is generally reversible with valve replacement.\textsuperscript{[512,513]}

Myocardial hypertrophy in aortic valve stenosis is caused by new myofibrils added in parallel to myocytes. No new myocytes are added, but existing myocytes become thicker, not longer, compared with normal myocytes. The hypertrophy of myocardial cells (increased myocardial cell diameter) is a determinant of both increased systolic load stress and decreased LV diastolic function found in aortic stenosis,\textsuperscript{[514]} and is also related to reduction in EF.\textsuperscript{[535]} Myocardial fibrosis exerts little effect.

Schwartz and colleagues found good systolic function and only hypertrophic myocardial cells when LV mass was less than 200 g · m\textsuperscript{-2}.\textsuperscript{[515,537]} When it was 200 to 300 g · m\textsuperscript{2}, degenerative changes were present but mild. When LV mass was greater than 300 g · m\textsuperscript{2}, systolic function was greatly depressed and multiple degenerative changes in ultrastructure were present (mitochondrial changes, disruption of sarcomeric units, nonoriented growth of fiber components, disappearance of organelles). Maron and colleagues also described these degenerative changes in detail.\textsuperscript{[536]} Krayenbuehl and colleagues found degenerative changes in the form of increased interstitial nonmuscular tissue in association with myocardial cellular hypertrophy.\textsuperscript{[535]} These changes are probably the morphologic basis for loss of inotropic (contractile) strength and irreversibility.

Thus, during the compensated phase, thickening of the LV wall keeps LV afterload (systolic wall stress) more or less normal (see “Ventricular Afterload” under Cardiac Output and Its Determinants in Section I of Chapter 5), preserving LV systolic function. LV compliance and diastolic function are gradually impaired, to a degree primarily related to extent of LV hypertrophy.\textsuperscript{[10]} At a more advanced stage, hypertrophy and wall thickness may increase less than LV systolic pressure (afterload mismatch\textsuperscript{[512]}); the resulting increase in afterload impairs LV systolic function. The degree of LV hypertrophy and decrease in contractility that ultimately develop are more often the cause of declining cardiac function.\textsuperscript{[614]} As indices of systolic function (EF, end-systolic volume, LV fractional shortening, velocity of circumferential shortening) decline, cardiac output decreases gradually or acutely, and LV diastolic function decreases with a consequent increase in LV end-diastolic pressure.\textsuperscript{[514]} By this time the condition is advanced, and chronic heart failure is present.

The atrial contribution to ventricular filling is of great importance with a thickened noncompliant ventricle. As long as sinus rhythm is maintained, left atrial and pulmonary venous pressure can remain near normal. However, loss of atrial contraction with the onset of atrial fibrillation can induce rapid clinical decompensation.\textsuperscript{[53]}

The hypertrophied ventricle may have reduced coronary perfusion per gram of muscle with diminished coronary vaso-vodilator reserve. Added myocardial oxygen demands with exercise or tachycardia may induce subendocardial ischemia and angina in the absence of coronary artery disease.\textsuperscript{[53,535]}

Occasionally, complete heart block develops in patients with extensive calcification of the stenotic aortic valve. It may be the result of gradually increasing pressure on the bundle of His by calcific deposits beneath the commissural area between the noncoronary and right coronary cusps.\textsuperscript{[58]} However, complete heart block sometimes occurs without calcific pressure on the bundle of His.\textsuperscript{[111]} Pressure in the LV is hypothesized to play a role. Rarely, relief of aortic stenosis relieves the heart block.\textsuperscript{[82]}

Aortic Regurgitation
Aortic regurgitation may develop acutely or more gradually as a chronic condition. Acute onset of severe regurgitation imposes a sudden large regurgitant volume on the LV, which has been normal.\textsuperscript{[556]} There is little time to accommodate to the volume load, and LV end-diastolic and left atrial pressures increase rapidly. Tachycardia is the primary compensatory mechanism but may be insufficient, and the clinical situation may quickly deteriorate to pulmonary edema and circulatory shock.

Patients presenting with chronic aortic regurgitation have combined volume and pressure overload of the LV.\textsuperscript{[550]} Compensatory mechanisms are primarily recruitment of preload reserve and LV hypertrophy. Most patients remain asymptomatic through a long compensatory phase that may last for decades.\textsuperscript{[550]}

The natural history of patients with aortic regurgitation depends primarily on its severity.\textsuperscript{[537]} Mild or moderate aortic regurgitation appears to affect activity and life expectancy minimally. LV structure and function begin to be adversely
affected, symptoms develop, and prognosis becomes more limited as severity of the regurgitation increases.

**Survival**

Even when aortic regurgitation becomes severe, there may be a long latent period (3-10 years), during which LV enlargement is only mild, symptoms are absent or mild, and the prognosis is good as long as the findings remain unchanged. Bonow and colleagues followed patients with chronic aortic regurgitation and normal EF. They found that 81% were alive without need of aortic valve replacement 5 years later. Less than 6% per year required aortic valve replacement because of symptoms or LV dysfunction at rest, less than 3.5% per year developed asymptomatic LV systolic dysfunction, and less than 0.2% per year died suddenly. Vasodilator therapy using nifedipine may benefit such patients and delay surgical intervention. When important symptoms develop, however, prognosis becomes severely limited (see Fig. 12-8).

The probability of death increases with development of specific risk factors. Symptoms of cardiac failure, development of ventricular premature beats, marked cardiomegaly (cardiothoracic ratio > 0.6), and ECG evidence of severe LV hypertrophy all increased the risk of death in a group of 180 surgically untreated patients with isolated severe aortic regurgitation of rheumatic etiology.

When severe aortic regurgitation develops acutely, as from infective endocarditis, the natural history is much less favorable. Only 10% to 30% survive more than 1 year after onset.

**Left Ventricular Structure and Function**

Cardiac size gradually increases in the presence of important aortic regurgitation. Quantitative angiography has shown that increased LV end-diastolic volume is directly related to the magnitude of aortic regurgitant flow.

Bonow and colleagues found a higher-risk subgroup within patients who are asymptomatic and have normal LV systolic function. Progressive enlargement (dilatation) of the LV or reduction in resting EF identified by serial echocardiography heralds onset of symptoms. Patients at risk for sudden death are those with extreme LV dilatation or an LV cavity dimension of 75 mm or more at end-diastole and 55 mm or more at end-systole (normal values are ≤55 mm and ≤35 mm, respectively). As LV size and end-diastolic volume steadily increase, eventually there is loss of LV reserve, and LV end-diastolic pressure then rises rapidly.

As the LV enlarges, LV hypertrophy begins to develop. In addition, the LV undergoes an increase in mass and wall thickness, and its shape and ultrastructure change. The myocardial cell hypertrophy and increase in interstitial nonmuscular tissue found in the pressure-overloaded LV of aortic stenosis are similar in the volume-overloaded LV of aortic regurgitation. Concomitant with hypertrophy, LV compliance decreases, compromising diastolic function. Finally, LV end-diastolic and left atrial pressures become elevated, with further increases during exercise.

At some point, LV stroke work fails to respond to increased wall stress (e.g., afterload increase by infusion of angiotensin). As LV systolic function decreases, LV end-systolic dimension steadily increases, and even in asymptomatic patients the rate of increase is about 7 mm per year.

Despite these changes and because of the complex interaction between aortic regurgitation and decreasing systemic vascular resistance, LVEF response to exercise is favorable for a considerable time. Eventually, however, it declines, and systolic function may even decrease during stress. Symptoms then worsen, and the decline in LV function accelerates.

**Bicuspid Aortic Valve**

Bicuspid aortic valve disease is usually asymptomatic in childhood, although rarely the presentation and natural history may take the form of critical congenital aortic stenosis (see Chapter 47). The clinical manifestations relate to the functional state of the valve (stenosis, regurgitation, or both), the aortopathy (aneurysm or dissection), and the potential for endocarditis. Longitudinal studies indicate that 25% to 40% of affected patients will have cardiac events (onset of heart failure, symptomatic aortic stenosis, stroke, endocarditis, or cardiac surgery) by age 50. More than one fourth of patients who are free of important aortic stenosis or regurgitation at initial diagnosis will require cardiac surgery within 20 years. Thus, many if not most patients with bicuspid aortic valve will eventually require surgical or catheter intervention.

Among adults, cusp calcification progressing to aortic stenosis is thought to be initiated by endothelial dysfunction and inflammation, lipoprotein deposition, and fibrosis, and contributed to by turbulent flow. Calcification is frequently present by age 40, and stenosis is often then progressive.

The natural history of aortic dilatation in patients with unoperated bicuspid aortic valve has been studied by Davies and colleagues. Compared with patients having a tricuspid aortic valve, aneurysm progression is greater (0.19 cm · y⁻¹ vs. 0.13 cm · y⁻¹), nearly twice as many undergo aortic surgery, and surgery occurs at a younger age. In a study using MRI and CT, additional involvement of the aortic root, aortic arch, or both was present in more than half the patients. Those with a bicuspid aortic valve are reported to have a ninefold increase in risk of acute ascending aortic dissection compared with those with a tricuspid valve, but the incidence of dissection remains low: 0.1% per patient-year of follow-up. Despite the risk for adverse cardiac events, 20-year survival in adults without important valve dysfunction at initial observation is equivalent to that of the general population.

**TECHNIQUE OF OPERATION**

**Isolated Aortic Valve Replacement**

**Initial Steps**

After the usual preparations and median sternotomy, cardiopulmonary bypass (CPB) is established at 34°C using a single two-stage venous cannula. A cardioplegia infusion catheter is positioned in the ascending aorta, and a coronary sinus perfusion catheter may be passed through a purse-string stitch in the right atrium and positioned in the coronary sinus. The cardioplegia infusion catheter, on one arm of a Y assembly on the cardioplegia infusion tubing filled with cardioplegic solution, is positioned in the ascending aorta. The other arm of the Y assembly, now clamped, also has two arms. One is connected to a second Y assembly, on each arm of which is an O-ring cannula to be used for direct cardioplegic infusion into the coronary ostia. The other arm can be attached to the
coronary sinus retrograde perfusion catheter (see Technique of Retrograde Infusion in Chapter 3).

Perfusate temperature is lowered and adjusted to 25°C to 28°C. The ascending aorta is occluded, promptly if ventricular fibrillation occurs, to prevent LV distention. The operation may be performed without a vent; alternatively, a vent may be introduced into the left atrium from the right side through the right superior pulmonary vein and advanced into the LV. The vent catheter may be introduced before aortic occlusion if ventricular fibrillation occurs or aortic regurgitation produces ventricular distension during cooling. Following aortic clamping, antegrade cold blood cardioplegia may be infused into the aortic root provided there is no aortic regurgitation. Even the slightest leak at the aortic valve will cause ventricular filling, although a properly functioning LV vent may prevent ventricular distention. Subsequent to cardiac electromechanical arrest, cold cardioplegia may be infused into the coronary sinus. Cardioplegic arrest may be accomplished by exclusive perfusion of the coronary sinus in the presence of important aortic regurgitation. A small aortotomy should be made or the aortic root vented when coronary sinus perfusion is performed. Alternatively, in the presence of aortic regurgitation, topical and systemic cooling of the vented LV may intentionally induce ventricular fibrillation, after which the aorta is promptly clamped, an aortotomy made, and direct coronary artery cardioplegia administered.

An initial aortotomy is made about 15 mm downstream from the origin of the right coronary artery. Its precise location is very important not only for surgical exposure but also because of space for intraaortic positioning of an allograft, autograft, or prosthetic valve, ease and security of closure, avoiding damage to the right coronary artery or its ostium, and facilitating aortic root enlargement if necessary. Exposure for this incision is facilitated by the first assistant’s retraction of the fat pad along the right atrioventricular groove over the aortic root. The pulmonary trunk may also need to be partially dissected from the aorta to avoid incising it. The initial incision is made directly anteriorly with scissors, facilitated by the collapsed state of the aorta. Once this small incision is made, the inside of the aortic root is visualized and a decision made as to whether an allograft, a pulmonary autograft valve, or a prosthesis will be used or repair performed (see “Nonreplacement Aortic Valve Operations in Adults” under Special Situations and Controversies later in this chapter).

The incision is extended. The surgeon has a choice depending on the operation to be performed:

- Extend the incision transversely (Fig. 12-9, A). This is the most common approach and has the advantage of providing good exposure of the aortic root without distorting it. The sinutubular junction is not disturbed. Exposure at the level of the aortic valve and below into the left ventricular outflow tract (LVOT) is usually very good.
- Extend the incision into the posterior commissure between the left and noncoronary cusps if posterior enlargement of the aortic root is required.
- Extend the incision obliquely (Fig. 12-9, B) into the noncoronary sinus to a point near the aortic anulus, to provide maximal exposure at the level of the aortic valve and below into the LVOT. This incision, which divides the sinutubular junction, can be extended into the anterior leaflet of the mitral valve for posterior aortic root enlargement.
- Extend the incision to divide the aorta (Fig. 12-9, C). This incision provides optimal exposure of the aortic root because the proximal aortic structures can be easily moved and displaced inferiorly and anteriorly so that the surgeon may visualize the intact aortic root and look directly into it. This incision is best for placing aortic allografts and stentless porcine bioprostheses inside the aortic root, as well as for aortic valve replacement with a pulmonary autograft or other procedures requiring replacement of the complete aortic root. It also provides excellent exposure for routine prosthetic valve implantation. Traction stitches are placed just above the aortic valve commissures for optimal exposure of the aortic root structures, regardless of type of incision.

The aortic valve is removed (Fig. 12-10, A). Unless the aortic valve disease is noncalcific, a short strip of narrow packing gauze can be inserted through the valve orifice into the LV (and some foolproof system is used to ensure its removal) to trap all calcific fragments that may escape during valvectomy. Neat, complete removal of the valve, particularly when heavily calcified, without damage to the LV-aortic junction, ventricular septum, or aortic wall, is one of the operation’s critical aspects. Usually an area exists in about the midportion of the right coronary cusp where an initial scissors cut can be made from the free edge to the point of cusp attachment. This incision allows entry of a knife blade to incise precisely along the attachment of the right coronary cusp toward the commissure between left and right coronary cusps. This commissure may also be calcified, but the incision can usually be carried between it and the aortic wall, often with scissors. The incision is then carried along the attachment of the left coronary cusp, stopping at a point about two thirds of the distance to the left coronary–noncoronary cusp commissure, because beyond that point, there is a tendency to carry the incision into the aortic wall or LV-aortic junction.

Returning to the right coronary cusp, the incision is extended toward the right coronary–noncoronary cusp commissure. In this area and in this commissure the calcification is often especially abundant, sometimes extending onto the underlying ventricular septum or, especially at the commissure, onto the aortic wall or underlying membranous septum. Thus, in dissecting this area, great care must be taken in deciding whether to cut through the calcific cusp attachment to the aortic wall or to go around some of the calcific material and leave it for later piece-by-piece removal. To the extent possible, one-piece removal is preferable, but perforation of the septum, LV-aortic junction, or aortic wall should not become a risk.

When the aortic valve is completely replaced by calcium deposits, or when the deposits extend into the sinus aorta or anterior leaflet of the mitral valve, it is useful to mobilize the calcified tissues by the endarterectomy technique. Using a scalpel, a shallow incision is made in the aortic intima along the calcified deposit. This allows insertion of an endarterectomy spatula (Freer septum elevator) to lift the intact hard deposit away from the soft underlying aortic or mitral valve tissues without fragmenting the calcified material. The incision is carried down along the attachment of the noncoronary
Figure 12-9  Initial steps for aortic valve replacement.  

**A.** Initial transverse incision into ascending aorta (*dashed line*) is 15 mm above right coronary artery. Lengthened just a little, it suffices for evaluating the aortic valve and deciding on procedure to be used. Lengthened further, it is sufficient for aortic valve replacement.  

**B.** Incision is extended into middle of noncoronary sinus of Valsalva, providing excellent exposure of aortic valve for its replacement with prosthetic device.  

**C.** Transverse incision may be extended to divide aorta above sinutubular junction. This permits working within the intact aortic root for correct positioning of aortic valve allografts or stentless xenografts below the coronary arteries (subcoronary technique).
Figure 12-10  Excision of aortic valve and débridement. A, A scissors cut is made in aortic valve cusp, extending to, but not into, aortic wall. Valve excision is along hinge line of aortic valve cusp. Careful excision of valve usually includes removing most calcium deposits along with the valve. B, Residual calcium deposits are débrided from aortic anulus and sinus aorta. Sellman or other forceps and bone rongeurs are instruments commonly used to accomplish this.
cusp, stopping about two thirds of the distance to the commissure between the noncoronary and left coronary cusps. The latter commissural area, which is at particular risk of junctional or aortic wall perforation during valvectomy, can then be approached with excellent visibility from both sides; the incision is carried through this area with firm upward traction on the valve.

After the valve is excised, the bed is examined and any loose calcific particles removed. Any remaining fragments are grasped with forceps or small rongeur and gently enucleated with a twisting motion (Fig. 12-10, B).

The downstream area of aorta is irrigated and examined for any loose calcific fragments, and the valve bed is wiped with gauze and irrigated with cold saline solution to remove any tiny fragments. The LV vent is turned off so that it will not suck fragments into the inaccessible depths of the ventricle, and the gauze is carefully removed from the LV cavity, most likely having trapped a few small calcific fragments. The LV cavity is then vigorously irrigated and aspirated with high suction and inspected for fragments. Generally, no fragments are found. With the precautionary measures against calcific embolization complete, the LV vent is again activated.

Prosthetic Aortic Valve
Insertion of a prosthetic aortic valve is the most common operation for replacing the aortic valve. The anulus is sized and an appropriate-size prosthesis selected. There is no advantage in choosing an oversized prosthesis that will erode the aortic anulus. Instead, if the aortic anulus is too small to accommodate a prosthesis that will provide adequate hemodynamic performance, a supraanular device may be chosen or the anulus enlarged (see “Managing the Small Aortic Root” under Special Situations and Controversies later in this chapter).

Interrupted Suture Technique Synthetic suture material is used, with a compressed PTFE pledget placed centrally and needles at each end. Alternating suture colors (green, white) simplifies sorting so that sutures may be held together as a group for each aortic sinus. Mattress stitches are taken through the aortic valve anulus beginning at the commissure between the left and right coronary cusps. The suture is placed through the sewing ring of the prosthesis after completing each anular pass. Stitches are placed in the right coronary anulus working clockwise toward the commissure between the right and noncoronary sinus (Fig. 12-11, A). Separate stitches are placed close to one another, and the space along the anulus is taken beneath the pledget of the mattress stitch. The prosthesis is held away from the aortic anulus until all stitches have been placed.

The anulus of the left coronary sinus of Valsalva is then approximated to the sewing ring of the aortic valve prosthesis, working counterclockwise from the commissure between the left and right coronary cusps (Fig. 12-11, B). The anulus of the noncoronary sinus of Valsalva is then approached to the valve prosthesis, working clockwise from the commissure between the right and noncoronary cusp toward the commissure between the left and noncoronary cusp (Fig. 12-11, C). Needles are passed through the anulus in a backhand manner. The three groups of sutures are then strongly retracted so that the prosthesis may be slid over the suture loops into the aortic anulus. Position of the occluder mechanism may be adjusted before the valve holder is removed.

Sutures are sorted and tied down in order, working first in the noncoronary sinus in a counterclockwise approach. The first suture in the left coronary sinus closest to the commissure between the left and right coronary cusps is tied to secure seating of the prosthesis directly across the anulus from those sutures already tied in the noncoronary sinus. The sutures of the left coronary sinus are tied down counterclockwise. Sutures are tied in the right sinus, working clockwise to complete the procedure (Fig. 12-11, D). For valve prostheses that have any part of the device projecting below the sewing ring, such that it is positioned partially below the anulus in the LVOT, the order of tying should be altered so that the prosthesis is first secured adjacent to the portions of the device below the anulus.

An alternative technique for placing the pledget stitches is used for the small aortic anulus (Fig. 12-11, E). Pledgets are placed below the anulus in the LVOT by passing a double-needle suture with center pledget as a mattress stitch from below the anulus and up through the prosthesis. A larger prosthesis is thereby secured above the anulus as the anulus is compressed between the pledget and device.

Continuous Suture Technique Continuous suture technique provides the advantage of tight approximation of the prosthesis to the aortic anulus, because the suture loops can slip through the tissues so that tension is equalized with heart motion. Inserting a slightly larger prosthesis may also be possible because an interrupted mattress suture technique may bunch tissues together.

The aortic anulus is divided into three segments by the commissures. During valve replacement, the anulus is further subdivided into six subsegments at the midpoint on the anulus between the commissures. Polypropylene suture (2-0) is used, with needles at each end and a compressed PTFE pledget in the center of the suture. An initial mattress stitch is placed at the center of the sinus of Valsalva through the anulus of the aortic valve and brought through the sewing ring of the prosthesis (Fig. 12-12, A). The prosthetic valve is held away from the anulus and positioned and retracted for added exposure. Exactly three stitches are placed between the initial pledgeted stitch and the commissure on each side of the sinus. The final stitch at each end is secured to the wound drapes by a hemostat. A loop of size 0 suture is placed around the polypropylene suture as the first suture loop is completed through the prosthesis in each subsegment. This suture loop is held by a hemostat to be used to adjust tension on the suture line.

Sutures in the right coronary anulus are placed from the center toward the commissures in the first and second subsegments. The initial stitch in the left coronary sinus passes through the sewing ring of the prosthesis opposite the last stitch of the second subsegment. Working from the center to the commissures in the left coronary sinus, the third and fourth subsegments are approximated to the prosthesis, and then the fifth and sixth subsegments are completed in the noncoronary sinus.

Traction is placed on the six size 0 silk loop sutures to pull the prosthesis into the anulus of the aortic valve (Fig. 12-12, B). The occluder of the prosthesis is opened, and the area below the prosthesis is checked to ensure that no loose suture loops exist in the LVOT beneath the prosthesis.
Aortic valve replacement with mechanical prosthesis or stent-mounted bioprosthesis, interrupted suture technique. 

**A**, Polytetrafluoroethylene felt pledget–reinforced 2-0 braided polyester suture is placed as interrupted horizontal mattress stitches passed from aortic side through aortic annulus. Needles are then passed through sewing cuff of replacement device. Suturing begins at commissure between left and right sinus of Valsalva and proceeds clockwise in right coronary sinus to commissure between right and noncoronary sinus. Alternating color of suture aids suture sorting.

**B**, Suturing continues in left coronary sinus of Valsalva in a counterclockwise fashion to commissure between left and noncoronary sinus.

*Continued*
Sutures surrounding anterior commissure should not penetrate tissues of membranous septum, to protect the His bundle from injury. Suturing is completed in noncoronary sinus of Valsalva. Prosthesis is passed over sutures into position on aortic anulus. Sutures are sorted and tied to fix prosthesis to aortic anulus.
because of the thickness of its wall. Therefore, it must be 1 to 2 mm smaller in internal diameter than the measured aortic anulus. This will allow some redundant aortic valve cusp to provide a larger than normal coaptation surface to accommodate the expected tissue shrinkage for several weeks after implantation.

The aortic allograft is removed from the liquid nitrogen freezer valve bank and thawed by protocol. The septal muscle is excised, with a finger placed inside the aorta to stabilize the graft, gauge the thickness of the trimmed graft, and remove endothelial cells that are antigenic. Excess aorta is trimmed from the valve cusps, leaving a 3- to 4-mm rim of aorta beyond attachment of the cusps. Most of the sinus aorta is removed from the right and left coronary sinuses, leaving the noncoronary sinus intact (Fig. 12-13, A). This technique was described by Ross and colleagues in London and has been used successfully for many years.

The allograft is implanted in anatomic position. Three stitches are used to attach it to the outflow tract. The first suture is 3-0 or 4-0 polypropylene, placed using two small (17-mm) strong half-circle needles. This suture is chosen for high needle strength and low tissue drag. The suture is placed through the patient’s aortic outflow tract below the medial commissure between the right and left coronary sinuses and through the septal myocardium below the corresponding commissure in the graft; the stitch is placed below the anulus of the aortic valve. The other two stitches are simply stay sutures placed to assist in aligning the allograft to the patient’s

Allograft Aortic Valve
Replacing the aortic valve with a transplanted human aortic valve became more feasible and available to surgeons because of improved commercial cryopreservation techniques.

Subcoronary Technique Because with this technique the graft is to be sewn in “freehand” using the natural aorta for support, a clear understanding of the anatomy and spatial relationships of the aortic root is essential. Important deformity of the aortic sinuses should be appreciated and corrected or the procedure abandoned in favor of conventional valve replacement or aortic root replacement techniques.

A transverse aortotomy is made initially. After assessing aortic valve morphology and anatomy of the aortic root, the incision is extended to transect the aorta (see Fig. 12-9, C). The aortic valve is excised and anulus débrided by usual techniques. Diameter of the aortic root at the level of the ventricular-aortic junction (anulus) is determined using standard sizing devices. This dimension must be accurately measured and clearly visualized. The aortic valve allograft to be placed inside the aortic root will consume space simply because of the thickness of its wall. Therefore, it must be 1 to 2 mm smaller in internal diameter than the measured aortic anulus. This will allow some redundant aortic valve cusp to provide a larger than normal coaptation surface to accommodate the expected tissue shrinkage for several weeks after implantation.

The aortic allograft is removed from the liquid nitrogen freezer valve bank and thawed by protocol. The septal muscle is excised, with a finger placed inside the aorta to stabilize the graft, gauge the thickness of the trimmed graft, and remove endothelial cells that are antigenic. Excess aorta is trimmed from the valve cusps, leaving a 3- to 4-mm rim of aorta beyond attachment of the cusps. Most of the sinus aorta is removed from the right and left coronary sinuses, leaving the noncoronary sinus intact (Fig. 12-13, A). This technique was described by Ross and colleagues in London and has been used successfully for many years.

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Figure 12-12 Aortic valve replacement with mechanical prosthesis or stent-mounted bioprosthesis, continuous suture technique. A, Polytetrafluoroethylene felt pledget–reinforced 2-0 polypropylene suture is placed through aortic anulus as a horizontal mattress stitch at midpoint of right coronary sinus. Stitch is brought through sewing cuff of prosthesis. Exactly three suture loops are placed through aortic anulus and sewing cuff between initial stitch and commissure. Tension loop is placed around first suture loop. After suturing right sinus, prosthesis is attached to left coronary sinus and finally to noncoronary sinus. B, Prosthesis is approximated to anulus of aortic valve by pulling up suture loops. Tension loops are pulled up to tightly approximate sewing cuff to deepest point in sinus of Valsalva. Suture ends at commissures are then pulled up to seat the valve in aortic root. Sutures are joined at commissures.
Figure 12-13  Aortic valve replacement with aortic valve allograft, subcoronary technique. A, Aortic allograft is chosen that is no more than 2 mm smaller in internal diameter than left ventricular (LV) outflow tract at aortic anulus. Cryopreserved aortic allograft is taken through the standard controlled thawing process. Its septal myocardium is thinned out and anterior leaflet of mitral valve removed along with tissues below aortic valve to create a level plane. Allograft aorta is removed from right and left coronary sinus of Valsalva, leaving 3 to 4 mm of aorta beyond hinge point of valve. Noncoronary sinus remains intact, maintaining relationships of commissures on each side of sinus. B, Patient’s aorta is divided above sinutubular junction so that valve replacement may proceed within the intact aortic root. Traction stitches are placed above each commissure. Allograft is inverted through its anulus into patient’s left ventricular outflow tract (LVOT). Allograft is attached to aortic anulus and below commissures in a generally level plane using continuous stitches of 3-0 polypropylene suture. C, Allograft is pulled back into aorta. Sinus aorta of allograft is attached to patient’s sinus aorta below the coronary ostia. Sutures proceed progressively up commissures to accurately recreate relations of aortic valve within aortic root. Suturing begins at lowest point of sinus of Valsalva and proceeds to top of each commissure. Separate sutures are used for each sinus and are joined at top of commissures. Intact noncoronary sinus of graft is sewn to patient’s aorta by continuous suture.
aortic root. These sutures will be removed because the primary suture line includes their position. They are placed beneath the appropriate commissure of the allograft and directly below the anterior and posterior commissures of the patient’s aorta.

The allograft valve is lowered into position in the patient’s aortic root. Commissures of the allograft are inverted through its anulus into the patient’s LV so as to expose the subvalvar edge of the allograft. A knot is placed in the primary suture, and the stay sutures are tightened to align the allograft with the LVOT. Stitches are placed between the allograft and the LVOT at or below the level of the anulus, attempting to make a level suture line (Fig. 12-13, B). Because the aortic anulus is not circular but crescent shaped, the stitches are well below the fibrous anulus in the subcommissural region and through this fibrous tissue of the anulus at the midpoint of the aortic sinus (see “Cardiac Valves” in Chapter 1). The stitches below the left coronary sinus are placed first. The suture line is taken to a point below the posterior commissure. Using the opposite needle, the stitches between the allograft and LVOT are placed below the right coronary sinus and completed below the noncoronary sinus (Fig. 12-13, B). Alternative suture techniques are equally effective, such as using three separate polypropylene sutures to facilitate placing multiple suture bites without “snuggling” the suture line to improve exposure, after which the sutures are tightened with a blunt nerve hook prior to tying. In the small aortic root, simple sutures of 4-0 polypropylene are also effective.

The commissures of the allograft are pulled out of the LV so that the allograft assumes its normal position and configuration. The allograft commissures are attached to the patient’s sinus aorta using continuous 4-0 or 5-0 polypropylene sutures. Separate sutures are used for each aortic sinus. The first stitch is taken deep in the sinus aorta at mid-position in the sinus slightly above the aortic anulus and then passed through the allograft. Suturing proceeds along the sinus aorta toward the commissure, so as to place the allograft flat against the patient’s aortic wall. The final stitch is placed at the top of the commissure, leaving the suture to be secured later (Fig. 12-13, C). Suturing proceeds in each aortic sinus until the allograft is completely attached. Either the right or left coronary sinus is completed first, sewing from the center point of the sinus to each of the commissures using opposite ends of the suture. The repair is completed in the noncoronary sinus by shortening the allograft aorta to approximate the height of the patient’s intact noncoronary sinus. The two edges of the aorta are simply oversewn by continuous suture so that the intact noncoronary sinus of the allograft is completely enclosed within the aorta. Optionally, the space between the allograft noncoronary sinus and the underlying native aortic wall can be partially obliterated with mattress sutures that are tied outside the native aorta. The ends of the patient’s aorta are then reanastomosed by continuous suture.

Intraoperative echocardiography is used to confirm aortic valve competence.

Root-Enlarging Technique An aortic allograft may be used for valve replacement as part of a root-enlarging operation. A transverse incision is made in the patient’s aorta. The incision is extended to the posterior aspect of the aorta and into the posterior commissure between the left and noncoronary sinuses. Incision into the triangular space of the commissure between the fibrous attachment of the native aortic valve opens the aortic root where there is little fibrous support so that the edges of the aortotomy will separate widely. The incision is taken to the upper edge of the anterior leaflet of the mitral valve, but it does not need to enter the leaflet tissue to provide the desired separation of the edges of the incision. The increased diameter of the patient’s aortic root is measured and an appropriately sized aortic allograft chosen. The allograft is trimmed, leaving the noncoronary sinus intact. The sinus aorta is removed from the left and right sinuses, leaving a few millimeters attached to the fibrous support of the cusps. The allograft is attached to the rim of the aortic-mitral anulus (without entering the actual anterior leaflet of the mitral valve) and superior aspect of the left atrium with interrupted 3-0 or 4-0 polypropylene sutures. The stitches are placed in the corresponding mitral valve and left atrium of the allograft’s noncoronary sinus. A PTFE felt strip is fashioned to slightly more than the length of the unsupported area of the separated aortotomy. The sutures of the noncoronary sinus are then tied down over the felt strip so as to incorporate it and fill in any potential defects in the suture line. The commissures of the valve are inverted into the LVOT, and the rest of the repair is completed according to the approach previously described under “Subcoronary Technique.” The allograft’s intact noncoronary sinus is used to close the aortotomy and widen the aortic root.

When greater enlargement of the LVOT is required, or when there is infective endocarditis with extension of anular abscess into the anterior leaflet of the mitral valve, the incision in the aorta is extended across the mitral valve anulus into the middle of the valve’s anterior leaflet. Anular abscesses are thoroughly débrided and much of the anterior leaflet of the mitral valve removed (Fig. 12-14, A). The anterior leaflet of the mitral valve is left attached to the aortic allograft and used to widen the LVOT or repair defects in the patient’s mitral valve (Fig. 12-14, B). The defect in the roof of the left atrium is closed with a patch taken from the aorta of the allograft or with bovine pericardium.

Aortic Root Replacement Technique An aortic allograft may be used to replace the patient’s aortic root completely when gross deformity is caused by infection or congenital anomaly, or it may be used to enlarge the root. Many surgeons use this technique routinely because aortic valve competence is virtually assured due to retention of the valve relationships within the intact aortic root of the allograft.

An initial transverse aortotomy is made (Fig. 12-15, A). After decision to proceed with aortic root replacement, the patient’s aorta is transected (Fig. 12-15, B). The sinus aorta is removed except for a rim surrounding the ostia of the coronary arteries. The aortic valve is removed and an appropriately sized aortic allograft selected. The allograft is used intact and in natural anatomic orientation, with only the excess of septal myocardium and the anterior leaflet of the mitral valve removed. Size match is not nearly as important as it is for freehand subcoronary valve replacement, but if the aortic anulus is more than 3 mm larger in diameter than the largest available aortic allograft, the patient’s aortic root should be narrowed to approximate the size of the allograft. This can be done conveniently by placing a pledged mattress stitch through the aortic anulus alongside the commissures so that when tied, the intecusp triangle below the commissure is obliterated (see “Method for Reducing Diameter of Dilated Aortic Anulus” later in this chapter).
Figure 12.14  Aortic valve replacement with allograft, aortic root enlarging technique, or repair of anular abscess. A, Aortotomy is extended through posterior commissure into abscess of patient’s mitral valve anterior leaflet. Abscess is débrided or simply incised if procedure is used to widen left ventricular outflow tract (LVOT). B, Anterior leaflet of mitral valve is left attached to allograft and used to widen, LVOT or repair defects caused by endocarditis. Anterior leaflet repair is done with interrupted stitches for greatest security. Defect in left atrium is closed with a patch of aorta from the allograft.
Figure 12-15  Aortic valve replacement, aortic root replacement technique. A, Transverse aortotomy is made. B, Traction stitches are placed in aorta above each commissure, and aortic valve is excised. When decision is made to proceed with complete replacement of aortic root, aortotomy is extended to divide aorta. Aorta is removed from sinuses of Valsalva, except for generous buttons around coronary artery ostia. C, Aortic allograft is minimally trimmed, removing anterior leaflet of mitral valve. Allograft root is attached to anulus of patient’s aortic valve with interrupted stitches of 3-0 or 4-0 polypropylene suture. Simple stitches are used.
D, Suture loops are tied down over a narrow strip of polytetrafluoroethylene felt or pericardium to support and fix diameter of aortic anulus and seal spaces between stitches. E, Left coronary artery button is anastomosed to opening in allograft created by excising left coronary artery of graft. Continuous stitches of 4-0 or 5-0 polypropylene are used, depending on thickness of tissues. F, Opening is made in allograft at position of right coronary artery unless patient’s aortic root was greatly dilated. Dilatation of aortic root displaces right coronary artery; in this case, it is advisable to complete the aortic anastomosis so that aorta may be filled under pressure to properly locate position for anastomosis of right coronary artery. G, End-to-end anastomosis of allograft to patient’s aorta completes the repair.
Figure 12-16  Aortic valve replacement, porcine xenograft stentless bioprosthesis. A, St. Jude Medical Toronto SPV bioprosthesis is presented with sinus aorta removed from all three sinuses of Valsalva. Device is covered with polyester fabric. Medtronic Freestyle porcine xenograft bioprosthesis is presented with intact aortic root with less fabric. There is an inflow sewing ring, and fabric covers portions of septal myocardium on aortic root. Aorta is removed by the surgeon from right and left coronary sinuses of Valsalva, leaving noncoronary sinus intact. B, Inflow sewing cuff of bioprosthesis (Freestyle) is attached to aortic valve anulus with continuous stitches of 3-0 polypropylene suture. Tension loops are placed around every third suture loop to make it easier to tighten suture and approximate bioprosthesis to aortic anulus. Alternatively, simple interrupted stitches of 2-0 or 3-0 braided polyester are used.
The allograft is attached to the LVOT at the aortic anulus and below the commissures by simple interrupted stitches of 3-0 or 4-0 polypropylene (Fig. 12-15, C). The key to a hemostatic proximal suture line is use of a PTFE felt collar. The felt is approximately 5 mm wide and long enough to encircle the allograft. The allograft is slipped over the sutures into the desired position in the LVOT. The sutures are then tied down, incorporating the felt strip within the suture loops (Fig. 12-15, D).

An alternative hemostatic method is to incorporate a double-suture-line technique in which the first suture line uses three separate polypropylene continuous sutures (one for each sinus), placing the sutures as in the interrupted technique. They are gently tightened with a nerve hook and tied. A second suture line incorporates the cut edge of the aortic wall adjacent to the anulus and the adventitia of the allograft immediately above the prior suture line.

The coronary ostia on the allograft are removed to create openings 5 to 10 mm in diameter (Fig. 12-15, E and F). The coronary arteries are anastomosed to the allograft by continuous 4-0 or 5-0 polypropylene suture using a small needle (exact size depends on thickness of the tissues). The left coronary anastomosis is created first (Fig. 12-15, E), followed by the right coronary anastomosis (Fig. 12-15, F). Repair is
completed by end-to-end anastomosis of the distal end of the allograft to the patient’s aorta (Fig. 12-15, G). Continuous stitches of 3-0 or 4-0 polypropylene are used.

**Cylinder Technique** The aortic valve allograft may be inserted as a cylinder within the aortic root, using a technique described by O’Brien and colleagues.\(^3\)

Buttons of sinus aorta are excised, including the ostia of the left and right coronary arteries of the allograft.\(^3\) The resultant opening may need to be extended proximally because the allograft valve now lies a little downstream from its native position.\(^3\) This technique has the potential disadvantage of too much open space between the allograft and native aortic walls.

In a slight modification of the cylinder technique, the center of each sinus is removed before inserting the cylinder of allograft, leaving an intact strut of aortic wall over each sinus.\(^8\) This approach maintains the integrity and special relationships of the allograft until the majority of the second (downstream) suture line of each sinus is complete and the bar over that sinus excised.
Porcine Xenograft Stentless Bioprosthesis

Several manufacturers supply porcine xenograft stentless aortic valves. The devices most frequently used are manufactured by St. Jude Medical and Medtronic (Fig. 12-16, A). The St. Jude medical device (Toronto SPV) is supplied for subcoronary valve replacement with the sinus aorta removed from all three sinuses of Valsalva. The device is covered with a thin polyester mesh. Proper insertion depends on near-normal diameter relationships of the aortic anulus and the sinutubular junction. The Medtronic device (Freestyle) is presented as the entire untrimmed aortic root.

Subcoronary Technique

The implant technique is similar to aortic valve replacement with aortic allografts. The aorta is divided about 1 cm above the sinutubular junction, or a transverse aortotomy is made in the same location. The proper size of xenograft is chosen using the sizing devices supplied by the manufacturer. The diameter of the aortic anulus is measured, and the same-size xenograft is chosen for implantation. Downsizing is not required because the xenografts are sized according to outside diameter of the device, in contrast to aortic allografts, which are sized according to inside orifice diameter. Some surgeons choose a xenograft 1 or 2 mm larger than the anulus because these flexible stentless bioprostheses fit easily into the aortic root. However, no advantage exists to greatly oversized xenografts increase the gradient across the valve.

The Medtronic Freestyle bioprosthesis requires trimming before implantation (see Fig. 12-16, A). The sinus aorta is removed from the right and left sinuses of Valsalva. The noncoronary sinus remains intact to fix the position of two of the three commissures of the valve. The lower edge of the aortic root of the xenograft is covered with polyester cloth to assist with implantation and to prevent shrinkage when xenograft septal myocardium is absorbed. This cloth limits how deeply the sinus aorta may be excised, especially in the right coronary sinus. Care should be taken not to disrupt the cloth covering.

The aortic valve is excised in the usual manner, and all calcific deposits are removed from the aortic anulus and sinus aorta. Exposure is enhanced by traction sutures placed at the sinus rim above each commissure. Markings on the cloth covering the lower edge of the xenograft correspond to each commissure. Continuous 3-0 polypropylene suture is used to attach the lower edge of the xenograft to the patient’s aortic anulus. A small needle with a taper-cut design is best to allow easier penetration of the polyester fabric. The suture line is started in the intercusp triangle below the commissure between left and right sinuses.

The prosthesis is held away from the anulus as suture loops are placed (Fig. 12-16, B). A heavy suture (0 or 2-0) is passed around every third suture loop to act as a tension-adjusting loop suture. These tension loops are secured by a small hemostat. Suturing proceeds below the right sinus to the commissure below the right and noncoronary sinuses. Stitches are placed mostly through the thick fibrous hinge of the aortic valve (anulus), attempting to level the plane of the suture line rather than strictly following the semilunar plane of the valve hinge (Fig. 12-16, C). From the midpoint of the right coronary sinus to the commissure between the right and noncoronary sinuses, the stitches must be through the anulus, not below and into the myocardium, to protect the conduction system from injury.

Suturing continues below the left sinus of Valsalva until below the commissure between the left and noncoronary sinuses. A separate suture is used for noncoronary sinus repair. Tension loops are placed around every third stitch. The prosthesis is seated in the aortic root by sequentially pulling up on the tension loops to approximate the fabric of the xenograft to the aortic anulus. Alternatively, the inflow suture line may be simple interrupted stitches placed with the xenograft held away from the anulus (see Fig. 12-16, B). Many surgeons prefer the interrupted stitch technique because it is similar to implanting prosthetic devices and avoids the possibility of a purse-string effect.

The sinus aorta of the xenograft is attached to the patient’s sinus aorta by continuous stitches of 4-0 polypropylene (Fig. 12-16, D). The initial stitch is placed in the patient’s sinus aorta just below the right coronary ostia. The suture line comes very close to the coronary ostia to achieve proper fit of the xenograft tissues to the patient’s sinus aorta. This is especially true for the right coronary sinus of the xenograft, which is covered with cloth quite high on its external surface. The commissure between the right and left sinuses of the xenograft must be carefully located so as not to distort the xenograft. Suturing continues beneath the left coronary artery to the top of each adjacent commissure (Fig. 12-16, E).

The noncoronary sinus repair is accomplished by trimming the xenograft to the same height as the patient’s noncoronary sinus aorta. The two edges of tissue are approximated by direct suture (see Fig. 12-16, E). Sufficient space usually exists in the patient’s noncoronary sinus of Valsalva to accommodate the xenograft without distortion. If the diameter (length) of the aorta at the sinutubular junction in the noncoronary sinus is greater than that of the sinutubular junction of the xenograft, the discrepancy can be compensated for by placing stitches more closely on the xenograft than the patient’s aorta. The repair is completed by anastomosis of the aorta or closure of the transverse aortotomy.

Aortic Root Replacement Technique

The Medtronic Freestyle device may be implanted as a complete aortic root replacement (Fig. 12-16, F). This method is employed when the aortic root is distorted or when it is dilated enough that support for the xenograft as a subcoronary valve implant will be inadequate. The aorta is divided just above the sinutubular junction. The left and right coronary arteries are mobilized, retaining a generous rim of sinus aorta around the coronary ostia, and the noncoronary sinus aorta is excised. The device is implanted as a complete root. The infow suture line is placed as for subcoronary implantation using continuous 2-0 polypropylene. The suture line is started in the intercusp triangle below the commissure between left and right sinuses.

The prosthesis is held away from the anulus as suture loops are placed (Fig. 12-16, B). A heavy suture (0 or 2-0) is passed around every third suture loop to act as a tension-adjusting loop suture. These tension loops are secured by a small hemostat. Suturing proceeds below the right sinus to the commissure below the right and noncoronary sinuses. Stitches are placed mostly through the thick fibrous hinge of the aortic valve (anulus), attempting to level the plane of the suture line rather than strictly following the semilunar plane of the valve hinge (Fig. 12-16, C). From the midpoint of the right coronary sinus to the commissure between the right and noncoronary sinuses, the stitches must be through the anulus, not below and into the myocardium, to protect the conduction system from injury.
Figure 12-17  Aortic valve replacement with pulmonary autograft (Ross procedure), aortic root replacement technique. A, Ascending aorta is divided, aortic valve is removed, and all aorta from sinuses of Valsalva is excised except for generous buttons around coronary artery ostia. Traction stitches are placed above each commissure. B, Pulmonary trunk is divided at bifurcation. Pulmonary valve is inspected to assure normal morphology. C, Dissection between medial commissure of aortic valve and pulmonary trunk enters infundibular septum. Plane between infundibular septum and right ventricular outflow tract (RVOT) is identified and dissection carried as far behind pulmonary trunk as is convenient. D, RVOT is opened anteriorly 5 mm below pulmonary valve.
E, Incision of RVOT is extended posteriorly to extent of previous dissection (C). F, Shallow incision is made below pulmonary valve posteriorly in RVOT, joining extent of RV incisions. Angle of scalpel is changed so that ventricular myocardium may be shaved off infundibular septum without injuring underlying first septal branch of left anterior descending coronary artery. G, Pulmonary autograft trunk is transferred to aortic position. Simple interrupted stitches of 3-0 polypropylene are used to attach pulmonary autograft to aortic anulus (see Fig. 12-15, B).
H, Narrow strip of polytetrafluoroethylene felt or pericardium is placed within suture loops. Pulmonary autograft is partially inverted into left ventricular outflow tract (LVOT). Sutures are tied to secure pulmonary autograft to anulus of aortic valve, making sure that there is direct tissue approximation and keeping support strip to the outside. I, An opening is made in posterior sinus of Valsalva of pulmonary trunk and a narrow strip of tissue removed from one side to create a site for anastomosis of left coronary artery. J, Left coronary artery is anastomosed to pulmonary trunk using continuous stitches of 5-0 polypropylene. K, Pulmonary trunk is anastomosed in end-to-end fashion to ascending aorta. Aortic occlusion clamp is removed temporarily to fill pulmonary autograft under pressure so that proper position for right coronary artery anastomosis can be located. A small opening is made into graft, and right coronary artery is anastomosed to it.
Figure 12-17, cont’d  L, A cryopreserved pulmonary allograft of appropriate size, having previously been selected and thawed, is anastomosed in end-to-end fashion to pulmonary artery bifurcation. Exposure for this anastomosis may sometimes be better if it is performed before aortic anastomosis. Proximal end of pulmonary allograft is anastomosed to RVOT using continuous stitches of 3-0 polypropylene. Stitches are placed through only partial thickness of infundibular septum posteriorly over location of first septal branch of left anterior descending coronary artery. M, Completed repair: aortic valve replacement with pulmonary autograft, pulmonary trunk replacement with pulmonary allograft.
in the porcine aortic root are closer together than in humans. It is usually necessary to create another opening into the right coronary sinus of the graft at an appropriate location to prevent kinking of the patient’s right coronary artery. The position is usually to the right of the right coronary artery of the porcine root, although it may be placed on part of the base of the porcine right coronary artery. Proper location of the right coronary artery is facilitated by filling the RV with blood from the pump-oxygenator. Any evidence of myocardial ischemia after aortic root replacement indicates need for revision of the location of the coronary anastomosis or for coronary artery bypass grafting.\textsuperscript{119}

**Autograft Pulmonary Valve**

The aortic valve may be replaced with the patient’s own pulmonary valve (pulmonary autograft) and a pulmonary allograft used to replace the pulmonary valve. This operation was devised by Ross and carries his name.\textsuperscript{119} The operation has the advantage of placing autogenous tissue in the high-pressure aortic position that theoretically should last indefinitely, assuming the procedure is technically correct. (See “Selection of Technique and Choice of Device for Isolated Aortic Valve Replacement” later in this chapter). The allograft tissue is placed in the low-pressure pulmonary position, where even if it should fail, valve regurgitation is tolerated for a long time.

CPB is established using two cannulae for venous drainage. A right-angle cannula is placed directly into the superior vena cava at the pericardial reflection. The other is placed in the inferior vena cava through the right atrium at the diaphragm (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Alternatively, a single two-stage venous uptake cannula may be used, placing the second-stage opening low in the right atrium near the inferior vena cava orifice. Vacuum-assisted venous return provides more safety and reserve when the single-cannula technique is used, reducing the risk and consequences of air lock, which may occur in a gravity drainage system when the RV is opened (see “Vacuum-Assisted Venous Return” in Section I of Chapter 2). Oxygenated blood is returned to the ascending aorta.

**Pulmonary Autograft Technique**

The aortic root is explored through the usual transverse incision. Once it is determined to proceed with the pulmonary autograft operation, the ascending aorta is divided, the aortic valve removed, and the entire sinus aorta excised except for a generous rim around the coronary ostia (Fig. 12-17, A). Traction stitches on the aorta above the coronary arteries are helpful. Only the fibrous connection of the aortic cusps remains for attachment of the pulmonary autograft. Traction stitches are placed above each commissure. Diameter of the aortic anulus is measured using Hegar dilator sizers.

The pulmonary trunk is separated from the aorta up to its bifurcation. It is divided at the bifurcation, taking care not to shorten the right pulmonary artery (Fig. 12-17, B). The pulmonary valve is inspected from above. If it is normal, operation may proceed. If it is abnormal, the pulmonary artery is reanastomosed and an aortic allograft used to replace the aortic root.

Dissection between the medial commissure of the aorta and the pulmonary trunk comes down onto the muscle of the right ventricular outflow tract (RVOT; Fig. 12-17, C). Thorough dissection between the aorta and pulmonary trunk, especially low onto the RV in the plane between the RVOT and the infundibular septum, makes removing the pulmonary trunk much easier.

The anterior intercusp triangle below the anterior commissure is identified as a reference point for opening the RVOT. A small right-angle clamp is placed precisely in the anterior intercusp triangle and pushed through the anterior wall of the RV. The small opening is carefully enlarged. The pulmonary trunk is separated from the RV, looking inside frequently to maintain appropriate length of the ventricle below the pulmonary valve (Fig. 12-17, D). Incision of the RVOT continues on the right side and posterior to the extent of previous dissection (Fig. 12-17, E).

The critical and unique part of the Ross operation is separating the pulmonary trunk from the RVOT above the infundibular septum. When done correctly, this part of the procedure makes the entire operation safe. Anatomy of the subpulmonary infundibulum is described in “Right Ventricle” under Cardiac Chambers and Major Vessels in Chapter 1. Injury to the underlying first septal branch of the left anterior descending coronary artery during dissection of the pulmonary trunk is a major source of morbidity in this operation. A shallow incision of the endocardial surface is made to join both ends of the partly excised pulmonary trunk (Fig. 12-17, F). The incision extends completely across the remaining undivided RVOT. The angle of the scalpel is immediately changed to shave off the ventricular myocardium almost parallel to the endocardial surface. This shaves off the pulmonary trunk without injuring the underlying first septal branch. This part of the operation should be performed deliberately and under precise control. The septal excision eventually separates the pulmonary trunk completely, leaving the left main coronary artery and the first septal branch behind and protected by a generous layer of tissue. The septal artery is occasionally seen in the myocardium.

The separated pulmonary trunk is placed in the pericardial sac for immediate use. The trunk is not removed from the operating field, to prevent its misplacement or inadvertent mixture with the allograft. At this point it is convenient to measure the dimensions of the pulmonary anulus using standard prosthetic valve sizers and to choose a pulmonary allograft for preparation for later use.

The pulmonary autograft is attached to the unmodified LVOT, using interrupted stitches of 3-0 polypropylene (Fig. 12-17, G). Size discrepancy between the pulmonary autograft anulus and aortic anulus should not exceed 2 mm. A larger discrepancy indicates the need to adjust the anulus of the aorta to match that of the pulmonary autograft (see “Method for Reducing Diameter of Dilated Aortic Anulus” later in this chapter). The autograft is marked below each of the commissures for orientation. The anterior commissure of the autograft is oriented to approximate the commissure between the right and noncoronary sinuses. Suturing proceeds below each sinus, separating the stitches into three groups. Stitches are placed through the strong fibrous tissue of the aortic anulus, keeping the plane of repair as level as possible. A strip of PTFE felt about 5 mm wide is used to fix the diameter of the proximal suture line and to ensure hemostasis between the sutures (Fig. 12-17, H). A strip of autogenous pericardium may also be used. A “supported” repair is favored to prevent dilatation of the pulmonary autograft at the proximal suture line. Some surgeons prefer a continuous suture line using absorbable stitches without prosthetic material, especially for children in whom growth of the pulmonary autograft is
desired. However, the accuracy of carefully spaced individual stitches and fixation support of the anulus seem best in adult patients. The felt or pericardial strip is placed within the suture loops so that it is incorporated as the sutures are tied down. The pulmonary autograft is partially inverted into the LVOT as the sutures are tied to ensure that tissue approximation is accurate and that the support ring is to the outside rather than interposed between the tissues of the autograft and the aortic anulus.

An opening is made into the left coronary sinus of the autograft using a scalpel (Fig. 12-17, J). Only minimal sinus tissue is excised, because the delicate pulmonary artery dilates and separates readily. The sinutubular junction of the autograft is preserved to maintain proper relationships of the commissures and cusps.

The left coronary anastomosis proceeds, working on the outside of the pulmonary autograft (Fig. 12-17, J). Continuous stitches of 5-0 polypropylene are used. As a practical matter, it is best to perform the right coronary anastomosis after completing the aortic anastomosis so that the pulmonary trunk can be distended by temporarily removing the aortic clamp (Fig. 12-17, K). The right coronary anastomosis typically fits high in the right sinus or even above the sinutubular junction on the anterior wall of the pulmonary trunk. It may also be advisable to anastomose the pulmonary allograft to the bifurcation of the pulmonary trunk before the aortic anastomosis if the medial aspect of the pulmonary anastomosis might be obscured by the overlying aorta (Fig. 12-17, L). Often the diameter of the aorta is larger than that of the pulmonary trunk, but the pulmonary trunk is usually sufficiently long that a bevel can be created to take up any size discrepancy. With gross aortic enlargement or aneurysm, the entire ascending aorta may be removed and the pulmonary trunk extended with a prosthetic graft (see “Method for Extending Pulmonary Autograft” later in this chapter).

**Pulmonary Allograft Technique** The cryopreserved pulmonary allograft is trimmed minimally. An end-to-end anastomosis of the allograft to the pulmonary bifurcation is performed using continuous stitches of 4-0 polypropylene (see Fig. 12-17, L). Retracting the LV inferiorly and placing the graft in the space between the pulmonary bifurcation and the RV makes it easier to perform the anastomosis of the posterior wall of the pulmonary arteries. It is sometimes preferable to perform this anastomosis before constructing the aortic anastomosis. The proximal end of the allograft trunk is anastomosed to the RVOT (see Fig. 12-17, L). Continuous stitches of 3-0 polypropylene are used. Needle penetration must be through only part of the thickness in the infundibular septum to avoid injury to the underlying first septal branch of the left anterior descending coronary artery. A potentially weak point on the anastomosis at the transition from the infundibular septum to the medial aspect of the RV free wall may be reinforced with a PTFE pledget worked into the suture line. The completed repair produces a remarkably normal anatomic appearance (Fig. 12-17, M).

**Method for Lengthening Pulmonary Allograft** The pulmonary allograft may be tailored to achieve greater length, reducing the chance that the graft will be too tight between the RVOT and pulmonary artery bifurcation. The entire left pulmonary artery may be retained on the graft. The right pulmonary artery is removed and closed by direct suture using 5-0 polypropylene to lengthen the graft (Fig. 12-18, A). The left pulmonary artery is cut back to the bifurcation to create a large circumference for anastomosis. Making the pulmonary allograft long or even slightly redundant may be important in maintaining proper allograft length, because myocardium below the pulmonary allograft valve is resorbed and replaced with contracting scar.

**Method for Reducing Diameter of Dilated Aortic Anulus** When the patient’s LVOT at the level of the anulus is more than 2 mm in diameter greater than the pulmonary autograft, the patient’s anulus may be narrowed to fit the autograft, taking up this variance in anular diameters. Interrupted mattress stitches of 2-0 braided suture reinforced with PTFE pledgets are placed through the fibrous tissue that supports the aortic cusps alongside each of the commissures. The stitches are placed across the intercusp triangle so that the triangle is obliterated after tying down the suture (Fig. 12-18, B).

**Method for Extending Pulmonary Autograft** When the ascending aorta is greatly dilated or aneurysmal, it is advisable to remove the affected aorta. A polyester tubular graft with the same diameter as the pulmonary autograft’s distal end at the sinutubular junction is selected for replacement of the ascending aorta as an interposition graft (Fig. 12-18, C).

**Method for Fixing Sinutubular Junction** Evidence indicates that the pulmonary trunk may dilate up to 30% in diameter and length when exposed to systemic arterial pressure. Schmidtke and colleagues found that the pulmonary trunk in the aortic position as a freestanding root assumed a diameter of 41 mm at the sinus level, compared with 32 mm when the autograft was placed within the natural aorta. When the pulmonary trunk may also dilate in the clinical setting of bicuspid aortic valve with dilated ascending aorta. Fixing the diameter of the sinutubular junction of the pulmonary autograft is desirable and may prevent or correct pulmonary autograft regurgitation. A segment of tubular polyester vascular prothesis equal to, or 1 to 2 mm greater than, the diameter of the pulmonary autograft sinutubular junction (10% larger) is placed on the outside of the autograft to fix its diameter at its normal dimension. The polyester segment is attached to the pulmonary autograft with a few simple stitches to prevent migration (Fig. 12-18, D). A PTFE felt strip works equally well, but the diameter of the finished band is more difficult to control. Surgeons not wanting to fix the diameter of the pulmonary autograft at the sinutubular junction may find that narrowing the graft with a felt strip corrects possibly important autograft regurgitation (Fig. 12-18, E). Because of the known tendency for the pulmonary autograft to dilate, some have advocated reinforcing the entire autograft with bovine pericardium, polyester, or as an intraaortic cylinder within the native aortic root.

**Replacement of Aortic Valve and Ascending Aorta, En Bloc**

Replacement of the aortic valve and ascending aorta, en bloc, is most frequently performed for anulaoortic ectasia and ascending aortic aneurysm accompanied by aortic valve regurgitation. Occasionally, en bloc replacement is performed for infective endocarditis of the aortic root with extensive abscess formation and in the setting of acute or chronic aortic dissection with aortic valve regurgitation, for which the technique of distal anastomosis may be somewhat different.
Figure 12-18  Methods for adjusting Ross operation in specific situations. **A,** Method for lengthening pulmonary allograft to prevent tension on graft between right ventricular outflow tract and bifurcation of pulmonary artery as right ventricular myocardium on allograft is reabsorbed and replaced with scar tissue. Left pulmonary artery is retained with pulmonary trunk; it may be cut back (broken line) to pulmonary bifurcation to create a large opening. Right pulmonary artery is removed and its origin closed by continuous suture. **B,** Method for reducing diameter of dilated aortic anulus for proper size match with pulmonary autograft. Pledget-reinforced horizontal mattress stitches are placed through the fibrous tissue adjacent to intercusp triangles posteriorly and medially to obliterate triangular space, thereby reducing anular diameter.

**Initial Steps**
The early steps of the en bloc operation differ somewhat from those of simple aortic valve replacement. The arterial cannula may need to be placed in the common femoral artery (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2). When the ascending aortic aneurysm stops short of the brachiocephalic artery origin, the distal ascending or proximal transverse arch can be cannulated in the usual manner.

A limited dissection is done, separating the right and contiguous portion of the pulmonary trunk from the back of the aorta and the aneurysm. This approach affords safe placement of the aortic occlusion clamp just proximal to the brachiocephalic artery. The procedure involves clean surgical separation of the right and contiguous portion of the pulmonary trunk from the back of the aorta and from the aneurysm, if possible.

CPB is established at 34°C using a single two-stage venous cannula and left atrial vent. The perfusate temperature is lowered to bring body temperature to 28°C. The aorta is occluded just proximal to the brachiocephalic artery. The ascending aorta is opened transversely in its midportion, stay sutures are applied, and cardioplegia is given.

The patient’s aortic root is disconnected from the LVOT and left atrium–mitral valve complex. The sinus aorta surrounding the coronary arteries is retained. The remaining
Figure 12-18, cont’d  
C. Method for extending pulmonary autograft when there is aneurysm or dilatation of ascending aorta. Aneurysmal aorta is removed. Pulmonary autograft is lengthened by attaching a tubular polyester graft of exactly the same diameter as the pulmonary trunk just above valve commissures. D, Method of fixing sinutubular junction of pulmonary autograft to prevent dilatation. A segment of tubular polyester vascular prosthesis 10% smaller than measured diameter of pulmonary valve is placed around outside of autograft at level of sinutubular junction. A few interrupted stitches are placed to attach graft to pulmonary trunk to prevent migration. E, Echocardiogram of pulmonary valve before aortic valve replacement with pulmonary autograft shows typical trivial central valve regurgitant jet. After pulmonary trunk is transferred to aortic position and subjected to systemic arterial pressure, there is moderate (2+) valve regurgitation. Narrowing the sinutubular junction with an external band restores valve to preoperative state of trivial regurgitation.

sinus aorta is excised, leaving only fibrous aortic valve attachments, which are normal and uninvolved with the disease process being treated. The ascending aorta is divided by extension of the transverse aortotomy.

Allograft Aortic Valve Cylinder
When the ascending aorta is replaced along with the valve, sizing of the allograft valve is less critical than in the case of isolated aortic valve replacement. Aorta is usually sufficient on the allograft to replace the ascending aorta. Length of the retained ascending aorta and arch are considered when choosing the graft (see Fig. 12-14). The distal aorta is tailored to fit the native aorta. The distal anastomosis is performed directly or under circulatory arrest with the patient’s body temperature at 18°C.

Autograft Pulmonary Valve Cylinder
In young patients it may be desirable to use a pulmonary autograft as part of the en bloc operation. The pulmonary autograft is used as an intact pulmonary trunk to replace the aortic root as described earlier for isolated aortic valve replacement (see Fig. 12-18, C). The abnormal dilated or
aneurysmal ascending aorta is excised. A crimped polyester tubular graft, collagen coated and of the same diameter as the distal end of the pulmonary autograft, is selected for replacing the ascending aorta. This graft is anastomosed to the distal end of the pulmonary trunk. The graft is shortened and beveled appropriately for end-to-end anastomosis to the distal ascending aorta.

**Composite Valve Conduit**

Replacing the aortic valve and ascending aorta as an en bloc procedure is most often done with a composite prosthesis containing a mechanical or bioprosthetic cardiac valve enclosed within a slightly larger tubular polyester graft. This operation is frequently referred to as the Bentall procedure. These grafts have a collagen or gel coating that makes them impervious to blood.

The patient is placed on CPB using a single venous two-stage cannula, with oxygenated blood returned to the femoral artery in most cases. Occasionally, the amount of ascending aorta is sufficient to allow it or the transverse portion of the aortic arch to be perfused. The ascending aorta is occluded by a vascular clamp, and a vent catheter is placed through the right superior pulmonary vein to the left atrium and LV. A vertical incision is made in the ascending aorta aneurysm. Cold cardioplegic solution is administered to the coronary sinus by a retrograde coronary perfusion cannula. Traction stitches are placed above each aortic valve commissure to expose the aortic root (Fig. 12-19, A). The aortic valve is excised. The coronary arteries are mobilized, retaining a generous button of sinus aorta. A limited dissection of the coronary artery is sufficient to ensure that excision of the coronary artery is complete and that the coronary button will move easily up to the composite prosthesis without kinking or creating undue tension on the artery. The remaining sinus aorta is removed.

Diameter of the anulus is calibrated, and an appropriately sized composite prosthesis, including the prosthetic aortic valve and attached crimped polyester tubular prosthesis, is selected. Stitches are placed through the anulus of the aortic valve and brought up through the sewing ring of the prosthetic valve is avoided. Ten-millimeter diameter of the anulus is calibrated, and an appropriately sized composite prosthesis is constructed by placing a prosthetic valve within a tubular polyester graft so that there is a short length of tubular graft extending below and a longer length of graft extending above the sewing ring of the valve (Fig. 12-19, C). The graft collar is used to cover the completed anastomosis for hemostasis (Fig. 12-19, D). Modifications are required when coronary artery ostia are either close to the anulus or widely separated laterally by an aortic aneurysm. When coronary artery ostia are bound tightly to the aortic anulus, usually by prior operation or valve replacement, it is impossible to create an accurate anastomosis to the tubular portion of a composite graft because the valve sewing ring may impinge on the coronary ostia. In this situation, a composite valve prosthesis is constructed by placing a prosthetic valve within a tubular polyester graft so that there is a short length of tubular graft extending below and a longer length of graft extending above the sewing ring of the valve (Fig. 12-19, D). The graft and sewing ring of the prosthetic valve are attached by continuous suture. The extension of the tubular graft below the prosthetic valve is attached to the aortic anulus, displacing the level of the prosthetic valve cephalad above the bound down coronary ostia. Obstruction of the coronary ostia from contiguous placement of the thick sewing ring of the prosthetic valve is avoided. Ten-millimeter extension grafts from the aortic graft above the prosthetic valve to the coronary ostia complete the repair.

When the coronary artery ostia have been carried laterally and superiorly from the usual location relative to the aortic
Figure 12-19 Replacement of aortic root and ascending aorta (en bloc) with composite prosthetic valve conduit. A, Aortic valve is excised. Aorta is removed from sinuses of Valsalva except for generous buttons around coronary ostia. Abnormal ascending aorta is removed. B, Composite prosthetic valve conduit is attached to anulus of aortic valve with pledget-reinforced horizontal mattress stitches of 2-0 braided polyester. Continuous suture technique may also be used. C, Sutures are tied to tightly approximate prosthesis to aortic anulus. D, An opening is made into graft posteriorly. Left coronary artery is anastomosed to graft using continuous stitches of 3-0 or 4-0 polypropylene.

Continued
Figure 12-19, cont’d  E, An opening is made into graft anteriorly. Right coronary artery is anastomosed to graft.  F, Generally, coronary arteries may be anastomosed to the graft directly, without special treatment. Dissection of aorta around coronary ostium may require repair with polytetrafluoroethylene (PTFE) felt “washers” placed on endothelial and adventitial surfaces to sandwich the aortic tissue. Biological glue may also be applied. When coronary ostia are widely displaced, a short segment of tubular polyester or PTFE graft may be placed between aortic graft and coronary ostium. A short segment of saphenous vein may be used as an interposition graft.
anulus by aneurysm or dilatation of the aortic root, it is necessary to create an extension from the composite prosthesis to the coronary arteries. Ten-millimeter tubular polyester grafts are attached to the coronary arteries and brought up to the anterior aspect of the composite prosthesis (Fig. 12-19, K).

Repair of Aortic Valve Regurgitation due to Aortic Dilatation or Aneurysm (Valve-Sparing Aortic Root Replacement)

Kunzelman and colleagues studied the relationships of the diameters at various levels in the aortic root, showing that the diameter at the sinutubular junction should be about 15% less than that at the base (anulus or ventricular-aortic junction)\(^{37}\) (Fig. 12-20). Grande and colleagues showed that minor dilatation of the aortic root (5%-15%) caused increased stress on aortic valve cusps.\(^{17}\) In response to dilatation of the aortic root, strain on the valve cusps changes in order to maintain coaptation. This method of compensation fails at 30% to 50% dilatation of the aortic root, and cusp tissue is insufficient to maintain coaptation, resulting in aortic valve regurgitation. Frater demonstrated that simply adjusting the dimensions of the sinus rim or sinutubular junction can correct such regurgitation.\(^{11}\)
Remodeling versus Reimplantation Procedures

Remodeling Procedure  The remodeling operation consists of removing the sinus aorta except for a small rim of aortic tissue around the coronary ostia and a rim of about 5 mm of aortic wall above the aortic valve anulus. Commissures are positioned to achieve good coaptation of the aortic valve cusps.

Choo and Duran point out that the aortic root is dynamic, responding to pressure changes during the cardiac cycle that expand the aorta at the sinutubular junction by 35%, but the area at the base (anulus) by only 5%. Thus, they propose measuring the aortic root diameter at the base of the cusps as the most reliable method for appropriate graft sizing. The method proposed here is based on the measured diameter of the aortic anulus and simple arithmetic. When the diameter of the aortic anulus is normal, a graft is chosen that will narrow the sinutubular junction by 10% to 15%. When the diameter of the aortic anulus is enlarged, it is adjusted to normal diameter for body size using a graft diameter approximately 10% less than the desired aortic anular diameter. The
geometry conveniently allows strips of the graft to support a reduction anuloplasty of five-sixths the circumference of the anulus (avoiding the conduction system) while the graft adjusts the diameter of the sinutubular junction.

David recommended that when aortic root remodeling procedures, such as the Yacoub operation, are performed in patients with Marfan syndrome, or when the aortic anulus is dilated, an aortic anuloplasty should be performed. A strip of prosthetic material is used on the outside of the LVOT below the aortic valve to correct dilatation of the fibrous components of the LVOT resulting from myxomatous changes in these tissues.

Reimplantation Procedure In this procedure, the aortic valve is reimplanted within a polyester tubular graft. The graft is secured to a level plane in the LVOT just below the valve, except in the one sixth of the circumference occupied by the conduction system. This fixes the diameter of the LVOT, but one may reduce the diameter if necessary. The aortic valve is attached (reimplanted) to the inside of the prosthetic graft. The graft determines the diameter of the sinutubular junction.

The reimplantation procedure has undergone a number of modifications by both David and other surgeons. However, the basic concept has been retained. Cochrane and colleagues modified the David operation to create pseudosinuses in the graft by removing three symmetric scallops from it, thereby lengthening the proximal suture line and restoring proper relationships at the sinutubular junction. The pseudosinus method (Cochrane) and sinus-tailored method (Yacoub) result in simulated cusp stresses that are closer to normal than does David’s cylindrical technique.

The graft is usually 30 to 32 mm in diameter, although 28- or 34-mm grafts are occasionally used.

Technique of Operation

After induction of anesthesia and before incision, intraoperative transesophageal echocardiography (TEE) is used to measure aortic root dimensions at the sinutubular junction and ventricular-aortic junction. Operations are performed on CPB using a single two-stage cannula for venous uptake, with oxygenated blood returned to a cannula placed high in the ascending aorta or arch or in the femoral artery. Hypothermic circulatory arrest is used when the aneurysm extends beyond the ascending aorta.

The aorta is divided above the sinutubular junction and the aortic valve thoroughly examined. Normal aortic valve cusps suggest the possibility of a valve-sparing operation. Diameters of the sinutubular junction and ventricular-aortic junction are measured using Hegar dilators or accurate valve sizers. Alterations of aortic root dimensions are noted and will guide the steps taken to restore dimensions to normal.

Aortic Anulus Normal, Normal Sinuses of Valsalva, Sinutubular Junction Enlarged A normal aortic anulus with enlarged sinutubular junction is found in patients with aortic ectasia and aneurysm of the ascending aorta not involving the aortic sinuses. The coronary arteries are not displaced from their usual location in relation to the anulus.

A vascular graft the same diameter as the aortic anulus is selected. A 4- to 5-mm segment of the graft is prepared for placement on the outside of the aorta at the sinutubular junction. The thickness of the aortic wall when compressed within the graft will reduce the inside diameter of the aorta to restore the normal dimension, which is 15% less than the diameter of the aortic anulus. Using this short segment of graft is easier and more accurate than attempting to attach a longer graft directly to the sinutubular junction.

Aortic Anulus Normal or Enlarged, Aneurysm of Sinus of Valsalva, Sinutubular Junction Enlarged An enlarged aortic anulus with enlarged sinutubular junction is found in patients with anuloaortic ectasia, some of whom have Marfan syndrome. Less commonly, patients with aortic regurgitation and sinus of Valsalva aneurysm will have a normal aortic anulus. Both the remodeling and reimplantation procedures have been recommended for this condition. Both are described here.

Remodeling Procedure

In the remodeling procedure, the aortic sinuses are removed. The aortic anulus is reduced to a diameter appropriate for the patient’s body size (Fig. 12-22), generally 25 mm for the average adult male, 27 mm for a large male, and 23 mm for an adult female. A vascular graft 10% to 15% smaller than that is selected. Two 4- to 5-mm segments (rings) of the graft are prepared to adjust the anulus diameter. The remaining graft is tailored by making three incisions and trimming the flaps for sinus reconstruction and replacing the ascending aorta.

To achieve an LVOT 25 mm in diameter at the ventricular-aortic junction, the circumference of the aorta must be reduced to 78 mm (25 \cdot \pi = 78). This reduction is accomplished by anuloplasty, using the short segments of graft to size the anulus accurately and to support the repair. Anuloplasty mattress stitches are placed in the LVOT at a level plane.
**Figure 12-21** Repair of aortic valve regurgitation caused by dilatation or aneurysm of ascending aorta when aortic anulus is normal and sinutubular junction is enlarged without aneurysmal enlargement of sinuses of Valsalva and without displacement of coronary ostia. A 4- to 5-mm segment of graft the same diameter as anulus is placed as a band on outside of aorta at sinutubular junction to reduce inside diameter by 10%. Ascending aortic aneurysm is resected and replaced with graft of same size.

**Figure 12-22** Remodeling method for restoring aortic root dimensions in an aortic valve–sparing operation when aortic anulus and sinutubular junction are enlarged, as in anuloaortic ectasia with Marfan syndrome. A vascular graft 10% to 15% smaller than desired diameter of aortic anulus is used to provide 4- to 5-mm strips of fabric that will support a reduction anuloplasty of five-sixths of circumference of left ventricular outflow tract (avoiding conduction system) just below aortic valve. Graft adjusts diameter at sinutubular junction. Sinuses of Valsalva are reconstructed as described in text.
just below the hinge point of the aortic valve. The stitches are placed beginning below the nadir or midpoint of the right coronary cusp of the aortic valve and working counterclockwise to the commissure between the noncoronary and right coronary cusps. This places the stitches on five sixths of the circumference, avoiding stitches in the one sixth of the ventricular septum that contains the conduction system. A strip of fabric to cover five sixths of the circumference and achieve a diameter of 25 mm is 65 mm in length (78 · 𝜋 · % = 65). It is convenient that a 22-mm crimped tubular polyester graft provides a strip of fabric 75 mm in length when the 4- to 5-mm segment is cut, opened, and stretched to length. From the strip of the graft, 10 mm of length is removed. The annuloplasty stitches are placed through the fabric strip and passed through the LVOT to the outside. Thickness of tissue through which the needles pass is about 3 mm. Thus, the outside diameter to be supported will be about 28 mm in diameter. The length of fabric needed to support this diameter is, conveniently, about 75 mm (28 · 𝜋 · % = 73). The anuloplasty stitches are passed through the outside fabric strip. A 25-mm-diameter Hegar dilator is placed in the LVOT while the sutures are tied down. This narrows the LVOT to a calculated diameter while distributing the tension equally over five sixths of its circumference.

The sinus aorta is reconstructed to the flap graft. Diameter of the sinutubular junction is accurately restored by the diameter of the graft chosen for the repair. Relationships just described should hold for the various graft sizes that might be chosen for reconstructing the aortic root. Intraoperative TEE is performed with the heart contracting and ejecting at normal pressure to determine adequacy of the repair.

**Reimplantation Procedure**

The reimplantation technique involves excising all three sinuses, leaving a rim of 4 to 5 mm of aortic wall and buttons of aorta around the coronary ostia (Fig. 12-23, A). An appropriately sized polyester graft (see later text for sizing details) is selected and marks are made on one end of it corresponding to position of the commissures. Multiple interrupted pledgeted horizontal mattress sutures of 2-0 polyester are passed from inside the LVOT immediately below the nadir of the aortic valve following a horizontal plane except in the region of the left anterior fibrous trigone (dense adherence of fibrous trigone to pulmonary trunk) and near the conduction system at the commissure between right and noncoronary sinuses (Fig. 12-23, B). (In these two commissural areas, the sutures follow the hinge point line of the valve cusps). These horizontal mattress sutures are then placed through the base of the polyester graft (placed slightly higher in the two commissural areas noted). Position of the commissures within the graft is then determined (the orientation being critical to competence of the aortic valve), and the aortic wall above each commissure is sutured to the graft with 4-0 polypropylene mattress sutures. The remainder of the suturing of the native aortic valve to the inside of the graft is similar to a subcoronary allograft procedure, described earlier under “Allograft Aortic Valve.” The suture line starts at the lowest point of each scallop and is continued to the top of each commissure. The valve is inspected for adequate cusp coaptation. If the free edge of one or more cusps is elongated and tending to prolapse, the free margin can be shortened by using 6-0 PTFE suture to imbricate the central portion of the cusp (nodulus of Aranti).

The coronary artery reimplantation steps are the same as described for the total root replacement operation (Fig. 12-23, C). The distal aortic anastomoses can be performed either with the same graft or with a separate smaller graft (see text that follows on creating pseudosinuses).

Two important technical considerations in the reimplantation procedure deserve special comment: commissure resuspension height and graft sizing with the construction of pseudosinuses.

**Commissural Resuspension Height**  
*Placing commissures at the appropriate height within the graft is of critical importance for long-term valve competence. They should be placed at a height that mimics normal geometry and avoids abnormal cusp coaptation. Experimental studies suggest that an abnormally low commissural resuspension level may compromise optimal cusp coaptation.*

**Graft Sizing with Construction of Pseudosinuses**

Multiple algorithms have been suggested for selecting the appropriate graft size, particularly when attempting to create pseudosinuses. Although it remains unproven that creating neosinuses adds to long-term valve competence, experimental studies dating back to Leonardo da Vinci and subsequently by others suggest that presence of vortices in the sinuses facilitates cusp closure in early diastole and reduces cusp stress.

In a study by Katayama and colleagues in which a finite element simulation was used to model aortic valve–sparing root replacement with and without pseudosinuses, distinct differences were observed in the closing dynamics of the cusps. In the model without neosinuses the aortic valve was open longer and the cusps had a faster closing velocity. In the pseudosinus model, vortex formation occurred, which facilitated a more gradual and smoother closure of the valve cusps. Furthermore, in the model without pseudosinuses, cusp stress and bending deformation was greater in the middle of the cusps. Aybek and colleagues studied aortic valve cusp dynamics in patients undergoing aortic valve–sparing root replacement with and without incorporation of pseudosinuses. Patients who underwent the reimplantation procedure with a straight graft had an aortic valve opening velocity of 61 cm · s⁻¹ (normal opening velocity 29 cm · s⁻¹) vs. 46 cm · s⁻¹ in those with pseudosinuses. Aortic valve closing velocity mirrored opening velocity. Therefore, although it is true that the opening and closing velocities of the aortic valve were closer to normal in patients with pseudosinuses, they remain abnormally high. A finite element model simulating aortic valve–sparing root replacement found that in the straight graft simulation, the diastolic cusp stresses and strains were mostly on the cusp belly and attachment edge, which are the regions closest to the graft. These are areas of the cusp that normally have high bending and flexing stresses during valve opening. In the pseudosinus graft simulation the aortic cusp stresses were still abnormal at the attachment edge, but less than that seen in the straight graft simulation. This biomechanical information suggests that incorporating pseudosinuses into the aortic valve–sparing root replacement procedure may confer some benefit in terms of aortic valve opening and closing velocities and cusp stresses, although they remain abnormal.

Thus, although it remains uncertain whether these biomechanical benefits will translate into long-term improved cusp...
appropriately on the graft, they will crimp the proximal graft down to the appropriate size while simultaneously creating pseudosinuses. Reducing of the diameter at the sinutubular junction to about 15% less than the desired aortic anulus diameter can be achieved either by placing plication sutures in the graft above each commissure, or, alternatively, by using a second graft for the distal ascending aortic replacement that approximates the anulus size and is sewn end to end to the larger proximal graft, effecting a reduction in diameter at the level of the sinutubular junction (“Stanford modification”). A commercially prepared graft with pre-constructed pseudosinuses (Gelweave Valsalva) is available in sizes 24-34.

Reducing the size of a dilated aortic anulus to increase cusp coaptation is an essential component of the operation. A Hegar dilator can be used to measure the anulus, and Svensson has recommended placing the Hegar through the aortic valve when tying the subanular sutures to guide the anuloplasty effect of the proximal graft suture placement. A 19-mm Hegar is selected for BSA of about 1.5 m², 21-mm Hegar for BSA 2.0 m², and 23-mm Hegar for BSA 2.5 m².

A larger graft (selected for creating pseudosinuses) can be “necked down” to an appropriate size at the anular end by placing multiple plication stitches in it with the appropriate valve sizer inside the graft to aid in achieving a desired diameter (Demers 2004, Miller 2007). Another option is to place the pledgeted sutures within the aortic root below the valve level to create an anuloplasty effect; when spaced appropriately on the graft, they will crimp the proximal graft down to the appropriate size while simultaneously creating pseudosinuses.

Reduction of the diameter at the sinutubular junction to about 15% less than the desired aortic anulus diameter can be achieved either by placing plication sutures in the graft above each commissure, or, alternatively, by using a second graft for the distal ascending aortic replacement that approximates the anulus size and is sewn end to end to the larger proximal graft, effecting a reduction in diameter at the level of the sinutubular junction (“Stanford modification”). A commercially prepared graft with pre-constructed pseudosinuses (Gelweave Valsalva) is available in sizes 24-34.

Adequacy of aortic valve–sparing operations is confirmed by intraoperative TEE.

**Alternative Aortic Valve–Sparing Techniques**

Alternative techniques generally focus on simplifying the operation by retaining aortic tissue and providing an external wrap to prevent further aortic enlargement. The advantage is a simpler procedure with fewer suture lines to bleed, which must be weighed against the potential for dissection in the retained aorta. The *Florida sleeve repair*
is a valve-sparing operation in which the ventricular-arterial junction, sinuses of Valsalva, and sinutubular junction are supported by a polyester conduit as a sleeve. In a technique reported by Laks and colleagues,\textsuperscript{12} aortic root aneurysms associated with bicuspid aortic valve regurgitation are treated with a combination of pericardial cusp extension, lining the sinuses of Valsalva with autologous pericardium (with holes punched to accommodate the coronary orifices), and wrapping the ascending aorta with polyester.

**Aortic Valve Replacement and Coronary Artery Bypass Grafting**

Preparing and draping the patient, and simultaneous preparation of the coronary bypass conduits, are the same as in simple coronary artery bypass grafting (CABG) (see Technique of Operation in Chapter 7). Purse-string sutures for aortic cannulation are placed, with care taken that they are far enough distally (downstream) from the aortic valve to allow room for both the aortotomy and any proximal venous graft anastomoses.

CPB is established. The operative procedure begins exactly as for isolated aortic valve replacement through excision of the aortic valve and selection of replacement device. The distal graft-to-coronary artery anastomoses are performed. Then the valve is replaced and the aortotomy closed. If vein grafts are used, they are routed and sized, and the proximal anastomoses to the aorta are performed. After de-airing the heart, CPB is discontinued and the operation completed as usual.

**Redo Isolated Aortic Valve Replacement**

Not all redo operations after primary aortic valve replacement involve a second valve replacement. Acute thrombosis may be treated by thrombectomy, and periprosthetic leakage of a mechanical valve or stent-mounted bioprosthesis may be successfully treated by simple resection of the area of dehiscence. Prosthetic valve endocarditis, central leakages of all types, and extensive periprosthetic leakage typically require valve re-replacement. The technique of operation embodies general principles of all redo cardiac operations (see “Secondary Median Sternotomy”\textsuperscript{12} under Incision in Section III of Chapter 2).

When a freehand-inserted allograft or xenograft requires replacement, the entire graft should be removed, including remnants of its aortic wall. The graft tissues are dissected from the sinus aorta and anulus using a Freer septum elevator, cutting suture material as required. This approach leaves an aortic root of good quality for inserting either another allograft or other replacement device.

When a stent-mounted bioprosthesis or mechanical prosthesis has been used, the device is removed by pulling on the knots with a needle holder and using a #11 scalpel to cut individual sutures that were placed at initial operation. Then, using a Freer septum elevator, a dissection plane is established between the fabric of the prosthesis sewing ring and aortic root tissues. The prosthesis is thus removed intact and aortic root tissues remain in good condition to accept another prosthesis. Mechanical prostheses can also be removed by first separating the mechanical device from the sewing ring by sharply dividing the ring with a scalpel. Incision of the sewing ring is taken completely through the retaining thread that holds the ring to the mechanical device. Once these retaining threads are cut, the mechanical device comes away from the sewing ring. Fabric of the sewing ring is then more easily separated from tissues by cutting the sutures placed at initial operation.

**Redo Aortic Valve and Ascending Aorta Replacement, En Bloc**

In the setting of a prior cardiac operation with an aneurysmal ascending aorta or ascending aortic graft, proximity of the ascending aorta or aortic graft to the underside of the sternum can be evaluated with CT studies. When the situation is considered high risk for direct adherence of the graft or aorta to the sternum, the following approach can be considered. The technique of reoperation needs to be modified from the standard approach because of an important risk of massive hemorrhage from the polyester tube graft at sternal reentry if the graft has adhered to the back of the sternum. Reentry is further complicated if aortic regurgitation is present. Under such circumstances, CPB is commenced through groin cannulation of the common femoral artery and vein using vacuum-assisted venous return (see “Vacuum-Assisted Venous Return” in Section II of Chapter 2). Core cooling is instituted to lower the nasopharyngeal temperature to about 20°C. When there is important aortic regurgitation, a limited left anterolateral thoracotomy may be made through the fifth intercostal space and a vent placed into the LV apex, monitoring LV end-diastolic pressure to maintain it at normal levels and prevent overdistention, even in the event of ventricular fibrillation. Alternatively, a large catheter (12F) is inserted percutaneously into the LV and its position confirmed by echocardiography. Adequate hypothermia permits the sternum to be opened with a vibrating saw without risk of exsanguinating hemorrhage. If the polyester tube is cut, CPB is stopped; blood escaping from the aorta is returned to the circuit by suction device, and control of the aorta distal to the tear is obtained before CPB is resumed.

Alternatively, to reduce the major increase in diffuse coagulopathy and generalized bleeding associated with the approach just described, the femoral artery and vein are dissected out and purse strings placed on their anterior surface with 4-0 polypropylene sutures in preparation for percutaneous arterial and venous cannulation for CPB if needed emergently. Using surgical towel clips through bone and xiphoid at the lower end of the incision to elevate the sternum, the oscillating saw is used to partially divide the sternum, taking care not to penetrate the posterior table. The posterior table is divided with scissors while elevating the lower sternum, so most of the sternal division is carried out under nearly direct vision. As the aneurysm or graft is approached, a portion of the periosteum or posterior table is left with the aortic graft by the appropriate dissection plane. If bleeding is encountered, the patient is promptly heparinized and the incision rapidly closed with numerous sharp surgical towel clips (as many as 20 clips may be needed). As long as the pleural spaces have not been entered during sternotomy, the completely closed incision (sufficient to eliminate any bleeding between towel clips) creates a closed space, and no further internal bleeding occurs after the space is obliterated. Hemodynamics are usually maintained while CPB is established through the femoral artery and vein. A decision can then be made to initiate hypothermic perfusion and temporary circulatory arrest as described in previous text or to remove the towel clips, collect
the aortic blood with a cardiotomy sucker, and obtain digital control while completing sufficient dissection to repair the aortic graft tear. Transient low-flow perfusion and moderate hypothermia are used to avoid ventricular fibrillation in the presence of important aortic regurgitation.

When infection is present, the prosthetic material should be removed entirely and replaced with an allograft. In the absence of infection, prosthetic material can be used again if desired.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Postoperative care after adult aortic valve surgery is generally the same as after other types of cardiac surgery (see Chapter 5). Patients receiving a mechanical prosthesis are begun on lifelong sodium warfarin anticoagulant therapy on the evening of the first postoperative day. Intensity of anticoagulation should be specific for both prosthesis and patient.

Modern mechanical prostheses are considered to have lower thrombogenicity than earlier devices. An international normalized ratio (INR) for prothrombin time of 2.5 is considered adequate to prevent valve thrombosis in the absence of abnormal intracardiac conditions. Atrial fibrillation alone does not raise the requirement for anticoagulation unless the left atrium is enlarged or LV function impaired. These additional risk factors dictate raising the intensity of anticoagulation to an INR of 3.0. Severe left atrial enlargement, greatly impaired LV function, or echocardiographic evidence of stasis in the left atrium require even higher levels of anticoagulation, with an INR of 3.5 to 4.0. Some evidence indicates that adding aspirin (81 mg daily) further reduces risk of thromboembolism. Aspirin at higher levels (200 mg daily) reduces total thromboembolic events but increases morbidity associated with bleeding. Newer platelet antagonists have not been completely evaluated as adjuncts to warfarin therapy.

Bioprostheses (human or xenograft) in the aortic position of stent-mounted or stentless design do not require anticoagulation with warfarin. It should be noted that optimal management protocols to prevent thromboembolism during the first several months after implantation of bioprosthetic aortic valves remain controversial. Recommendations from the 2006 ACC/AHA Guidelines include warfarin for the first 90 days. A study by El Bardissi and colleagues supported the use of warfarin only in the higher risk settings of small prosthesis size (19 mm) and New York Heart Association (NYHA) functional class III/IV symptoms preoperatively in patients in sinus rhythm. For most patients in sinus rhythm, it is judicious to use aspirin therapy (81 mg daily) for at least 1 month, when risk of thromboembolism is greatest.

Patients in atrial fibrillation for more than 48 hours after operation are anticoagulated with warfarin until sinus rhythm is restored.

The thick-walled hypertrophied LV secondary to aortic valve disease requires a higher-than-usual filling pressure to distend it. Thus, a mean left atrial pressure of 8 to 10 mmHg, considered appropriate under many circumstances, may be inadequate to develop optimal LV preload early after operation in patients with important LV hypertrophy (see “Cardiac Output and Its Determinants” in Section I of Chapter 5). Reduction in myocardial compliance that occurs during cardiac surgery further increases the disparity between the usual mean left atrial pressure (LV filling pressure) and optimal preload.

For these reasons, unless cardiac performance is already optimal, left atrial pressure should be maintained at 15 to 18 mmHg by appropriate fluid infusion during the early hours after adult aortic valve surgery, particularly for severe aortic stenosis. This need is often less critical when operation has been done for aortic regurgitation, when the sudden reduction in LV stroke volume by eliminating the aortic regurgitant flow improves left compared with RV performance (see Chapter 5). Therefore, mean left atrial pressure may not be as elevated early postoperatively as when operation has been done for aortic stenosis.

Sinus tachycardia is frequently observed after operations on the aortic valve. When heart rate exceeds 100 beats·min$^{-1}$ for several days and shows no signs of returning to normal, a β-blocker should be administered to reduce the rate. It may be necessary to continue this therapy for 2 to 3 months until heart rate control mechanisms are restored.

**RESULTS**

**Early (Hospital) Death**

The Society of Thoracic Surgeons (STS) National Database reports a 2.6% and 3.3% 30-day mortality for isolated aortic valve replacement for the years 2009 and 2011, respectively. Risk is higher for women than men (3.9% vs. 3.0%). When CABG is added to aortic valve replacement, the current risk of hospital death among STS National Database participants rises to 4.2%. Isolated reoperative aortic valve replacement does not appear to increase early mortality in the current era.

**Time-Related Survival**

Overall survival (including hospital deaths) after aortic valve replacement in heterogeneous groups of patients is about 75% at 5 years, 60% at 10 years, and 40% at 15 years (Fig. 12-24, A). These percentages are less than those in an age-gender-race–matched general population, except for elderly patients (see Fig. 12-25). Many factors likely contribute to this, including the possible palliative nature of the operation, incomplete regression of LV remodeling after valve replacement, poor control of chronic anticoagulation in patients receiving mechanical prostheses, reoperation for structural valve deterioration of bioprostheses, and other prostheses-related morbidity. Grunkemeier and colleagues report risk-unadjusted data suggesting that after adjusting for age differences, late survival is similar for mechanical and bioprosthetic valves.

The hazard function for death after aortic valve replacement is similar to that after other valve replacement operations in adults (Fig. 12-24, B). The early, rapidly declining hazard phase gives way to a late phase about 6 months after operation, which begins to rise as early as 5 years after operation.

**Modes of Death**

Of the few deaths early after aortic valve replacement, most are related to acute cardiac failure, neurologic complications, hemorrhage, and infection. Most late deaths are unrelated to
Device-related modes of death include thromboembolism, although the frequency may have decreased in recent years. Some patients, but its occurrence in patients with an allograft 20% of late deaths. It may result from thromboembolism in death occurs with surprising frequency, accounting for about cardiac infarction are the most common modes of death, as the specific replacement device used. Cardiac failure and myo-

colleagues.## B37,B42,F14,K9,L26

Figure 12-26. Overall survival curves are a composite of patients of increasingly higher risk being operated on during increasingly safer years of calendar time. Older age at operation is a risk factor both early and late after aortic valve replacement, as after most cardiac operations.## B37,B42,F14,K9,L26 However, elderly patients with any chronic illness are at increased risk of dying, and only death in the early phase is specific to the cardiac operation (Fig. 12-26).

Strength of the risk factor of older age is less than might be expected,## F14 even in an earlier era (Fig. 12-27). Risk of death early after operation is about 1% at age 40 and about 8% in patients over 70.## B29,F14 Risk of operative mortality for isolated aortic valve replacement among STS National Database participants is at least doubled when the operation is performed in patients over age 65 (4.9%) vs. those under 65 (2.3%)## F14; with associated coronary artery disease requiring CABG, the risk for patients over age 65 increases to 7.6%, compared with 3.3% for those under age 65. Levinson and colleagues reported that hospital mortality was 9.4% among these elderly patients, and most reported a satisfactory lifestyle. Similar results were observed by Azariades and colleagues.## A21 Rizzoli and colleagues reported a 5- and 10-year survival after aortic valve replacement in patients over

the specific replacement device used. Cardiac failure and myocardial infarction are the most common modes of death, as after all valve replacement operations (Fig. 12-25). Sudden death occurs with surprising frequency, accounting for about 20% of late deaths. It may result from thromboembolism in some patients, but its occurrence in patients with an allograft indicates other causes.

About 20% of deaths may be related to the device inserted, although the frequency may have decreased in recent years.## 16 Device-related modes of death include thromboembolism

Figure 12-25. Survival after aortic valve replacement stratified by age group. For each age group, an age-gender-ethnicity–matched population life table curve is shown by lavender. Note that the younger the patient, the more marked the departure from normal life expectancy. (From Blackstone and colleagues.## B36,B57,C44

Incremental Risk Factors for Premature Death

Table 12-3 summarizes incremental risk factors for premature death.

Older Age at Operation

Age of patients at operation has increased steadily since the beginning of aortic valve replacement and now approaches a mean above 70 years.## 224 Overall survival curves are a composite of patients of increasingly higher risk being operated on during increasingly safer years of calendar time. Older age at operation is a risk factor both early and late after aortic valve replacement, as after most cardiac operations.## B37,B42,F14,K9,L26 However, elderly patients with any chronic illness are at increased risk of dying, and only death in the early phase is specific to the cardiac operation (Fig. 12-26).

Strength of the risk factor of older age is less than might be expected,## F14 even in an earlier era (Fig. 12-27). Risk of death early after operation is about 1% at age 40 and about 8% in patients over 70.## B29,F14 Risk of operative mortality for isolated aortic valve replacement among STS National Database participants is at least doubled when the operation is performed in patients over age 65 (4.9%) vs. those under 65 (2.3%)## F14; with associated coronary artery disease requiring CABG, the risk for patients over age 65 increases to 7.6%, compared with 3.3% for those under age 65. Levinson and colleagues reported that hospital mortality was 9.4% among these elderly patients, and most reported a satisfactory lifestyle. Similar results were observed by Azariades and colleagues.## A21 Rizzoli and colleagues reported a 5- and 10-year survival after aortic valve replacement in patients over
Table 12-3  Incremental Risk Factors for Death Early and Late after Isolated and Combined Aortic Valve Replacement

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Hazard Phase</th>
<th>Risk Factors</th>
<th>Hazard Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Early</td>
<td>Late</td>
<td>Coexisting coronary artery disease</td>
</tr>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
<td>Coexisting aneurysm of ascending aorta</td>
</tr>
<tr>
<td>(Older)</td>
<td></td>
<td></td>
<td>Prosthetic valved conduit</td>
</tr>
<tr>
<td>Age</td>
<td>•</td>
<td></td>
<td>Allograft aortic valved conduit</td>
</tr>
<tr>
<td>African American</td>
<td></td>
<td></td>
<td>Autograft pulmonary valved conduit</td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
<td>(Greater) left ventricular hypertrophy (grades 0–4)</td>
</tr>
<tr>
<td>(Higher)</td>
<td>•</td>
<td></td>
<td>(Greater) left ventricular dysfunction</td>
</tr>
<tr>
<td>NYHA functional class (I–V)</td>
<td></td>
<td></td>
<td>(Greater) left ventricular diastolic dysfunction</td>
</tr>
<tr>
<td>(Greater)</td>
<td></td>
<td></td>
<td>Surgical</td>
</tr>
<tr>
<td>Left ventricular enlargement (grades 0–4)</td>
<td>•</td>
<td></td>
<td>(Earlier) Era</td>
</tr>
<tr>
<td>(More)</td>
<td></td>
<td></td>
<td>(Longer) Global myocardial ischemic time</td>
</tr>
<tr>
<td>Aortic regurgitation (grades 0–5)</td>
<td>•</td>
<td></td>
<td>Type of replacement device:</td>
</tr>
<tr>
<td>Functional mitral regurgitation</td>
<td></td>
<td></td>
<td>Mechanical prosthesis</td>
</tr>
<tr>
<td>Angina</td>
<td>•</td>
<td></td>
<td>Bioprosthesis</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>•</td>
<td></td>
<td>Allograft</td>
</tr>
<tr>
<td>Ventricular arrhythmia</td>
<td>•</td>
<td></td>
<td>Autograft</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
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<td>Smaller prosthesis</td>
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<td>Renal dysfunction</td>
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<td>Previous aortic valve replacement</td>
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<tr>
<td>(Lower)</td>
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<td></td>
<td>Concomitant CABG</td>
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<td>Hematocrit</td>
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<td>Peripheral arterial disease</td>
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</tr>
<tr>
<td>Smoker</td>
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<td></td>
<td></td>
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<tr>
<td>Severe COPD</td>
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<td></td>
<td></td>
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<tr>
<td>Diabetes</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(More)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>More severe aortic stenosis</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(More)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of previous aortic valve</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>replacement operations (grades 0–3)</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

*Risk factors classified based on experience and published reports, and not all obtained by multivariable analysis.

Key: CABG, Coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association.

Figure 12-26  Hazard functions for each mode of death after primary aortic valve replacement in a group of 1533 patients. (An age-gender-ethnicity-matched general population has an incidence of deaths - month⁻¹ of 0.001 across a 5-year period, similar to that for deaths in uncertain mode, marked K.) (From Blackstone and Kirklin.)
However, risk of premature death late postoperatively is meaning hemodynamic instability or cardiogenic shock. Ability is so advanced or acute that it is NYHA class V, which is often not highly correlated with functional status, as reflected in NYHA functional class III. Poor functional status, as reflected in NYHA functional class III, is a risk factor for death, usually in cardiac failure, primarily after isolated aortic valve replacement. Nomogram of multivariable logistic equation. Key: NYHA, New York Heart Association. (From UAB group, 1975 to July 1979; n = 842.)

Age 80 equivalent to that of the general population. Age is not so dominant a risk factor as to negate the effect of the other risk factors in elderly patients. Risk of operation for aortic valve replacement combined with CABG in patients over age 80 is 10% (95%; CL 6.9%-13%), compared with 7.9% (95%; CL 6.6%-9.2%) in patients under age 80. Death early after operation in elderly patients tends to be related to excessive bleeding (in part attributable to the poor quality of the tissues), pulmonary dysfunction (in part related to generalized weakness and consequent delay in weaning from intubation and ventilation), and susceptibility to infection. Precise surgical techniques and acceleration of convalescence, with departure from the intensive care unit as quickly as possible, are helpful in neutralizing these risks.

Older patients may be more subject to important neurologic complications. Levinson and colleagues reported neurologic sequelae in 9% of 64 patients age 80 to 89 years undergoing isolated or combined aortic valve replacement. Alexander and colleagues reported associated neurologic events (15% vs. 9.1%, P < .05) and renal failure (12% vs. 6.8%, P < .05) were higher in patients over age 80 than in younger patients. These data were compiled from results in 2035 patients having operations in 22 centers in the United States.

Race
African Americans appear to be at increased risk of death late after aortic valve operations. The reasons for this are unclear, but may include socioeconomic and genetic factors that predispose individuals to hypertension.

Functional Status
Poor functional status, as reflected in NYHA functional class, is a risk factor for death, usually in cardiac failure, primarily early after isolated aortic valve replacement. The effect on premature death late postoperatively is less, probably because later survival is related preoperatively more to LV function, which is often not highly correlated with functional status. Risk of death is particularly increased when the disability is so advanced or acute that it is NYHA class V, meaning hemodynamic instability or cardiogenic shock. However, risk of premature death late postoperatively is affected to some degree as well. Preoperative left atrial enlargement has been found to be one of the most powerful risk factors for premature death after aortic valve replacement for aortic stenosis.

Aortic Regurgitation
Aortic regurgitation is probably a risk factor for death early postoperatively under some circumstances. However, the interrelationship between aortic regurgitation and abnormalities of LV structure, size, and function indicates that these are likely the incremental risk factors.

Gender
Gender is a risk factor for late mortality after operation for aortic valve regurgitation. Klodas and colleagues reported increased late mortality after aortic valve operations for women with aortic regurgitation in a multivariable analysis that considered patient size, LV dimension, and concomitant replacement of the ascending aorta for aneurysm. McDaid and colleagues found that this late mortality was influenced by coexisting aortic pathology and subsequent rupture of the aorta. Female gender (and BSA < 1.8 m²) are risk factors for early mortality in patients older than 80.

Angina
Angina in patients with aortic valve disease increases the likelihood of coexisting coronary artery disease. Unless coronary artery disease is excluded or treated by concomitant CABG, angina becomes a risk factor for death after the operation.

Atrial Fibrillation
Using Cox regression analysis (univariable, multivariable, and age adjusted) to study 2359 patients with aortic valve replacement, Kvidal and colleagues found that atrial fibrillation was associated with a hazard ratio greater than 2 beyond 30 days of operation.

Coexisting Coronary Artery Disease
Coexisting coronary artery disease is a complex risk factor for premature death after operation. Among STS National Database participants, aortic valve replacement with concomitant CABG carried a higher early mortality (4.2%) during the early phase after operation than either aortic valve replacement alone (2.6%) or CABG alone (1.9%). However, patients with both diseases are generally older at operation and have more functional disability, more angina,
more previous myocardial infarctions, and a higher prevalence of hemodynamic instability than those with isolated aortic valve disease. These patients also usually require longer aortic occlusion time. Many of these factors have been found to increase risk of death after the combined operation. Some authors have not found concomitant CABG to be a risk factor for death during the early or intermediate period (up to 5 years) after aortic valve replacement operations, but others have observed a somewhat lower 5- to 10-year survival than after isolated aortic valve replacement (Fig. 12-28).

Most important, despite the variability in comparisons of outcome after isolated aortic valve replacement with that after operation combined with CABG, patients who have combined aortic valve and coronary artery disease who undergo only aortic valve replacement have a lower survival than patients who undergo concomitant CABG. Also, Czer and colleagues found sudden death late postoperatively to be more common in patients with combined aortic valve and coronary artery disease when concomitant CABG had not been performed than when it had.

**Acute Aortic Valve Endocarditis**

Surprisingly, native valve endocarditis at valve replacement is not a risk factor for long-term mortality. For replacement valve endocarditis, radical débridement of infected tissue and aortic root replacement with cryopreserved aortic allografts can be accomplished with low early risk.

**Coexisting Ascending Aortic Aneurysm**

Coexisting aneurysm of the ascending aorta has been associated with slightly decreased hospital and intermediate-term survival. However, it has not been shown to be a risk factor overall, and the decreased survival may be attributable to other factors, including longer periods of global myocardial ischemia and CPB required for ascending aorta plus aortic valve replacement than for simple aortic valve replacement. Overall survival in patients with this combination who undergo only valve replacement probably is considerably lower.

Survival after combined replacement of the aortic valve and ascending aorta is partly determined by the replacement device. When a composite valve conduit has been used, 1-month and 1-, 5-, 10-, and 15-year survival, as reported by Kouchoukos and colleagues, has been 95%, 88%, 74%, 57%, and 32%, respectively (Fig. 12-29). Survival was somewhat better in patients with anuloaortic ectasia than in those operated on for ascending aortic dissection. Early (hospital) death was 4.7% (CL 2.8%-7.5%), although it was less in patients with anuloaortic ectasia or chronic aortic dissection (Table 12-4), as also reported by Gott and colleagues.

With methods of myocardial management now in use, early...
Hospital Mortality after Composite Prosthetic Valve-Graft Replacement of Aortic Valve and Ascending Aorta

<table>
<thead>
<tr>
<th>Aortic Disease</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anuloaortic ectasia</td>
<td>69</td>
<td>2</td>
<td>2.9</td>
<td>1.0-6.8</td>
</tr>
<tr>
<td>Chronic aortic dissection</td>
<td>39</td>
<td>1</td>
<td>2.6</td>
<td>0.3-8.5</td>
</tr>
<tr>
<td>Acute aortic dissection</td>
<td>12</td>
<td>2</td>
<td>17</td>
<td>6-11</td>
</tr>
<tr>
<td>Others*</td>
<td>7</td>
<td>1</td>
<td>14</td>
<td>2-41</td>
</tr>
<tr>
<td>TOTAL</td>
<td>127</td>
<td>6</td>
<td>4.7</td>
<td>2.8-7.5</td>
</tr>
</tbody>
</table>

Data from Kouchoukos and colleagues.\textsuperscript{531}  
*Includes syphilitic aortitis, replacement valve endocarditis, and extreme poststenotic aortic dilatation.

Key: CL, 70% confidence limits.

limited. Results presented by Okita and colleagues from the experience of Ross suggest poorer overall survival with allograft replacement, but this is related primarily to higher hospital mortality than that reported by Kouchoukos and colleagues.\textsuperscript{531} Also, the distribution of primary pathologies is quite different in the two series. However, Yacoub and colleagues reported 94% survival at 10 years in 74 patients having aortic root replacement with unprocessed viable (“homovital”) aortic allografts.\textsuperscript{51} They also reported a larger series of aortic root replacements with aortic allografts that included the homovital group plus a greater number of antibiotic-sterilized allografts.\textsuperscript{522} Survival at 20 years was 71%, excluding patients operated on for endocarditis or aneurysm of the ascending aorta or dissection, so this series does not provide the actual incremental risk for coexisting ascending aortic aneurysm.

Aortic root replacement with a stentless porcine bioprosthesis is also associated with low early mortality.\textsuperscript{526} In a multicenter trial (21 centers), 226 patients with mean age 70 ± 8.6 years received a Medtronic Freestyle porcine aortic root bioprosthesis.\textsuperscript{1,2} Two thirds were operated on for aortic valve regurgitation or mixed stenosis-regurgitation, and 24% required ascending aorta replacement. Operative mortality was 11% in the older age group of patients with a high proportion of aortic pathology. Hemodynamic performance has been excellent, and risk of thromboembolism leading to permanent neurologic deficit has been 1.0% per year over 6 years. The Freestyle bioprosthesis may be the device of choice for replacing the aortic root in patients over age 70 years.

Too few long-term follow-ups have been reported to define the intermediate-term results after use of an autograft pulmonary valve cylinder for replacement of the aortic valve and ascending aorta.

Era

Risk of hospital mortality has declined with each passing year since the beginning of operations to replace the aortic valve (Table 12-5). Even in the current era, risk of early death after aortic valve replacement continues to decrease.
Global Myocardial Ischemic Time

Global myocardial ischemic time remains a risk factor for death early after isolated or combined aortic valve replacement. Although most aortic valve operations are performed using cold cardioplegia, it is difficult to document that mortality after aortic valve replacement has been improved by abandoning continuous coronary perfusion or hypothermic ischemic arrest as the method of myocardial management. The duration of relatively safe global myocardial ischemia has increased considerably with widespread use of cold cardioplegia (see “Cold Cardioplegia [Multidose]” under Methods of Myocardial Management during Cardiac Surgery in Chapter 3). As is always the case, the incremental risk of duration of global myocardial ischemic time is additive to, and at times interactive with, the effects of other risk factors. Thus, the risk of 120 minutes of global myocardial ischemia using cold cardioplegia is relatively low in patients with aortic stenosis. Risk is also low in patients who are in NYHA class II (Fig. 12-32, A) preoperatively, but higher in preoperative class V patients with aortic valve regurgitation and hemodynamic instability (Fig. 12-32, B).

When the hemodynamic state is unstable before CPB, the period of relatively safe global myocardial ischemia seems longer with current techniques of antegrade plus retrograde infusion of the cold cardioplegic solution, controlled aortic root reperfusion, and warm induction of cardioplegia and substrate enhancement of the cardioplegic solution (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and When Needed Warm Cardioplegic Induction” in Chapter 3). These techniques should translate into increased survival.

Type of Replacement Device

Survival for at least 15 years is probably unrelated to the type of aortic valve replacement device used.\(^{31,15}\) This inference has been supported by two randomized trials.\(^{40,41,31,32}\) However, valve-related complications are more numerous in patients receiving mechanical valves, the result of considerably more nonfatal bleeding episodes in that group.\(^{31,11}\)

The literature is replete with nonrandomized studies comparing various cardiac valve replacement devices and claims of survival superiority of one over the other. Grunkemeier and colleagues presented data that, after correcting for age differences between groups, showed no survival advantage for use of either a mechanical or tissue valve.\(^{24}\) They suggested that important clinical differences, such as structural failures or bleeding, do not require randomized trials to demonstrate statistical differences in properly controlled clinical evaluations.\(^{23}\)

Stentless Valves

Increased rapidity and greater reverse remodeling of the LV after valve replacement are assumed to result in better survival. Statistical methods to prove this are still in the primitive stages of development, but in a study of 8905 postoperative echocardiograms after 3850 aortic valve replacements with a stented bioprosthesis, no influence of rapidity and completeness of reverse remodeling was found to correlate with time-related survival. A Framingham study showed that LV hypertrophy has important prognostic implications even for patients free of clinically apparent cardiovascular disease.\(^{13}\) Levy and colleagues followed 3220 subjects older than 40 for 4 years, correcting for age, diastolic blood pressure, pulse pressure, treatment of hypertension, cigarette smoking, diabetes, obesity, and lipid ratios.\(^{13}\) They found that for each 50 g · m\(^{-2}\) in LV mass corrected for height, the hazard ratio for death from all causes was 1.49 in men and 2.01 in women. However, inferences about the association of LV hypertrophy secondary to systemic hypertension may not be entirely transferable to that secondary to aortic valve disease. The former has complex systemic humoral, cellular, and vascular aspects not generally present in the latter.

Evidence supporting superiority of stentless aortic valve heterografts over stented heterograft prosthetic valves in reducing LV hypertrophy after valve replacement has been conflicting, but several recent randomized trials indicate similar survival and regression of LV hypertrophy with either
a stented bovine pericardial valve prosthesis or a stentless heterograft. In a randomized trial comparing the Toronto Stentless porcine valve (St. Jude Medical Inc., St. Paul, Minn.) with the PERIMOUNT stented bovine pericardial valve (Edwards Lifesciences, Irvine, Calif.), regression of LV hypertrophy and mortality out to 12 years were similar.\textsuperscript{28} These results are supported by other randomized trials.\textsuperscript{A4,C14,R9}

Studies comparing other stentless bioprostheses for aortic valve replacement are also inconclusive for differences in survival.\textsuperscript{22} Yacoub and colleagues showed promising results with almost no decline in survival for the first 10 years after aortic valve replacement with homovital aortic allografts.\textsuperscript{71} Cartier and colleagues compared stentless replacement devices for aortic valve replacement:\textsuperscript{16} survival at 5 years was 96% for pulmonary autografts (mean age 34 ± 16 years), 84% for aortic allografts (mean age 47 ± 19 years), and 84% for stentless porcine xenografts (mean age 68 ± 8 years), with major differences in the age of patients in each group. Aklog and Yacoub compared pulmonary autografts and aortic allografts (as an aortic root replacement) in a prospective randomized trial and found similar early risk and 5-year survival,\textsuperscript{A2} but at 10 years survival was 97% in the autograft group and 83% in the allograft group ($P = .006$).\textsuperscript{E3} Allograft aortic root replacement compares with aortic root replacement using a pulmonary autograft because of similarly exposed suture lines. After aortic valve replacement with a pulmonary autograft, death would be unusual, if not rare, as a result of bleeding from the pulmonary allograft used for RVOT reconstruction. Serious hemorrhage more typically results from the aortic root reconstruction. Risk of infection or heart failure after either procedure is similar. Follow-up is insufficient, however, to determine durability of the repair.

Use of an allograft replacement device sewn frechand (subcoronary technique) into the aortic position has had no adverse effect on early survival. This is evident from the previous discussions in this chapter, from the experience of O’Brien and colleagues\textsuperscript{44} (Fig. 12-33), and from the UAB experience (1981-1988) of no deaths (0%; CL 0%-2.5%) among 70 patients undergoing isolated aortic valve replacement and 7 undergoing concomitant.\textsuperscript{E20}

**Stent-Mounted Porcine Xenograft Valves** These valves have not been shown to affect survival adversely when further replacements can be performed.\textsuperscript{E20} However, Lytle and colleagues found that the combination of a stent-mounted bioprosthesis and chronic anticoagulation decreased 10-year survival.\textsuperscript{L28}

**Mechanical Valves** Mechanical replacement devices have not had an adverse effect on survival, but only because most bleeding complications from warfarin therapy are not fatal, although clinically important.\textsuperscript{126,127} Zellner and colleagues followed patients having aortic valve replacement with the St. Jude Medical prosthesis and analyzed competing risks of outcomes\textsuperscript{22} (Fig. 12-34). At 15 years, deaths related to the prosthesis reduced survival to 79%. Complications related to the valve (e.g., reoperation, endocarditis, thromboembolism, anticoagulant-related bleeding) that were not fatal occurred in 37% of patients, leaving only 42% free of death or complications related to the prosthetic valve. Non–valve-related deaths reduced the number of patients living and free of all complications to 23%.

Studies comparing different modern mechanical prostheses generally do not show clinical advantages among them.\textsuperscript{D23}

**Pulmonary Valve Autograft** The potential for adverse effects from a pulmonary valve autograft as a replacement for the aortic valve has not been evaluated completely. Earlier information suggested no adverse effect,\textsuperscript{G4,G11,R16} but more recent data suggest that 30-day mortality for this operation is 3.5% to 5.1% higher than for other replacement methods.\textsuperscript{E10,G34,539} (Table 12-6).

**Hospital Morbidity**

**Complete Heart Block**

Infrequently, replacement of severely calcific aortic valves leads to complete heart block. It usually results from trauma to the bundle of His after removal of calcium from the region of the membranous septum and right trigone beneath the noncoronary cusp–right coronary cusp commissure. Although this complication occasionally is unavoidable, care in removing calcium from these areas and rigorous avoidance of suture penetration of the membranous septum near its junction with the muscular septum should reduce its occurrence greatly. Heart block may be transient rather than permanent.

**Neurologic Deficits**

Neurologic complications after aortic valve replacement may mar an otherwise routine operation. The current risk of neurologic complications among STS National Database participants is 3.5%.\textsuperscript{G34} With known arteriosclerotic cardiovascular disease, the risk increases; when CABG is combined with aortic valve replacement, risk increases to 5.7%. Attention to the details of avoiding loss of calcific fragments during valve resection and to techniques for removing air from the heart after closing the aorta are the only methods available to reduce early risk of neurologic complications associated with aortic valve replacement. Late neurologic events appear to correlate more with degree of vasculopathy than with bioprosthetic aortic valve replacement itself.\textsuperscript{E329}
Symptomatic Improvement

The functional status of most surviving patients is good after aortic valve replacement. About 90% of patients traced 5 to 10 years are in NYHA functional class I or II.\(^{58}\) About 70% of preoperatively in NYHA class IV are in class I or II postoperatively, as are 80% of those preoperatively in class III and 90% of those preoperatively in class II. Hemodynamically efficient replacement devices appear to favor good functional results. After aortic valve replacement with aortic allografts in the subcoronary position, Prager and colleagues reported that at an average follow-up of 4.2 years, 100% and 97% of patients were in NYHA class I and II, respectively, when a root replacement technique was used.\(^{522}\) Doty and colleagues reported 94% of patients in functional class I and 4% in class II after aortic valve replacement with an allograft at an average follow-up of 4.6 years.\(^{146}\) The authors also reported 92% of an older group of patients (mean age 71 ± 8.4 years) in class I or II after aortic valve replacement with stentless porcine aortic bioprosthesis at an average follow-up of 2.3 years.\(^{143}\)

Exercise capacity tested objectively can approach normal after aortic valve replacement, as shown in patients with aortic stenosis, depressed preoperative exercise capacity, and near-normal resting LV end-diastolic pressure.\(^{11}\) In other situations, such as in many patients with aortic regurgitation and preoperatively increased LV end-diastolic pressure, exercise capacity is improved after operation but remains subnormal.\(^{511}\) Exercise capacity testing after aortic valve replacement with a pulmonary autograft has yielded impressive results. The Ross procedure provides excellent hemodynamic results at rest and exercise, with values indistinguishable from normal,\(^{521}\) including exercise capacity sufficient for athletic competition and ability to achieve extraordinarily high cardiac output with low pressure gradient across the LVOT.\(^{101}\)

Left Ventricular Structure and Function

The degree of improvement in LV structure and function, if any, after aortic valve replacement depends primarily on such factors as the type and extent of secondary cardiomyopathy at operation, coexisting disease, extent (if any) of permanent intraoperative LV damage, and energy loss and regurgitation across the valve replacement device.

Aortic Stenosis

Completeness of return of LV mass toward normal after normalization of LV systolic pressure by aortic valve replacement depends on extent of myocardial degenerative changes (and thus degree of LV hypertrophy) and related loss of LV reserve.\(^{823}\) When LV end-diastolic pressure is still low at operation, LV wall thickness and mass regress substantially, the latter from an average of 206 g · m\(^{-2}\) to 133 g · m\(^{-2}\) \((P < .05)\) in a study by Kennedy and colleagues.\(^{511}\) The regression continues for more than a year postoperatively,\(^{537}\) but completely normal LV mass is rarely relieved.

In addition to reduction in mass, reversal of LV remodeling gradually returns the LV to a more spheroidal shape.\(^{537}\) When LV end-diastolic pressure has become importantly elevated before aortic valve replacement, either because of afterload mismatch (see Natural History earlier in this chapter) or reduced contractility, LV mass may be importantly reduced after operation.\(^{58,511,516}\) However, at this stage many patients fail to show a reduction in LV mass, presumably because of irreversible myocardial degenerative changes. Krayenbuehl and colleagues showed that the preoperatively enlarged muscle fiber diameter shortens within 1 to 2 years after aortic valve replacement as part of this process, but with some increase in interstitial fibrosis.\(^{535}\) Interstitial fibrosis tended to decrease thereafter, but the myocardium did not return to normal, retaining some permanent fibrosis.

Rate and completeness of LV mass reduction after aortic valve replacement may be related to type of replacement device used and other factors at operation. LV function early after operation for aortic valve replacement with LV hypertrophy appears to be better when cold blood cardioplegia is
employed vs. other methods of myocardial management.\textsuperscript{111} Jin and colleagues showed more complete resolution of LV hypertrophy and greater improvement in LV function when an aortic allograft or stentless porcine bioprosthesis was used to replace the aortic valve than when a stent-mounted bioprosthesis or mechanical valve was employed.\textsuperscript{112} Walther and colleagues found regression of LV hypertrophy in all patients after aortic valve replacement in a randomized study comparing stentless and stent-mounted bioprostheses.\textsuperscript{113} but patients with stentless bioprostheses had greater regression at 6 months. Maselli and colleagues reported similar findings favoring aortic allografts and stentless bioprostheses, with the most rapid resolution of LV hypertrophy occurring when aortic allografts were used.\textsuperscript{114} Basarir and colleagues also found a greater decrease in LV hypertrophy with aortic allografts than with mechanical prostheses after aortic valve replacement.\textsuperscript{115}

Kleine and colleagues demonstrated that turbulence, and thus energy loss, caused by mechanical heart valves can be reduced simply by optimal orientation of the device relative to flow patterns created by LV ejection.\textsuperscript{116} They state that turbulence may be an important factor in reversing ventricular remodeling after implantation of a prosthetic heart valve, as well as in relief or reduction of pressure gradient across the LVOT. The premise is based on the observation that blood is ejected from the LV eccentrically at the level of the aortic valve. In humans (and pigs) the eccentric flow is toward the right posterior wall of the aorta, the location of the noncoronary sinus of Valsalva. Mechanical valves oriented to place the major flow orifice to take advantage of the eccentric flow pattern in the aorta have optimal performance in that orientation. Thus, a tilting-disc valve properly oriented can perform better than a bicuspid device, even though the latter is perceived as the better replacement device.

Functional response of the LV to sudden surgical normalization of systolic pressure can be anticipated from morphologic response.\textsuperscript{117} LV end-diastolic and end-systolic volume indices decrease and EF increases within 6 months after aortic valve replacement.\textsuperscript{118} However, Hwang and colleagues found that 66% (CL 54%-76%) of patients with preoperative LV dysfunction still had abnormal values 6 months postoperatively.\textsuperscript{119} When LV wall stress is essentially normal at operation because of appropriate LV hypertrophy and increased wall thickness, indices of LV systolic function (including EF) remain normal or become supra-normal postoperatively.\textsuperscript{120,121} By the time of operation, when LV hypertrophy is insufficient to prevent afterload mismatch, the reduced EF and elevated end-diastolic pressure still may return to normal.\textsuperscript{122,123} However, when these indices of LV function have deteriorated because of reduced contractility, usually associated with marked cardiomegaly, they often show little improvement after operation.

Hwang and colleagues developed a logistic risk factor equation for postoperative LV dysfunction after aortic valve replacement for aortic stenosis.\textsuperscript{124} Risk factors were lower preoperative EF, one or more myocardial infarctions preoperatively, low preoperative aortic valve gradient (low cardiac output), and unrevascularized coronary artery disease.

**Aortic Regurgitation**

The increase in LV mass that develops in patients with important aortic regurgitation can occur insidiously and in the absence of symptoms. Also, LV mass can become much greater in these patients than in those with aortic stenosis.\textsuperscript{125} At least experimentally, abolishing LV volume overload must be performed within 6 months of its inception to permit regression toward normal mass.\textsuperscript{126} This observation helps explain why reduction in LV mass after valve replacement for aortic regurgitation is often moderate in degree and unpredictable, even when indices of LV systolic and diastolic function improve after operation.\textsuperscript{127,128} When these indices do not improve, the often massive increase in LV mass fails to regress and may even worsen several years after operation.

Regression of muscle fiber diameter after aortic valve replacement described for patients with aortic stenosis also occurs after operation for aortic regurgitation.\textsuperscript{129} Decrease in interstitial fibrous content is greater after valve replacement for aortic regurgitation, however.

Thus, it is not surprising that when LV contractility and EF are good and LV end-diastolic pressure is only mildly elevated, LV mass becomes almost normal late after replacing a regurgitant aortic valve.\textsuperscript{130} When already severely diminished at valve replacement, LV systolic and diastolic function often remain compromised late postoperatively, and LV mass fails to regress.

When LV systolic function (estimated by resting and exercise EF, as well as end-systolic volume, LV fractional shortening, and velocity of circumferential shortening) is truly normal at aortic valve replacement (found in only about 10% of patients with symptomatic aortic regurgitation),\textsuperscript{131} LV diastolic function is usually normal and, with systolic function, remains normal postoperatively. When preoperative LV systolic function and diastolic function are mildly or moderately depressed at rest or with stress testing (usually associated with only moderate cardiomegaly and increased LV mass), regression (but not normalization) of impaired resting function usually characterizes the postoperative period, but response of systolic function to stress usually remains abnormal.\textsuperscript{132,133} Impaired preoperative exercise capacity adversely affects the probability of important recovery of LV systolic function after valve replacement.\textsuperscript{134} Also, even with other factors equal, the longer the duration of preoperative limitation of LV systolic function, the less likely the possibility of appreciable return toward normal.\textsuperscript{135} When systolic function improves within 6 months of valve replacement, however, it usually improves still further over the next several years,\textsuperscript{136} although about one third of patients show no additional improvement. Severe preoperative reduction of resting or stressed LV systolic function often indicates irreversible deterioration.\textsuperscript{137,138} Some patients may even show a progressive deterioration in LV systolic function and an increase in LV diastolic volumes leading to death with heart failure a few months to a few years after operation.

Although LV diastolic function is often not improved by aortic valve replacement for aortic regurgitation,\textsuperscript{139,140} the characteristically large LV end-diastolic volume is usually reduced toward normal within 10 days of ablation of regurgitation (and thus decrease in stroke volume).\textsuperscript{141} Further volume reduction occurs late postoperatively in many patients, with the greatest reduction in those with lesser degrees of abnormal LV structure and function preoperatively. Bonow and colleagues found that preoperative exercise capacity correlated well with postoperative reduction of LV end-diastolic dimensions.\textsuperscript{142} These fell strikingly and occasionally to near-normal values in patients with good preoperative exercise tolerance, whereas in patients with impaired exercise ability,
some hearts were larger postoperatively, and few regressed in size late postoperatively (Fig. 12-35).

Failure of LV end-diastolic volume to regress toward normal indicates irreversible morphologic and functional LV damage and portends poor long-term results. By the time exercise ability has become impaired, the diastolic properties of the LV may have even become irreversibly impaired, and fixed cardiomegaly may be present (Fig. 12-36). These relationships are particularly important because exercise capacity becomes limited earlier in the course of aortic regurgitation than in aortic stenosis.

These same considerations apply to patients with periprosthetic leakage late postoperatively. The hemodynamic and functional variables after operation for aortic regurgitation appear to be very sensitive to the LV volume overload of periprosthetic leakage. Thus, Schwarz and colleagues found that such patients had importantly reduced LV systolic function late postoperatively compared with patients who had no periprosthetic leakage.

In summary, patients overall experience considerable reduction of LV diastolic volume, decrease in end-systolic volume, and increase in EF after aortic valve replacement for aortic regurgitation. However, about 60% of patients with preoperative dysfunction have dysfunction postoperatively. Some of the variability among reports of postoperative LV function may relate to the variable interval between operation and postoperative testing; LV systolic performance at rest and particularly during exercise improves still further after 1 year. Borer and colleagues reported improvement between the second and third postoperative years and observed no subsequent deterioration in patients who improved.

LV systolic dysfunction preoperatively is the most predictive variable for postoperative LV dysfunction.

**Left Ventricular–Aortic Energy Loss**

All devices placed within the aortic root for replacement of the aortic valve are obstructive to some degree. This inherent obstruction may be minimized by complete replacement of the aortic root with an aortic allograft, stentless bioprosthesis, or pulmonary autograft. These operations are more complex than replacement of the aortic valve with a mechanical or stent-mounted prosthesis.

Gradients are minimal after freehand insertion of an aortic allograft or stentless aortic bioprosthesis, but are pronounced in patients receiving mechanical or stent-mounted
Chapter 12 Aortic Valve Disease

The magnitude of gradient varies greatly depending on characteristics of the prosthesis, size of the device relative to size of the patient, cardiac output (study done during rest, exercise, or pharmacologic stimulation), and abnormal conditions in or around the replacement device.

Fisher and colleagues evaluated mechanical and stent-mounted bioprosthetic valves in vitro with regard to pressure gradients generated at various flow rates. In vivo measurement of pressure gradient across mechanical or bioprosthetic cardiac valves by Doppler ultrasound has been complicated by complex blood flow velocity profiles associated with the prosthetic valve. Doppler ultrasound, although noninvasive, tends to overestimate energy loss resulting from pressure gradient across prosthetic valves. In addition, aortic curvature, arterial distensibility, arterial impedance, and unsteady flow appear to affect interpretation of pressure measurements.

Despite these limitations, reproducible estimates of pressure gradient are possible in vivo using Doppler ultrasound techniques. These values have been used to compare various prostheses and bioprostheses according to label size (Tables 12-7A and 12-7B). Resting gradient under 10 mmHg is desirable. Comparative figures are subject to interpretation, recognizing that most values are obtained during rest, and even then, cardiac output (flow) may vary considerably from patient to patient. In addition, label size among different types of device is associated with widely variable valve orifice size. Comparing studies is also complicated by what is reported: peak LV to aortic systolic gradient or mean systolic gradient, for example. After considering these confounding factors, however, hemodynamic performance characteristics clearly have improved with newer prosthetic valve designs. Also, most cardiac valve replacement devices function well at rest if greater than 23 mm in diameter. Some 21-mm devices are satisfactory, but 19-mm devices may have higher than desirable gradient even at rest.

Virtually all mechanical prostheses and bioprostheses larger than the 21-mm size can provide satisfactory performance in most adults. Some 21-mm mechanical prostheses and first-generation bioprostheses have high energy loss during periods of increased cardiac output. Among the 21-mm mechanical prostheses, the St. Jude Medical valve performs well in this regard. Other prostheses of either tilting-disc or bicuspid design also have good hemodynamic performance.

Because of the variability in the gradient usually present across the prostheses used for aortic valve replacement, unusual gradients may be difficult to identify. However, such abnormalities develop from fibrous ingrowth below or above the device, dense clot around the valve (thrombotic encasement), or leaflet calcification of a bioprosthesis. Gradients

![Figure 12-37](image-url) In vitro evaluation of mechanical and stent-mounted bioprosthetic valves. Bench testing of these devices for cardiac valve replacement compares root mean square (RMS) forward flow through device to pressure gradient generated. Mechanical and stent-mounted pericardial prostheses show a performance advantage compared with first-generation stent-mounted porcine bioprostheses. (From Fisher and colleagues.)

### Table 12-7A Systolic Left Ventricular–to-Aortic Pressure Gradient (mmHg): Mechanical Prostheses

<table>
<thead>
<tr>
<th>Prosthesis</th>
<th>Label Size (mm)</th>
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<tbody>
<tr>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Starr-Edwards 1260</td>
<td></td>
</tr>
<tr>
<td>Medtronic-Hall</td>
<td></td>
</tr>
<tr>
<td>Monostrut</td>
<td></td>
</tr>
<tr>
<td>St. Jude</td>
<td>16-22</td>
</tr>
<tr>
<td>CarboMedics</td>
<td>17-19</td>
</tr>
</tbody>
</table>

Data from references A14, A17, C7, C9, C12, C13, C18, C30, C31, C43, D5, J15, K15, L7, L8, L12, M38, N5, P9, P13, P24, R25, R26, T5, W13, W15, W19, and Z1.

### Table 12-7B Systolic Left Ventricular–to-Aortic Pressure Gradient (mmHg): Biological Prostheses

<table>
<thead>
<tr>
<th>Prosthesis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Carpentier-Edwards porcine</td>
<td>32</td>
</tr>
<tr>
<td>Hancock porcine</td>
<td>34</td>
</tr>
<tr>
<td>Hancock MO</td>
<td>17</td>
</tr>
<tr>
<td>Hancock II</td>
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</tr>
<tr>
<td>Carpentier-Edwards pericardial</td>
<td>17-24</td>
</tr>
<tr>
<td>Medtronic Freestyle</td>
<td>13</td>
</tr>
<tr>
<td>St. Jude SPV</td>
<td></td>
</tr>
</tbody>
</table>

Data from references A14, A17, C7, C9, C12, C13, C18, C30, C31, C43, D5, J15, K15, L7, L8, L12, M38, N5, P9, P13, P24, R25, R26, T5, W13, W15, W19, and Z1.

*Data represent in vivo mean pressure gradient measured by Doppler ultrasound.
of 85 to 100 mmHg may be produced, but they can be much lower and more difficult to define as abnormal when cardiac output is reduced by these developments.

**Effective Orifice Area**

Acoustic anomalies caused by mechanical prosthetic valves after implantation make it difficult, if not impossible, to measure prosthetic valve area by ultrasound (echocardiography) using pressure half-time estimates. These methods are most applicable to bioprosthetic heart valves. Mechanical prostheses cause changes in the flow velocity patterns across the aorta, and in vivo measurements are often subject to question as to sampling sites. A modified Bernoulli equation appears to be the most reproducible and accurate method for calculating prosthetic valve area by ultrasound. The mathematical constants of these equations are loaded into modern echocardiographic equipment to facilitate estimating valve area.

**Hemolysis**

Patients with allograft valves sewn freehand into the aortic root do not have abnormal red blood cell hemolysis, even when there is periprosthetic or central leakage. Well-functioning stent-mounted xenografts generally do not produce hemolysis when central leakage develops, but they may do so with periprosthetic leakage. All well-functioning mechanical valves produce at least a small degree of hemolysis, with disc-type valves producing less than ball valves. Periprosthetic and intraprosthetic leakage produces increased amounts of hemolysis, the magnitude of which is related to the amount of regurgitation. Thrombotic narrowing of a prosthetic orifice also importantly increases hemolysis.

**Replacement Device Regurgitation**

**Periprosthetic Leakage**

Periprosthetic leakage may occur after replacing the aortic valve with an allograft or stentless porcine bioprosthesis placed as a freehand subcoronary implant. Elimination of the dead space between graft and the patient’s aorta by sutures is thought to reduce occurrence of leakage, although these sutures may actually cause periprosthetic leakage. Periprosthetic leakage in the presence of aortic allografts or freehand subcoronary-implanted bioprostheses is related to technical problems at the outflow or upper suture line. Buckling of the graft or dehiscence of sutures from the aortic wall results in dissection of blood along the patient’s aortic wall into the space between the graft and aorta. Eventually, a passageway is created to the inflow or lower suture line. Although placing sutures between the graft and aorta may reduce the space or may more securely approximate the graft and aorta at operation, it is virtually impossible to obliterate the space until healing has occurred. Sutures between the graft and aorta other than at the inflow and outflow suture line could actually open tracts to this space along the sutures and needle holes. The best preventive measure against periprosthetic leakage is a secure outflow suture line, as confirmed by intraoperative echocardiography and a strict policy to repair any leakage found at operation.

With use of mechanical prostheses or bioprostheses, important periprosthetic leakage is uncommon in the absence of infection, although minor leakage may occur. Periprosthetic leakage usually becomes evident during the early months after operation. Shean and colleagues reported a prevalence of minor periprosthetic leakage of 17% in the Massachusetts General Hospital series. In addition, 6% of patients (CL 5%-7%) had clinically recognizable hemolysis.

When periprosthetic leakage develops and no infection is present, the area of dehiscence is usually small and can be repaired with one or two pledgeted mattress sutures. The prosthesis does not have to be removed and replaced unless the area of dehiscence is large.

**Central Leakage**

**Allograft Aortic Valves**

Allograft valve central leakage has a variety of causes and a variable prevalence that relate to valve preparation, storage, and insertion techniques. For antibiotic-sterilized, wet-stored (at 4°C) valves, degeneration (cusp rupture with or without minor calcification) is the most common cause (Fig. 12-38), with a 10-year prevalence of up to 15% to 18%. The Stanford group reported a 30% 10-year prevalence of degenerative valve failure with antibiotic-treated valves. Differences in prevalence relate primarily to the definition of degenerative failure, which in the Stanford series was the appearance of a new regurgitant murmur, in the O’Brian series was reoperation, and in the Barrett-Boyes series was moderate or severe regurgitation. Patients with mild or trivial regurgitation are not considered examples of valve failure, because this may develop early after operation from imperfect cusp coaptation. Kirklin and colleagues reported an 85% freedom from valve failure (implantation for cusp failure or moderately severe or severe

![Figure 12-38](image-url)
Aortic root diameter is also a continuously vari-

Fig. 12-39 summarizes the incremental risk factors for allograft regurgitation or 3+ or greater aortic regurgitation on follow-up echocardiography. Dashed lines enclose 68% confidence limits. (From Kirklin.220)

**Table 12-8** Incremental Risk Factors for Central Leakage from Cusp Degeneration of Allograft Aortic Valves Used for Aortic Valve Replacementa

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Freedom from important allograft aortic valve regurgitation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allograft preparation and storage:</td>
<td></td>
</tr>
<tr>
<td>Chemical sterilization (β-propiolactone)</td>
<td></td>
</tr>
<tr>
<td>Sterilization by irradiation</td>
<td></td>
</tr>
<tr>
<td>(Greater) Donor age</td>
<td></td>
</tr>
<tr>
<td>(Larger) Aortic root diameter</td>
<td></td>
</tr>
<tr>
<td>(Younger) Recipient age</td>
<td></td>
</tr>
<tr>
<td>Native valve regurgitation</td>
<td></td>
</tr>
<tr>
<td>Technique of insertion:</td>
<td></td>
</tr>
<tr>
<td>Stent mounting</td>
<td></td>
</tr>
<tr>
<td>Faulty freehand insertion</td>
<td></td>
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</tbody>
</table>

*aRisk factors assembled based on experience and published reports, not obtained by multivariable analysis.

Although difficult to examine, imperfect freehand insertion of an allograft results in altered stress and strain on the cusps, storage, and implantation within a few days (homovital).71 These techniques reduce cusp degeneration and central leakage to a prevalence of 2% to 10% by 10 years after insertion.227,2048 Histologic findings in allograft cusps preserved by these techniques after implantation in animals,220 or retrieval after implantation in humans,204 indicates better preservation of cusp architecture and fibroblasts than when other methods are used. The allograft valve is antigenic,113 however, and both endothelial cells and fibroblasts are probably destroyed by an immunologic process. Antibiotic sterilization and cryopreservation are thought to reduce antigenicity of allograft valves,22 but low-grade rejection still may occur and promote graft degeneration. Tissue matching and immunosuppressive therapy fail to reduce degeneration.72

Donor age appears to be a continuous variable that affects the rate of cusp degeneration, but its effect is weak until after about donor age 50 years. The effect is probably produced by age-related structural changes in the cusps. Cusp calcification is also more common in valves from older donors, which presumably explains why most allograft valves that develop stenosis come from donors over age 60.116 The age effect is such that prevalence of valve degeneration by 10 years after insertion is 8%, 25%, and 40% when donor age is under 20 years, 20 to 50 years, and over 50 years, respectively.216 (Fig. 12-40).

Although aortic root diameter is also a continuously variable risk factor, its effect becomes strong only when it is greater than 30 mm (corresponding to an allograft inner diameter of greater than 28 mm). Thus, central leakage within 10 years is approximately 40% when the aortic root diameter is at least 30 mm and 10% when it is less than 30 mm.817,837 (Fig. 12-41).

The incremental risk of young age on cusp degeneration and central leakage is much weaker than with stent-mounted xenograft valves. However, an analysis by Kirklin and colleagues identified younger recipient age as the primary predictor of late cusp failure.220

A second, less common, cause of important central leakage after freehand insertions is technical error, with cusp distortion and prolapse or progressive host aortic root dilatation associated with bicuspid aortic valve or cystic medial necrosis of the aorta. The free edges of the cusps are overstretched and fail to meet centrally, but are otherwise intact. The latter mechanism can be prevented by avoiding freehand insertion in patients who have large aortic roots.

A third cause of central leakage is endocarditis (see “Replacement Device Endocarditis” later in this chapter).

Table 12-8 summarizes the incremental risk factors for central leakage caused by cusp degeneration. In allograft preparation and storage, integrity of cusp ground substance and fibroblasts is maintained either by short-duration, low-concentration antibiotic disinfection followed by cryopreservation204 and later insertion, or by sterile collection, wet

Figure 12-39 Hazard function for presumed cusp failure (reoperation for allograft regurgitation or 3+ or greater aortic regurgitation on follow-up echocardiography). Dashed lines enclose 68% confidence limits. (From Kirklin.220)

Figure 12-40 Freedom from important allograft aortic valve regurgitation according to age of donor, providing nonviable valves. Only regurgitation from valve wear (degeneration) is included. Numbers at risk are noted. (From Barratt-Boyes and colleagues.816)
which in turn predispose to rupture in the cusp belly or even at the commissures where stresses are minimal in the native valve. Asymmetric location of the graft valve commissures at implantation or distortion of the commissural location during closure of an oblique aortotomy that extends into the noncoronary sinus of Valsalva may be an important cause of altered stress on the graft cusp tissues. Fig. 12-42 shows how a commissural positional abnormality results in lengthening and stretching of the right and left coronary cusps, compared with redundancy of the noncoronary cusp. Calcium deposits are greatest in the anulus and sinus of the redundant cusp, whereas the stretched cusps are subject to cusp tear or disruption. Septal myocardium left on the allograft is broken down and absorbed, because no myocardium is seen on the graft at explantation. This may explain why an aortic valve allograft inserted by the subcoronary freehand technique may show perfect function at operation but become regurgitant within a few weeks or months. In support of this, the prevalence of aortic regurgitation several months after operation is considerably greater with freehand aortic allografts than with aortic valve allografts or pulmonary autografts inserted as part of a full or “mini” root replacement.

Stent mounting of allograft aortic valves used as aortic valve replacements has resulted in a higher prevalence of cusp degeneration and valve regurgitation than has freehand insertion. Risk factors are incremental, so results appear to be best with cryopreserved or homovital valves when donor age is restricted to younger than age 50, recipient age is older than age 15, and aortic root diameter is less than 30 mm. These restrictions could reduce central leakage to 6% at 9 years, although the prevalence rises sharply thereafter.

Pulmonary Autograft. Cusp degeneration or central regurgitation of a pulmonary autograft implanted freehand into the aortic valve position (Ross procedure) may result from technical factors similar to those associated with freehand-inserted aortic valve allografts. It is important to note, however, that the majority of pulmonary autografts are now inserted by the full aortic root replacement technique.

When early regurgitation occurs in this situation, it is likely caused by technical problems with insertion, cusp shrinkage (which should be minimal or absent), and progressive changes of connective tissue related to genetic factors either in the native aortic root tissues that support the pulmonary autograft or in the autograft itself. Technical problems at operation relate primarily to matching diameter of the pulmonary autograft to the LVOT at the position of attachment. The LVOT should be sized up or down to a diameter within 2 or 3 mm of that of the autograft. The autograft should not be stretched over a larger LVOT, and the size of the autograft should not be “taken up” during implantation to a

\[\text{Figure 12-41} \text{ Freedom from important regurgitation according to aortic root diameter after allograft aortic valve insertion. Data set and format are as in Fig. 12-40. (From Barratt-Boyes and colleagues.}\]

\[\text{Figure 12-42} \text{ Effect of commissural position error in aortic valve replacement with an aortic allograft. A, Minor position error. Explanted aortic allograft is shown in surgeon's view, with diagram of major findings alongside. Distance (length of aorta) between commissures bordering noncoronary sinus of Valsalva is shorter than that between commissures bordering left coronary sinus and commissures bordering right coronary sinus. Presumably this is the result of closing an oblique incision in the noncoronary sinus with some aortic tissue loss. This commissural positional abnormality places stress on right and left coronary cusps. Calcium deposits appear greatest in noncoronary cusp. B, Major position error. Explanted aortic allograft is shown in surgeon's view with diagram alongside. Commissure between left and noncoronary sinuses is drawn far to the right above noncoronary sinus rather than following natural position posteriorly. Commissure between right and noncoronary sinuses is drawn far to the right, producing a similar deformity so that commissures nearly touch in noncoronary sinus. This is the result of closure of an oblique incision in noncoronary sinus of Valsalva with large tissue bites, which draws adjacent commissures toward each other, as well as simply not following anatomic contours of aortic valve. Stress on left and right coronary cusps resulted in leaflet tear; noncoronary cusp is redundant, prolapsed, and contains calcium deposits.}\]
substantially smaller aortic anulus. Use of an interrupted suture technique probably provides the most accurate method of suture placement for implanting the autograft and may result in near-perfect valve function later. Addition of a support or reinforcement ring to the LVOT suture line is associated with greater freedom from pulmonary autograft regurgitation (Fig. 12-43).

Connective tissue abnormalities, such as fibrillin deficiency associated with Marfan syndrome, are considered contraindications to aortic valve replacement with a pulmonary autograft because the pulmonary trunk will likely have the same tendency for dilatation as the aorta. Elkins and colleagues noted fibrillin or elastin abnormalities in the resected aorta in a high proportion of patients undergoing the Ross procedure for aneurysm or dilatation of the ascending aorta. Changes in pulmonary autograft dimensions did not correlate with the observed changes in fibrillin or elastin. Concern about potential dilatation of the pulmonary autograft, resulting in aortic valve regurgitation of a bicuspid aortic valve and dilatation of the aortic root and ascending aorta, appears to be overstated. Long-term series do not report this complication when the neoaortic anulus is supported and its diameter fixed.

Although aortic root dilatation is common late after autograft root replacement, it is probably not related to bicuspid aortic valve disease or preexisting degenerative changes in the pulmonary trunk. Histologic abnormalities of the pulmonary trunk are rare and equally prevalent in patients with bicuspid and tricuspid aortic valves. As noted in “Autograft Pulmonary Valve” under Isolated Aortic Valve Replacement earlier in this chapter, the pulmonary trunk may dilate up to 30% when subjected to systemic arterial pressure. Although the precise mechanism remains unclear, the tendency for late anular dilatation in some patients and its association with valve regurgitation has been well documented.

David and colleagues found a higher risk of late dilatation of the neo-aortic root with the root replacement technique than with the root inclusion method in which the autograft is implanted within the native aortic root. reported 10-year follow-up of 218 patients undergoing the Ross operation, 148 with root replacement and 70 with the intraaortic (inclusion) technique. Freedom from autograft reoperation at 10 years was 81% and 84%, respectively. Similar results were reported by Kouchoukos and colleagues.

Autograft dilatation is the main cause of failure following root replacement, and autograft valve prolapse is the main failure mode after the inclusion technique. Following root replacement, the rate of autograft dilatation has been reported to 0.5 mm · year$^{-1}$ in the adult population and 2 mm · year$^{-1}$ in a mixed pediatric and young adult population. Presence of preoperative aortic regurgitation is an independent predictor of autograft dilatation. Systemic hypertension may also play a role. Long autografts may be more prone to dilatation of the supracommissural segment, and some have recommended keeping the autograft as short as possible. Juthier and colleagues reported absence of neoaortic regurgitation at a mean follow-up of 4 years when the autograft was reinforced with a polyester tube.

Whether current methods to stabilize the neoaortic valve at the anular and sinutubular levels following root replacement, or wrapping the entire autograft with bovine pericardium or polyester, will affect late freedom from moderate or worse valve regurgitation has been incompletely studied. However, an analysis of the German-Dutch Ross registry (more than 1500 patients) identified preoperative aortic regurgitation and the nonreinforced full root technique as factors associated with late autograft failure (8-12 years). Elkins and colleagues reported an 83% freedom from autograft failure at 16 years, and also identified preoperative aortic regurgitation as a risk factor for late valve failure. Among patients undergoing valve implantation by the inclusion technique, late reoperation is normally associated with progression of early discrete aortic regurgitation, which likely results from a geometrically imperfect implant.

Increases in neoaortic anulus diameter over time in excess of that expected by somatic growth has also been observed in the pediatric population. Among pediatric patients, freedom from autograft valve-related reoperation is about 86% at 12 years following aortic root replacement. Shinkawa and colleagues reported a 95% freedom from autograft reoperation at 10 years, but only 64% by 15 years among neonates and infants. A meta-analysis of reports published between 2000 and 2008 indicates that durability limitations of the Ross procedure in children and young adults become apparent by the end of the first postoperative decade.

**Stent-Mounted Xenograft (Porcine) and Pericardial (Bovine) Glutaraldehyde-Treated Aortic Valves**

These valves, mounted on a cloth-covered stent, may develop central leakage because of cusp rupture either in the commissural region or in the cusp belly. Rupture is often associated with cusp calcification, in contrast to allograft valves inserted freehand. Also, calcification may produce stenosis rather than rupture. Although most ruptures in this type of bioprosthesis are precipitated by collagen fatigue and fracture and subsequent invasion of the cusp by macrophages, some may be caused by abrasion of the cusp against a stent. A few cases have resulted from cusp perforation by long, cut ends of rigid suture material projecting inward from the sewing ring toward the cusp base. Detachment of the valve’s aortic remnant from the stent pillar, in contrast to stent-mounted allograft valves and previously used formaldehyde-treated stent-mounted xenografts, is rare and associated with failure of host tissue overgrowth across the polyester bias strip onto the graft. Presumably the collagen cross-linkage from glutaraldehyde preservation of porcine aortic and bovine...
Figure 12-44 Nomogram of estimated risk-adjusted probability of bioprosthetic degeneration within 5 years of inserting first-generation stent-mounted porcine xenografts, according to patient’s gender and age at insertion. (From Blackstone and Kirklin.81)

pericardial valves strengthens the aortic tissue sufficiently to prevent tearing and detachment.

Among 478 patients who received a bovine pericardial prosthesis in the premarket approval stage, 70 experienced structural valve deterioration.518 Pathology was pure regurgitation in 23, pure stenosis in 18, and mixed in 20 (uncertain in 9). Modes of failure were calcification (39%), noncalcific degeneration (30%), fibrosis (7.1%), dehiscence (5.7%), and a combination of these (14%). Calcification and degeneration appeared to accelerate with time, and these modes of degeneration were particularly accelerated by younger age at implant.

Thus, risk factors for central leakage from degeneration (structural valve deterioration [SVD]) of the cusps of a stent-mounted glutaraldehyde-fixed xenograft include female gender and younger age of recipient (Fig. 12-44). This accelerated rate of degeneration of xenograft valves in the aortic position rapidly declines with advancing age. In patients older than about 65 years, failure at 10 years is less than 5%.837 Jamieson and colleagues showed that degeneration of first-generation porcine xenograft valves was related to younger age, decreasing after age 60 and almost imperceptible in patients over 70.36.39 A similar age-related effect on durability of bovine pericardial bioprostheses has been observed (Fig. 12-45); chance of valve explant for structural deterioration is less than 10% at 15 years in patients over age 65 years89 (Fig. 12-46). Statistical methodology also affects interpretation of the apparent frequency of degeneration625 (see “Computing Risks” in Section IV of Chapter 6). Kaplan-Meier analysis estimates accurately the biological frequency of SVD among living patients as an isolated event; competing risks analysis places SVD into the context of mortality before SVD occurs. Thus, in older patients, not only does the biological behavior of the xenograft contribute to a lower occurrence of SVD, but mortality decreases the probability that the patient will survive long enough to experience the event (Table 12-9).

Method of valve preservation is also probably a risk factor, because glutaraldehyde fixation at pressures above zero abolishes the normal collagen crimp and diminishes cusp pliability (distensibility). As a result, the cusp kinks rather than stretches on opening, leading to compression fracture of the collagen at sites of kinking.866,866 In contrast, zero-pressure fixation retains collagen crimp and produces a more pliable cusp with mechanical properties that closely approach those of fresh cusp tissue.3410 Second- and third-generation zero-pressure-fixed bioprostheses may perform better over time than first-generation pressure-fixed valves.35 Also, substances introduced into the fixation protocol may reduce risk of cusp calcification.

Accumulating data demonstrate that second- and third-generation bioprostheses last longer than first-generation devices.32,32 (Fig. 12-47). The Hancock II porcine aortic xenograft with improved stent and anticalcification treatment (T6) and the Edwards Lifesciences bovine pericardial valve with flexible stent and anticalcification treatment (T80) are showing less degeneration beyond 10 years than first-generation devices.38 Cryopreserved and homovital aortic allografts appear on the same curve as second-generation xenografts. Data are limited beyond 12 years with third-generation stentless porcine valves, but structural integrity appears good and on the same trajectory as aortic allografts.45
Stentless Xenograft (Porcine) Aortic Valves  Absence of a stent has the theoretic advantages of making the device less stenotic and decreasing perivalvar leakage. Also, by analogy with allografts, degeneration may occur more slowly in stentless than in first-generation stent-mounted xenografts. Experimental and short-term clinical results in a small number of patients are compatible with this hypothesis. Midterm data show that the prevalence of primary periprosthetic leak at 4 years is 2.2% and that virtually no central aortic valve regurgitation of I+ or greater occurs with the Medtronic Freestyle. Changes in the aorta, however, independent of degeneration of the valve may affect performance of the Toronto SPV bioprosthesis; dilatation of the sinutubular junction may result in aortic valve regurgitation and may be prevented by restricting the aorta above the valve with a circumferential band.

Mechanical Valve Replacement Devices  Mechanical replacements develop important central leakage only with mechanical failure (e.g., poppet escape, catastrophic structural failure or entrapment of a suture. Also, tissue or thrombosis may encroach into the seating area of the device, although the occurrence appears low.

Replacement Device Endocarditis  Endocarditis on the device used for aortic valve replacement is an uncommon but serious complication; overall, only about
PART III  Acquired Valvar Heart Disease

gram-negative cocci, or mixed organisms. The rare fungal infection is typically fatal. Replacement device endocarditis occurring late after operation is the result of a transient bacteremia, most often with streptococcal organisms.

Incremental Risk Factors

Incremental risk factors for developing endocarditis after primary aortic valve replacement (the same as after primary mitral valve replacement) (Table 12-10) are different from those after reoperation (Table 12-11). When the valve replacement operation is performed for endocarditis on either the native valve or a previously inserted replacement device, no risk factors for subsequent endocarditis other than the endocarditis have been identified, probably because of the dominant risk of infection already present.

Of particular therapeutic importance is the finding that a mechanical prosthesis is a risk factor for replacement device infection because of the higher early phase of hazard associated with its use (Fig. 12-50). The allograft aortic valve, inserted freehand into the aortic position, is unique in having no early hazard phase (Fig. 12-51), even when the operations are performed on already infected native valves or replacement devices. Bioprostheses seem less likely to develop prosthetic valve endocarditis than mechanical prostheses.

Presence of native valve endocarditis has some adverse effects on subsequent freedom from replacement device endocarditis. Replacement device endocarditis tends to develop after a redo operation more often than after an original valve operation (Fig. 12-52).

Table 12-10  Incremental Risk Factors for Replacement Device Endocarditis after Primary Operation

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Early</th>
<th>Constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic variables:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male gender</td>
<td>⬤</td>
<td>⬤</td>
</tr>
<tr>
<td>African American</td>
<td>⬤</td>
<td>⬤</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>⬤</td>
<td>⬤</td>
</tr>
<tr>
<td>Surgical variables:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mechanical prosthesis</td>
<td>⬤</td>
<td>⬤</td>
</tr>
</tbody>
</table>

Data from Blackstone and Kirklin.837

Table 12-11  Incremental Risk Factors for Replacement Device Endocarditis after Reoperations on Valve

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Single Hazard Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>⬤</td>
</tr>
<tr>
<td>Mitral replacement at original operation</td>
<td>⬤</td>
</tr>
</tbody>
</table>

Data from Blackstone and Kirklin.837

30% of patients are long-term survivors.16 Infective endocarditis is discussed in detail in Chapter 15.

Prevalence and Incidence

The prevalence of endocarditis on an aortic valve replacement device is low, with 95% to 97% of patients free of this complication 5 years postoperatively (Fig. 12-48). Risk of endocarditis generally is greatest about 6 weeks after insertion of the replacement device, then gradually declines to a low constant hazard function by about 9 months837,838,16 (Fig. 12-49).

Etiology

Endocarditis early after valve replacement (early peaking hazard phase) is usually caused by organisms already present in the operative field or introduced at operation or within the next few days. The organisms are usually staphylococci, The rare fungal infection is typically fatal. Replacement device endocarditis occurring late after operation is the result of a transient bacteremia, most often with streptococcal organisms.16
This result, however, may reflect operations performed in patients with less extensive infections than those requiring aortic root replacement techniques for aortic root abscesses, as well as infectious processes extending beyond the aortic valve cusp tissues. In contrast, Sabik and colleagues reported that radical débridement and aortic root replacement with a cryopreserved aortic allograft resulted in 5- and 10-year survival of 73% and 56%, respectively.32

Table 12-12 lists the risk factors for death after valve replacement for native or prosthetic valve endocarditis.

### Table 12-12  Incremental Risk Factors for Death after Aortic Valve Replacement for Acute Infectious Endocarditis

<table>
<thead>
<tr>
<th>Hazard Phase</th>
<th>Risk Factors</th>
<th>Early</th>
<th>Constant</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Higher) NYHA functional class (I-V)</td>
<td>•</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Larger) Number of previous aortic valve procedures</td>
<td>•</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data from Haydock and colleagues.16

*Nonuse of an allograft aortic valve inserted by freehand technique did not remain in the final model (equation);  P was .3 in early hazard phase and .9 in constant hazard phase.

*No risk factors in constant phase.

*When number of previous aortic valve procedure was 0, endocarditis was on the native valve.

Key: NYHA, New York Heart Association.

### Thromboembolism

Risk of thromboembolism is approximately constant beyond the first month after operation. The authoritative report by Edmunds indicates that the overall linearized rate of thromboembolism in patients with aortic mechanical device replacement is 2 ± 1 per 100 patient-years and about half that value in patients with stent-mounted xenograft valves.34 The comprehensive study of Grunkemeier and colleagues showed considerable variance in rate of thromboembolism among published series of patients.32 Thromboembolism rate is about the same for the various mechanical devices; median rate for the St. Jude valve is 1.33% · year⁻¹; for the Medtronic-Hall, 1.20% · year⁻¹; and for the CarboMedics valve, 1.16% · year⁻¹. Rates for stent-mounted bioprostheses are also similar; median rate for the Hancock porcine is 0.78% · year⁻¹, for the Carpentier-Edwards porcine, 0.87% · year⁻¹; and for the Carpentier-Edwards bovine, 1.22% · year⁻¹. The rate is lower for allografts, with a median of 0.23% · year⁻¹. All these rates fall below the objective performance criteria required for U.S. Food and Drug Administration (FDA) approval of 3.0% · year⁻¹ for mechanical valves and 2.5% · year⁻¹ for bioprostheses. Adequacy of warfarin therapy is the key determinant of...
the rate in patients with mechanical aortic valves. Thromboembolism is rare in patients receiving aortic allografts or pulmonary autografts in the aortic position.

Thrombosis of the replacement device itself is uncommon. The linearized rate for mechanical prostheses is about 0.1% - year\(^{-1}\). Thrombosis occurs even less often in patients with stent-mounted xenograft valves.

**Complications of Anticoagulation**

Complications of chronic warfarin therapy in patients who have undergone aortic valve replacement are the same as in other patients (see “Complications of Long-Term Anticoagulation” under Results in Section I of Chapter 11). Excessive anticoagulation is accompanied by threat of bleeding. Antiocoagulant levels above therapeutic values but with INR less than 5 indicate need to withhold warfarin until INR returns to therapeutic range, then restart the medication at a lower dose. Warfarin is withheld in patients with INR of 5 to 9, and oral vitamin K (1.25-2.5 mg) is considered if the patient is at increased risk of bleeding. Vitamin K\(;\) (2.5-5 mg) is given orally to patients with INR greater than 9, and if the patient has serious bleeding, it is given intravenously (10 mg) accompanied by transfusion of fresh frozen plasma.

Frequent questions arise about managing potential bleeding in patients with mechanical heart valves taking warfarin who require cardiac catheterization, percutaneous catheter intervention, noncardiac surgery, or a dental procedure. Most dental procedures can be managed without interrupting anticoagulation. For patients with minimal risk of thromboembolism, warfarin should be stopped about 3 days before elective operation so that the procedure may be performed when INR is 1.5 or less. Warfarin is restarted as soon as risk for bleeding has ceased, usually 24 to 48 hours after completing the procedure. Where there is increased risk (atrial fibrillation with large atria, enlarged or poorly contractile LV), unfractionated heparin (enoxaparin) is administered when INR is less than 2. The short-acting anticoagulant is discontinued for the procedure, restarted along with warfarin after risk of bleeding has ceased, and continued for a 3- to 5-day overlap until INR is again therapeutic. Enoxaparin administered to patients prior to cardiac operations, however, increases risk of postoperative bleeding requiring re-entry. When emergency operation is required, operation proceeds immediately as indicated, with reversal of warfarin’s effect by transfusion of fresh frozen plasma as required to achieve adequate clotting.

More accurate control of level of anticoagulation by self-testing of prothrombin time has been associated with a reduction in major bleeding events. In a randomized trial of 325 patients, Byeth and Landefeld reported reduction of major bleeding events in the first 6 months of therapy with warfarin. Providing appropriate devices to allow patients to measure prothrombin time themselves and teaching them how to adjust the warfarin dose early after operation is effective in reducing complications related to anticoagulant therapy.

Aortic Root Complications

**Aneurysms**

At operation, a secure full-thickness closure must always be obtained to prevent not only acute postoperative bleeding but also late aneurysm formation. Three unexpected small aneurysms were found among 100 patients studied by aortography 6 to 9 months after aortic valve replacement by Bjork and colleagues. One was at the aortotomy suture line, and two seemed to originate from the left coronary sinus.

After composite graft reconstruction using the inclusion technique, there has been an important occurrence of aneurysm, most often arising from partial dehiscence of the anastomosis to the graft of the aorta around the coronary ostia and less often from the distal graft to aorta suture line. To overcome dehiscence, Cabrol and colleagues recommend routine use of a separate 8-mm polyester tube graft, the extremities of which are anastomosed to the aorta around the right and left coronary orifices. A large side-to-side anastomosis is then made between the center of this graft and the front of the 30-mm polyester tube. Alternatively, and probably preferably, an aortic button containing the coronary ostium is anastomosed directly to a window in the polyester graft (see Technique of Operation earlier in this chapter). Dehiscence at the distal graft suture line is avoided by using a prosthetic collar (cut from the primary graft) to cover the distal suture line.

False aneurysm at the proximal suture line has been observed when the full root replacement technique is employed for implanting an aortic allograft or pulmonary autograft (Ross procedure). This rare complication may be eliminated by routine use of a support collar at the proximal suture line and partial inversion of the graft while it is tied to the aortic anulus to ensure direct tissue approximation during implantation.

**Aortic Aneurysm Following Aortic Valve Replacement for Bicuspid Aortic Valve**

Progressive aortic enlargement in patients with a bicuspid aortic valve who undergo isolated aortic valve replacement requires special comment. Available data indicate that aortic valve replacement by itself does not ameliorate the adverse natural history of progressive aortic dilatation, suggesting that aortic dilatation results from inherent weakness of the aortic wall rather than hemodynamic factors. A study by Borger and colleagues concluded that among patients undergoing isolated aortic valve replacement, subsequent aortic complications and reoperation were more common when the aortic diameter was 4.5 cm or greater. This is consistent with current recommendations to replace the ascending aorta at the time of bicuspid aortic valve replacement if the aortic diameter is 4.5 cm or greater (see Special Situations and Controversies).

**Cessation of Gastrointestinal Bleeding**

In patients with aortic stenosis who have a history of gastrointestinal bleeding, an unusual but characteristic syndrome, nearly all (93% of 91 patients in one study) are free of bleeding after aortic valve replacement. In contrast, abdominal procedures for gastrointestinal bleeding are successful only occasionally.

**Reoperation**

Reoperation may be necessary early or late after aortic valve replacement. The nature of the reoperation varies with its
indication. When performed for acute thrombosis, thrombectomy can be an effective procedure, although valve replacement is often required. When performed for periprosthetic leakage, simple suture repair is often possible and effective. Valve replacement is required in a few patients when dehiscence of the valve from aortic root tissues is extensive. When the reoperation is for endocarditis, re-replacement is indicated when there is active infection. In unusual circumstances, when infection has been controlled and arrested for weeks or months and there is residual periprosthetic leakage, it may be possible to repair the leak and retain the valve.

Although hospital mortality can be low for a first-time aortic valve re-replacement (3.9%; CI 2.4%-6.0% in one study), replacement of an already replaced aortic valve has serious implications. Jones and colleagues have shown that operative mortality for repeat heart valve surgery has declined with each decade of experience. Mortality for aortic valve re-replacement was 6.4%. Risk increased with increasing age of the patient, presence of coronary artery bypass grafts, and indication for operation (particularly for valve thrombosis or endocarditis). Replacing a dysfunctional mechanical valve had 2.25 times the risk of replacing a bioprosthetic valve. Hasnat and colleagues reported an early mortality of 3.4% (CL 1.9%-5.8%) for replacing an aortic valve allograft with a second one. In their experience a second aortic valve allograft was associated with good long-term survival; accelerated degeneration did not occur. Byrne and colleagues reported 11% hospital mortality for aortic valve allograft re-replacement in 18 patients, 14 of whom (67%) received mechanical prostheses at reoperation. At least in the case of prosthetic and bioprosthetic valves, after each reoperation there is an increasing prevalence of still another reoperation (Fig. 12-53), of periprosthetic leakage (Fig. 12-54), and of prosthetic valve endocarditis (see Fig. 12-54). In addition, each reoperation increases the risk of death. Many factors contribute to the increasing prevalence of unfavorable outcome events as the reoperations accumulate, including increased fibrosis and decreasing local vascularity in the interior of the aortic root. This emphasizes the importance of making the first valve replacement operation the only one whenever possible.

The prevalence and incidence of a first reoperation vary to some extent with the circumstances. Thus, the shape of the hazard function for reoperation for mechanical devices differs from that for stent-mounted xenografts (Fig. 12-55). Mechanical replacement devices have an early peaking hazard phase and a constant hazard phase; in that for bioprostheses, there is an early peaking phase and a second rising late hazard phase. (From Blackstone and Kirklin.)
inserted, without the prevalence of early regurgitation attributable to technical error, there is no early hazard phase of reoperation, but rather a gradually increasing late postoperative phase (see Fig. 12-39).116,320,34

Late reoperation may be required after composite prosthetic graft reconstruction for graft or prosthetic valve infection, for prosthetic valve thrombosis or periprosthetic leakage, and for pseudoaneurysm. Freedom from reoperation was 81% at 7 years in one series.321

Reoperations after Valve-Sparing Aortic Root Replacement

The major reason to reoperate after valve-sparing aortic root replacement is progressive aortic regurgitation. In general, freedom from reoperation for both remodeling and reimplantation techniques has been good. In the absence of external fixation at the level of the aortic anulus, Yacoub and colleagues reported 85% freedom from reoperation at 15 years.34 David and colleagues310 suggest better late aortic valve preservation with the reimplantation technique than with the remodeling method (10-year freedom from moderate or severe aortic regurgitation of 94% with reimplantation vs. 75% with remodeling; \( P = .04 \)). The reimplantation technique appears particularly advantageous in Marfan syndrome and similar connective tissue disorders prone to progressive anular dilatation because of more secure anular fixation. However, others, such as Schaefers and colleagues, report excellent long-term valve function after the remodeling procedure.310 Whether the remodeling procedure will be enhanced by routine placement of an external aortic anuloplasty ring15 or prove superior in the setting of a bicuspid aortic valve (possibly enhanced early valve competency) will require long-term studies.

The situation in pediatric patients is even less clear. Late results of valve-sparing operations are confounded by aggressive connective tissue disorders often found in the pediatric phenotype of Marfan syndrome, Loeys-Dietz syndrome, and Ehlers-Danlos syndrome. Long-term follow-up is limited, but the reimplantation techniques appear to offer similar outcomes as in adults when an adult-sized conduit can be implanted.311

INDICATIONS FOR OPERATION, SELECTION OF TECHNIQUE, AND CHOICE OF DEVICE

Advances in diagnostic techniques, understanding of natural history, and operative procedures for aortic valve disease have resulted in enhanced diagnosis, more scientific selection of patients for surgery, and increased survival of patients with aortic valve disorders. The extensive literature on valvar heart disease, however, consists mostly of single-institution experiences in relatively small numbers of patients. ACC/AHA charged the Committee on Management of Patients with Valvular Heart Disease with the task of compiling an information base and making recommendations for diagnosis and treatment. The task force’s 2006 report, “ACC/AHA Guidelines for the Management of Patients with Valvular Heart Disease,” represents the most definitive treatise on this subject.850

Box 12-1 summarizes the indications for operation in patients with aortic valve disease.

<table>
<thead>
<tr>
<th>Box 12-1 Indications for Operation for Aortic Valve Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aortic Stenosis</strong></td>
</tr>
<tr>
<td>1. Symptomatic patients with severe stenosis (see Table 12-2)</td>
</tr>
<tr>
<td>2. Patients with moderate or severe stenosis having operation for coronary artery disease, other heart valve disease, or aortic disease</td>
</tr>
<tr>
<td>3. Asymptomatic patients with severe stenosis</td>
</tr>
<tr>
<td>a. LV systolic dysfunction (EF ≤ 50%)</td>
</tr>
<tr>
<td>b. Abnormal response to exercise (hypotension)</td>
</tr>
<tr>
<td>c. Ventricular tachycardia</td>
</tr>
<tr>
<td>d. Marked LV hypertrophy (≥ 15 mm)</td>
</tr>
<tr>
<td>e. Aortic valve area &lt; 0.6 cm²</td>
</tr>
<tr>
<td><strong>Aortic Regurgitation</strong></td>
</tr>
<tr>
<td>1. Symptomatic patients with severe chronic regurgitation</td>
</tr>
<tr>
<td>a. LV systolic function preserved or moderately depressed (EF &gt; 25%)</td>
</tr>
<tr>
<td>b. Advanced LV dysfunction (EF &lt; 25%, end-systolic dimension &gt; 60 mm), risk increased</td>
</tr>
<tr>
<td>c. Progressive LV dilatation, declining EF, or positive exercise test performance</td>
</tr>
<tr>
<td>d. Angina without coronary artery disease</td>
</tr>
<tr>
<td>2. Symptomatic or asymptomatic patients</td>
</tr>
<tr>
<td>a. Mild to moderate LV dysfunction (EF 25%-49%)</td>
</tr>
<tr>
<td>b. Patients with moderate or severe AR having operation for coronary artery disease, other heart valve disease, or aortic disease</td>
</tr>
<tr>
<td>3. Asymptomatic patients</td>
</tr>
<tr>
<td>a. Chronic severe AR and LV systolic dysfunction (EF ≤ 50%) at rest</td>
</tr>
<tr>
<td>b. Chronic severe AR with normal LV systolic function (EF &gt; 50%), but with severe LV dilatation (end-diastolic dimension &gt; 75 mm or end-systolic dimension &gt; 55 mm)</td>
</tr>
<tr>
<td>c. Chronic severe AR and normal LV systolic function at rest (EF &gt; 50%) when the degree of LV dilatation exceeds an end-diastolic dimension of 70 mm or end-systolic dimension of 50 mm, when there is evidence of progressive LV dilatation, declining exercise tolerance, or abnormal hemodynamic response to exercise.</td>
</tr>
<tr>
<td>4. Acute and severe aortic regurgitation</td>
</tr>
</tbody>
</table>

Modified from Bonow and colleagues.310
*Consider lower threshold values for patients of small stature of either gender. Key: AR, Aortic regurgitation; EF, ejection fraction; LV, left ventricular.

**Aortic Stenosis**

**Symptomatic Patients**

Patients with symptoms of angina pectoris, dyspnea, or syncope caused by aortic valve stenosis have symptomatic improvement and increased survival after aortic valve replacement, even with LV dysfunction.829,121,332 Therefore, aortic valve replacement is indicated in virtually all symptomatic patients. Patients with severe symptomatic aortic valve stenosis associated with low transvalvular pressure gradient also have hemodynamic improvement and better functional results.564 Elderly patients over age 85 with severe heart failure and associated coronary artery disease may be exceptions and are candidates for transcatheter aortic valve replacement.530 Even severe concomitant noncardiac disease rarely contradicts aortic valve replacement, although advanced chronic obstructive pulmonary disease, widespread arteriosclerosis, and advanced neurologic disease may greatly increase the risk
of operation or render it inadvisable. Advanced age per se is not a contraindication for operation; improved quality of life has been reported in octogenarians 1 year after aortic valve replacement.

The urgency of operation in patients with important aortic stenosis and syncope (or near-syncope) as the only complaint has been debated. This presentation generally does not make operation urgent but does make it advisable.

**Asymptomatic Patients**

Controversy surrounds the approach to patients with absent or trivial symptoms. When stenosis is clearly severe (mean gradient > 40 mmHg, valve area < 1.0 cm², valve area indexed to BSA < 0.6 cm² · m⁻², jet velocity > 4.0 m · s⁻¹), operation is usually advisable even when patients are asymptomatic. Some clinicians, however, may be reluctant to proceed. Even though the perioperative risk of operation is low, long-term morbidity and mortality related to the replacement device may be appreciable. The combined risk of operation and late complications of the replacement device may exceed the 1% per year risk of sudden death in asymptomatic patients. Some asymptomatic patients may be at higher risk for sudden death without surgery, although supporting data are limited. Of clear importance, however, is the accurate identification of subtle symptoms of severe aortic stenosis and not denying such patients the opportunity for surgical therapy. Freed and colleagues noted a 14% mortality within 15 months in a patient cohort where symptoms were missed.

Patients with LV systolic dysfunction, abnormal response to exercise (hypotension), ventricular tachycardia, marked LV hypertrophy (≥15 mm), left atrial diameter over 4 cm, or valve area under 0.6 cm² are likely at higher risk with medical therapy and thus should be considered for surgical intervention. Such high-risk patients are usually symptomatic but if not will become so in a short time. Lancellotti and colleagues reported that the echocardiographic indices of peak aortic jet velocity 4.4 m · s⁻¹ or greater, valvar-arterial impedance (an estimate of LV afterload that is the sum of systolic arterial blood pressure and mean transvalvar pressure gradient divided by stroke volume index) 4.9 mmHg · mL⁻¹ · m⁻² or greater, and an indexed left atrial area 12.2 cm² · m⁻² or greater were predictive of subsequent cardiac events and could justify surgical intervention. An algorithm for managing patients with severe aortic stenosis as recommended in the 2006 ACC/AHA Guidelines is presented in Fig. 12-56.

**Patients with Ischemic Heart Disease**

Patients with severe aortic valve stenosis and important ischemic heart disease should have aortic valve replacement at the time of CABG. The approach is less clear if aortic valve stenosis is moderate or even mild, because it is difficult to predict when these patients will develop severe aortic stenosis after coronary revascularization. Some patients manifest rapid progression of aortic valve stenosis of up to 0.3 cm² · year⁻¹ and an increase in pressure gradient of up to 15 to 19 mmHg · year⁻¹. Most patients, however, show little or no change. The average rate of reduction in valve area seems to be about 0.12 cm² · year⁻¹. Mean time to reoperation for aortic valve replacement after CABG is 5 to 8 years. Experienced surgeons tend to be more aggressive in treating mild and moderate aortic valve stenosis in conjunction with coronary artery disease because of the unpredictable progression of the aortic valve disease. Patients over age 45, those over 35 with angina as a part of their symptomatology (which makes coexisting coronary artery disease more likely), and those with a strong family history of arteriosclerotic disease require coronary angiography before operation.

**Patients with Other Heart Valve or Thoracic Aorta Disease**

Patients with moderate (gradient 30 mmHg or greater) or severe aortic valve stenosis should have aortic valve
replacement in conjunction with operations on the aorta or other heart valves.

**Aortic Regurgitation**

Patients with pure, chronic aortic regurgitation should have aortic valve replacement only if the regurgitation is severe (see Box 12-1). Patients with symptoms and only mild or moderate aortic regurgitation may have other conditions, such as coronary artery disease, hypertension, or cardiomyopathy.

**Symptomatic Patients**

Aortic valve replacement is recommended for patients with normal systolic function (EF ≥ 50% at rest) and symptoms in NYHA functional class III or IV or angina pectoris in Canadian Heart Association class II to IV. Patients with new onset of mild symptoms require special attention and are usually considered for operation, even without reaching threshold values for LV size and function.

**Symptomatic Patients with Left Ventricular Dysfunction** Patients having symptoms of heart failure or angina pectoris and mild to moderate LV dysfunction (EF 25%-49%) should have aortic valve replacement. Postoperative survival and recovery of systolic function are reduced, however, compared with less symptomatic patients. Symptomatic patients with advanced LV dysfunction (EF < 25%, end-systolic dimension > 60 mm) present more difficult management problems; some recover LV function after aortic valve replacement, but many do not because of irreversible myocardial changes. Operative mortality in these patients approaches 10%. Chance of good results is better in patients with recent onset of symptoms in NYHA functional class II or III. Operation is usually recommended for patients with class II symptoms and normal EF who show evidence of progressive LV dilatation or declining EF at rest on serial echocardiographic or radionuclide studies. Even in the high-risk group with NYHA class IV symptoms, aortic valve replacement is usually a better alternative than the higher risks of long-term medical management.

**Asymptomatic Patients**

Aortic valve replacement in asymptomatic patients with aortic regurgitation is controversial, but most agree that operation is indicated in patients with LV systolic dysfunction. Aortic valve replacement is generally recommended for asymptomatic patients when EF is less than 50%. Severe LV dilatation (end-diastolic dimension greater than 75 mm, end-systolic dimension greater than 55 mm) is also an indication for operation, even if EF remains normal, because these patients have an increased risk of sudden death and postoperative results are good. Patients with systemic hypertension, coronary artery disease, concomitant mitral valve stenosis, or who are women deserve special attention and may be recommended for aortic valve replacement at reduced LV dimension thresholds. Reduced EF during exercise, mild decline in EF (but still within normal limits), or minor increases in LV dimensions less than those just detailed are not usually indications for operation in asymptomatic patients with aortic regurgitation. Improving methods of aortic valve replacement, however, may reduce objective thresholds for recommending operation.

**Patients with Ischemic Heart Disease, Other Heart Valve Disease, or Aortic Disease**

Coronary artery disease coexists with aortic regurgitation less frequently than with aortic stenosis. Patients having CABG or other heart valve replacement usually have aortic valve replacement for moderate or severe aortic regurgitation. Mild aortic valve regurgitation has a long natural history and is usually not an indication for aortic valve replacement in association with other cardiac operations.

Operations for primary disease of the aorta with associated aortic regurgitation require special attention and are discussed under Special Situations and Controversies.

**Native Aortic Valve Endocarditis**

Native aortic valve endocarditis in a hemodynamically stable patient should be treated in the hospital with appropriate antimicrobial therapy and serial echocardiographic examination of the aortic valve and root. If aortic regurgitation develops, if evidence of aortic root or mitral annular abscess appears, or if septic embolization or vegetation is observed, operation must be undertaken promptly, before hemodynamic deterioration increases the risks associated with operation.

An allograft valve is the replacement device of choice in these patients and may be used even when an aortic root abscess is present. A pulmonary autograft may also be used in patients with active endocarditis on aortic valve cusps, limited anular involvement with no associated medical comorbidity, and a life expectancy exceeding 20 years. Extensive aortic root destruction indicates aortic root replacement with an allograft aortic root. Rarely, the infected valve may be repaired rather than replaced. A detailed discussion of surgery for infective endocarditis is found in Chapter 15.

**Selection of Technique and Choice of Device**

After more than 50 years of experience with heart valve devices, it would seem reasonable that a single type of device should have emerged that is ideal for all circumstances when aortic valve replacement is necessary. This is not the case. The surgeon must choose from an ever-increasing number of replacement devices; new devices are constantly being designed, tested, and added to the market after short-term clinical trials. By the time midterm or long-term performance data are known, an equal number of valves are discarded in favor of new and unproven devices.

**Type of Replacement Device**

The type of operation performed on the aortic valve has changed over time as replacement devices have changed and improved. Current practice indicates a trend toward less frequent use of mechanical prostheses and more use of bioprosthetic devices (Table 12-13). Photographs of current mechanical and biological prosthetic valves for the mitral position are found in Chapter 11. Allograft aortic valve procedures are limited by donor availability to about 2% of aortic valve replacements.

Comparative information concerning performance specifications of the various valves is confusing. The body of literature on valve performance and outcome statistics is enormous; an individual surgeon cannot assimilate sufficient data to
The Starr-Edwards valve is a first-generation mechanical valve. Label size (mm) expresses prosthesis size (diameter) and is larger than the primary (geometric) orifice diameter.

Internal orifice area (measured geometric orifice in cm²) is larger than in vitro orifice area (measured in pulse duplicator).

In vitro orifice area is generally larger than the area measured in vivo by Doppler ultrasound after the valve is implanted (the exception is bioprostheses tested at low steady flow rates). The orifice area calculated either in vitro or in vivo is also called the effective orifice area (EOA, cm²), which may be indexed to body size by dividing by BSA (indexed EOA = EOA ÷ BSA). BSA is calculated from both height and weight, however, so obesity may distort this figure (however, see discussion under “Normal Pathways” in Chapter 1).

Devices for replacement of the aortic valve are divided into two groups: mechanical prostheses and bioprostheses, the latter commonly referred to as “tissue valves.” A complete listing of all available devices would serve little useful purpose. The focus here is on the devices that have been most widely used throughout the world. Generally, valves within these groups have similar performance characteristics, and choice is usually based on surgeon preference, handling characteristics of the device, availability, technical and service support, and cost.

### Mechanical Aortic Valve Replacement Devices

#### Ball-in-Cage Devices

Starr-Edwards Silastic Ball-Valve Prosthesis (Model 1260). The Starr-Edwards valve is a first-generation device of historical importance. The first device in this line was used in the first successful human orthotopic valve replacement operation. In small sizes in the aortic position, the model 1260 valve has somewhat more energy loss across it than other devices. It is no longer available in the United States.

**Omniscience, Omnicarbon Valve.**

The Omniscience valve (Medical CV Inc.) is an evolution of the discontinued Lillehei-Kaster pivoting disc valve. The Omnicarbon valve is an all-pyrolytic carbon design, a ceramic material that is extraordinarily hard.

### Bileaflet Devices

St. Jude Medical Valve. The St. Jude Medical bileaflet valve was introduced in 1977. The valve mechanism, unchanged since its first clinical use, consists of two semicircular leaflets with small ears that pivot in a butterfly-shaped recess in the housing of the device. It is manufactured from pyrolytic carbon and is durable, with leaflet fracture virtually nonexistent.

The St. Jude valve is available in a variety of models, all based on variations of the sewing ring; the basic mechanical device is the same in all models. It is available in rotatable and nonrotatable, standard, expanded, or reduced sewing ring; the basic mechanical device is the same in all models. It is available in rotatable and nonrotatable, standard, expanded, or reduced sewing rings and with silver impregnation to prevent infection (see “Silver-Coated Sewing Rings” under Special Situations and Controversies later in this chapter). Hemodynamic performance of even the 19-mm device is adequate, and sizes 21 mm and larger show good performance. Freedom from thromboembolism is good.
CarboMedics Valve. The CarboMedics valve is available in various designs of sewing cuff, but the basic mechanical valve is the same in all models. The bileaflet design has flat, pyrolytic carbon-coated leaflets in a pyrolytic carbon housing strengthened by a radiopaque titanium ring.

Edwards Tekna Valve. The Edwards Tekna device was originally called the Duramedics valve. Its unique design features are curved leaflets and a hinge mechanism below the inflow edge of the housing. After initial mechanical failures, minor modifications have apparently corrected the problems.

Sorin Bicarbon Valve. The Bicarbon device was introduced in 1990. It has a solid titanium housing and a bileaflet carbon mechanism. The sewing ring is carbon coated.

ATS (Advancing the Standard) Open Pivot Valve. The ATS valve, introduced in 1995, is unique in that the hinge socket is on the cusp, whereas the protrusion of the hinge mechanism is on the housing. The purpose is to reduce thromboembolism by better washing of the pivot mechanism.

MCRI (Medical Carbon Research Institute) On-X Valve. The On-X device is manufactured from an improved and more pure form of pyrolytic carbon for greater strength. It has an elongated housing and flared inlet to provide hemodynamic advantages.

Specifications for Mechanical Prostheses Table 12-14 lists manufacturers’ reported primary orifice area for the common mechanical cardiac valve prostheses. Compared with in vitro pulse duplicator studies, the effective orifice is smaller than measured geometric orifice (Table 12-15). In vivo performance studies of mechanical heart valves are often subject to error artifacts caused by turbulence and alterations of blood flow patterns by the prosthetic material in the LVOT. Also, some manufacturers’ labeled-size valves are mechanically equivalent, meaning that the same housing is used but the sewing rings are different, enabling the manufacturer to label the device differently. For the St. Jude prostheses, HP valves have label size 2 mm less than the standard valve sharing the same-size housing.

Mechanical cardiac valve prostheses produce sounds that are audible to patients. Occasionally the sound is disturbing. Sezai and colleagues interviewed patients 1 month and 1 year after aortic valve replacement with the St. Jude Medical or ATS prostheses. Many patients (52% St. Jude Medical, 8.3% ATS) reported that the valve was audible 1 year after implantation. The sound was sometimes disturbing in 9% of patients with the St. Jude Medical valve (0% ATS) and resulted in sleep disturbances in 9% and a desire for a less noisy valve in 9%. Reported loudness of the valve sound is the best measurement of a patient’s adverse reaction to the sound; this may be modified by hearing loss in patients. Erickson and colleagues studied mechanical heart valve sound loudness in vitro and found that the quietest valves were the St. Jude Medical and the CarboMedics. The Sorin Bicarbon valve was 10% louder. Loudness was doubled with the Edwards Tekna and Monostrut valves. The St. Jude Medical valve was confirmed as quiet in another study. Sezai and colleagues’ data, however, indicate that the ATS valve may be quieter.

Bioprosthetic Aortic Valve Replacement Devices

Stent-Mounted Xenografts The many stent-mounted bioprosthetic devices in clinical use include those with valve cusps made of xenograft aortic valves, pericardium, fascia lata, and dura mater. Theoretically, according to the physical characteristics of biological materials, only cusp tissue should be considered appropriate for this purpose, but pericardium has proved to be remarkably durable.

Carpentier-Edwards Glutaraldehyde-Preserved Porcine Xenograft (Edwards Lifesciences). The Carpentier-Edwards bioprosthetic model 2625 is used for aortic valve replacement. The EOA in smaller sizes of this device may be slightly smaller than equivalent mechanical prostheses, but EOA in bioprostheses, unlike mechanical prostheses, is flow dependent. Incidence of thromboembolism is low, so the device may be implanted without anticoagulating the patient. Durability is better in the aortic position than in the mitral position and is related to patient age. The device is more durable in patients over age 60 (see Table 12-9). The Hancock Glutaraldehyde-Preserved Porcine Xenograft (Medtronic). The original Hancock I valve (standard model) has an appreciable gradient across it in all sizes in the aortic position. This bioprosthesis is also available with a modified orifice. In the modified version, the right coronary cusp, with its muscular bar at the base, is replaced by a muscle-free noncoronary cusp from a second valve. This modification has not reduced the device’s long-term durability. The Hancock Modified Orifice bioprosthesis has been free of structural deterioration in 78% of patients over age 65 (7% cumulative incidence of SVD) and 84% of patients over 70 (3% cumulative incidence of SVD) at 19 years. It differs from the Hancock I in having a lower gradient across the valve.

Hancock II Glutaraldehyde-Preserved Porcine Xenograft (Medtronic). The Hancock II porcine xenograft is a second-generation device with a porcine aortic valve fixed at low pressure. The anticalcification agent sodium dodecyl sulfate surfactant (T6) is added to the fixative. A flexible,
high-strength stent is made of acetyl homopolymer with reduced implant height. Flow area is maximized. The stent is covered with polyester and is less bulky so that a larger valve can be implanted. The inflow edge and sewing ring are scalloped to allow supraaunlar implantation of a larger valve. Hemodynamic performance, reduced thromboembolic complications, and durability are improved compared with first-generation devices. Anticoagulation is not required.

**Intact Glutaraldehyde-Preserved Porcine Xenograft (Medtronic).** The Intact xenograft is a newer generation glutaraldehyde-treated porcine valve in which the fixation pressure is zero and toluidine blue is added to inhibit calcium deposition. Zero-pressure fixation preserves the collagen crimp of the porcine aortic valve so that it is more flexible and presumably more durable. This device has been used in large series of patients in New Zealand, Canada, and South Africa. Jamieson and colleagues report freedom from SVD at 12 years of 94% ± 3.3% for patients age 61 to 70 years and 98% ± 1.1% for those over age 70, and Corbineau and colleagues report similar results at 13 years.

**Biocor (St. Jude Medical).** The Biocor stent-mounted aortic valve bioprosthesis was developed in Brazil. This porcine aortic valve is fixed at zero pressure, and the stent has a supraannular configuration.

**Mosaic Glutaraldehyde-Preserved Porcine Xenograft (Medtronic).** The Mosaic xenograft is a third-generation stent-mounted bioprosthesis in which the porcine valve is subjected to physiologic aortic root fixation. Glutaraldehyde at 40 mmHg pressure is applied in the LVOT below the valve and also to the aorta above the valve. The effect is to apply zero net pressure to the valve cusps to preserve collagen crimp and flexibility while applying sufficient pressure to the aorta and sinuses of Valsalva to fix the aorta in anatomic relationships. Mechanical properties are such that they can withstand stress equivalent to normal valve cusps. α-Aminooleic acid, an anticalcification agent, is chemically bound to glutaraldehyde for permanence in the tissues. Jamieson and colleagues report freedom from reoperation for SVD at 12 years of 93% ± 2.6% for patients aged 60 years or older, and 76% ± 9.3% for those younger than 60.

**PERIMOUNT Glutaraldehyde-Preserved Bovine Pericardial Xenograft (Edwards Lifesciences).** The PERIMOUNT pericardial xenograft is a second-generation bioprosthesis. Bovine pericardium is fixed in glutaraldehyde at low pressure and applied to a flexible stent with distensible struts by intraaortic or subcoronary valve implantation. The anticalcification agent polysorbate (Tween 80) is added. The prosthesis has proved to be durable, with 80% freedom from SVD at 14 years in the aortic position. The postapproval Investigational Device Exemption Center (IDE) study showed 84% freedom from structural valve deterioration. The stent and method of tissue mounting provide for a very good EOA. Stent-mounted pericardial bioprostheses have superior hemodynamic performance compared with porcine aortic xenografts in sizes of 21 mm or less, which may translate into greater reduction in LV mass.

**Mitroflow.** The Mitroflow bioprosthesis is constructed from bovine pericardium mounted on a stent. It was introduced to clinical practice and received the CE mark of the European Community for the international market in 1997. A multicenter Italian study revealed reoperation for SVD at 18 years was 66%, but 78% in patients older than 70 at implant.

**Stentless Xenografts** Stentless xenografts are constructed from porcine aortic valves or bovine pericardium that use less cloth for stabilization and sewing than stented valves. The major advantages of stentless valves over stent-mounted xenografts are improved hemodynamic efficiency. They have a potential advantage in small aortic roots to avoid a root enlargement procedure, and flexibility of implantation as a subcoronary valve, intraaortic cylinder, or root replacement.

Although the larger EOA may translate into more complete regression of LV mass with stentless than with stented bioprosthetic valves, studies fail to demonstrate a consistent advantage. Observational data indicate a low risk of SVD at 8 to 10 years, but evidence for improved durability over stented xenograft valves is lacking. Some studies indicate an increasing hazard for structural valve failure after about 8 years. In addition to cusp calcification and cusp tear, rupture of the porcine aortic wall has been reported as a cause of valve failure. Their major disadvantage is increased complexity of implant (similar to allograft aortic valves) compared with stented valves. Reoperation for replacement also may be more difficult.

**Freestyle Glutaraldehyde-Preserved Porcine Aortic Root Bioprosthesis (Medtronic).** The Freestyle porcine bioprosthesis is a third-generation device presented as the complete porcine aortic root with a thin polyester covering of the septal myocardium. It has no support stent. The tissue is fixed in glutaraldehyde using the physiologic root pressure technique described for the Mosaic valve: there is zero net pressure applied to the valve cusps to preserve collagen crimp while the aorta is distended to normal configuration. The valve is designed to be implanted as a valve replacement in the subcoronary position, as an inclusion root cylinder, or as a full aortic root replacement. Thus, as the name Freestyle implies, the surgeon may choose the method of implantation. Hemodynamic performance of the device is excellent because without a stent, a large EOA valve may be implanted. Short-term durability has been excellent, with 97.7% freedom from SVD at 5 years. However, at 10 years, freedom from reoperation was 90% ± 5% in the Royal Brompton randomized trial comparing allograft and Freestyle aortic root replacement, an experience considerably less favorable than 97% ± 5% at 9 years reported by Ennker and colleagues.

α-Aminooleic acid is added to prevent or retard calcification. Effectiveness of anticalcification treatment is not known, but evidence suggests that it is beneficial. Electron beam CT shows a low amount of calcification in the aortic wall of the Freestyle bioprosthesis compared with homovital aortic allografts at 18 months. Calcium deposits have been noted in the aortic wall of the graft, but the cusps remain free of calcification up to 4 years. A Freestyle bioprosthesis removed at autopsy 68 months after implantation showed minimal calcification in the aortic tissue at the commissures and no calcium deposits in cusp tissue.

**Toronto SPV Glutaraldehyde-Preserved Porcine Xenograft (St. Jude Medical).** The Toronto SPV (stentless porcine valve) is a low-pressure glutaraldehyde-fixed porcine aortic valve. The aortic tissue is removed from all three sinuses, and the graft is covered with a thin coat of polyester. It can only be implanted as a subcoronary valve replacement. With no support stent, a large valve can be implanted with greater EOA compared with stented devices. Hemodynamic performance has been excellent and equivalent to the Medtronic
Freestyle device. Durability has been good, with freedom from structural valve deterioration of 85% at 9 years.399

Edward Prima. The Prima device is a low-pressure glutaraldehyde-fixed porcine aortic root similar to the Freestyle device. Markings on the outside of the aortic root guide the trimming of the aorta for subcoronary valve implantation. The hazard for structural valve failure rises after about 8 years.418

CryoLife-O’Brien. The CryoLife-O’Brien stentless porcine aortic valve is a manufactured composite of the noncoronary sinus and cusp from three porcine aortic roots. It is designed to be implanted below the coronary arteries in a supraannular position in the sinuses of Valsalva by a single suture line. Experience is limited to a few centers, and the technical aspects of implantation may be more difficult than with other stentless bioprostheses.

Pericarbon Freedom (Sorin Group). The Pericarbon Freedom stentless valve is composed of two sheets of bovine pericardium sewn together to produce a cylindrical shape and fixed with glutaraldehyde.825 The implant procedure requires two suture lines. A modification of this prosthesis, the Freedom Solo, can be implanted with a single continuous suture line in the subcoronary supraannular position. Five-year follow-up suggests hemodynamic benefit similar to other stentless xenografts.399

Cryopreserved Aortic Allograft. Human donor aortic valve allografts are presented as the complete aortic root, ascending aorta, and some or all of the aortic arch. The anterior leaflet of the mitral valve usually remains attached unless it has been removed for a mitral valve graft. The tissue is harvested under sterile conditions, the internal diameter at the ventricular-aortic junction measured, quality of the valve assured, and the graft packaged. The tissue is frozen using liquid nitrogen with the temperature drop controlled at 1°C per minute between +5°C and −40°C in tissue culture media containing 10% dimethyl sulfoxide (DMSO) to facilitate water transfer across cell membranes during the freezing process. The tissue is placed in liquid nitrogen for storage at −180°C. Cryopreserved aortic allografts are free of structural deterioration in 80% of patients at 15 years.45

Pulmonary autograft and cryopreserved pulmonary allograft. The patient’s own pulmonary trunk, including the pulmonary valve, may be used to replace the aortic valve, usually as a full aortic root replacement. The pulmonary trunk is then replaced with a cryopreserved pulmonary allograft as described earlier. This operation (Ross procedure) is hemodynamically superior to other procedures for replacing the aortic valve, because the patient’s own pulmonary valve is properly sized to accept cardiac output with little or no pressure gradient, even during the high cardiac output state of extreme exercise.415 In fact, the pulmonary valve is usually slightly larger than the aortic valve (see “Dimensions of Normal Cardiac and Great Artery Pathways” in Chapter 1). The pulmonary valve in the aortic position appears to function well over time (see Special Situations and Controversies).

Mechanical differences are minimal between aortic and pulmonary valve tissues, and the tensile strength of pulmonary valve cusps equals or exceeds that of aortic valve cusp tissues.412,422 Goffin and colleagues studied tissues removed at autopsy 17 months after the Ross procedure.49 Pulmonary autograft valve cusp tissues showed essentially normal histology, with preserved fibroblasts and some endothelial cells on the surfaces. Schoof and colleagues showed in growing pigs that developing pulmonary autograft wall in the aortic position becomes normally revascularized, remains viable without major degenerative phenomena, and retains morphologic features typical for pulmonary artery rather than remodeling to thickness similar to aorta.411 Smooth muscle rearrangement and increased collagen were observed in response to increased pressure on the vascular matrix, strengthening the vascular wall without increasing wall thickness. A meta-analysis based on current evidence calculated average reoperation-free life expectancy of the pulmonary autograft as 16 years after implantation.71

The cryopreserved pulmonary allograft is extensively devitalized, with valve cusps devoid of endothelial cells and few fibroblasts present.49 This phenomenon is likely immunologically mediated, as measured by presence of classes I and II anti-HLA antibodies after implanting cryopreserved allograft material in patients.418,420 Degree of histocompatibility, however, does not appear to be related to humoral response.434 Implanting decellularized human valve allografts does not provoke a panel reactive antibody (PRA) response nor encourage host recellularization.429 Stenosis of the pulmonary allograft (pressure gradients across the graft of 30 mmHg or more) occurs in 17% of patients after the Ross procedure, with a mean follow-up of 48 months; only 3% of patients, however, require reoperation.438 Cause of stenosis appears to be an inflammatory reaction to the pulmonary allograft leading to extrinsic compression or shrinkage. The reaction may be immunologically mediated, but could also be related to other as yet unexplained mechanisms.

Specifications for Bioprostheses. Manufacturer specifications for bioprostheses are more complicated than they are for mechanical cardiac valve prostheses. It is impractical to measure true internal orifice area because of the irregular shape presented by the biological tissues mounted within the stent. Therefore the manufacturers’ specifications refer to the inner diameter or the outside diameter of the mounting stent. The actual outside diameter including the sewing ring is always considerably larger than the diameter of the mounting stent, which is used for the label size (actually from midpoint to midpoint of the mounting stent).

Table 12-16 presents comparison data of widely used first- and second-generation stent-mounted bioprostheses. Stentless bioprostheses are labeled as the outside diameter of the device. In this respect, Medtronic Freestyle and St. Jude Medical Toronto SPV devices are equivalent. In vitro studies allow benchmarking of the EOA (cm²) of the various devices (Table 12-17). Second-generation stent-mounted bioprostheses (Hancock II, Carpentier-Edwards pericardial) have larger EOAs than first-generation devices because of improved mounting stents. Third-generation stentless bioprostheses (Medtronic Freestyle, St. Jude Toronto SPV) have even larger EOAs because the mounting stent has been eliminated, and generally a graft with a larger label size can be implanted.

Selection of Technique and Choice of Device for Isolated Aortic Valve Replacement

Mechanical Prostheses. Mechanical prostheses are useful because of their durability under all circumstances and because of their good performance, even in relatively small aortic roots.533 Although these prostheses carry the disadvantages of thrombogenicity requiring lifelong anticoagulation with its complications of thromboembolism and bleeding, they are
Table 12-16  Primary Orifice Diameter (mm): Manufacturer’s Specifications for Biological Prostheses

<table>
<thead>
<tr>
<th>Prosthesis</th>
<th>Label Size (mm)</th>
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<tbody>
<tr>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Carpentier-Edwards porcine</td>
<td>17</td>
</tr>
<tr>
<td>Hancock porcine</td>
<td>16</td>
</tr>
<tr>
<td>Hancock MO</td>
<td>16</td>
</tr>
<tr>
<td>Hancock II</td>
<td>—</td>
</tr>
<tr>
<td>Carpentier-Edwards pericardial</td>
<td>18</td>
</tr>
</tbody>
</table>

Data from manufacturers’ package inserts.
Key: I.D., Internal (stent) diameter; O.D., outer (suture ring) diameter.

Table 12-17  Effective Orifice Area (cm²) from In Vitro Studies on Biological Prostheses

<table>
<thead>
<tr>
<th>Prosthesis</th>
<th>Label Size (mm)</th>
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<tbody>
<tr>
<td></td>
<td>19</td>
</tr>
<tr>
<td>Carpentier-Edwards porcine</td>
<td>1.17</td>
</tr>
<tr>
<td>Hancock porcine</td>
<td>1.15</td>
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<tr>
<td>Hancock MO</td>
<td>1.22</td>
</tr>
<tr>
<td>Hancock II</td>
<td>—</td>
</tr>
<tr>
<td>Carpentier-Edwards pericardial</td>
<td>1.56</td>
</tr>
<tr>
<td>Medtronic Freestyle</td>
<td>1.84</td>
</tr>
</tbody>
</table>

Data from Yoganathan and colleagues.¹⁶

Table 12-18

Chapter 12  Aortic Valve Disease

rarely contraindicated; exceptions include premenopausal women (because of risk to fetus and mother from warfarin) and those with unusual risk of hemorrhage, such as from severe peptic ulcer disease, ulcerative colitis, or hazardous occupation. Mechanical valves are particularly indicated for patients at any age who are willing to avoid undue physical hazards, who can follow a regimented medical protocol, and who prefer the low risks of chronic warfarin therapy to the lower potential risk, but greater anxiety and discomfort, of a second valve replacement operation.

Stent-Mounted Glutaraldehyde-Preserved Porcine Xenograft Valve  This type of valve is appropriate in patients over age 70, particularly those in sinus rhythm, because of its excellent hemodynamic performance and no requirement for warfarin anticoagulation. Long-term outcomes are unknown, but at midterm (5-10 years), performance and durability are good.

Cryopreserved Aortic Allograft Valve  Inserted freehand inside the aorta, the allograft valve has been chosen for aortic valve replacement because of excellent hemodynamic performance, lack of thromboembolism, no need for warfarin anticoagulation, and resistance to infection in patients requiring valve replacement for infective endocarditis of either native or prosthetic aortic valves. Allograft aortic valve replacement is primarily indicated in patients under age 55 and in selected older patients, generally for endocarditis. Primary contraindications include an aortic root with an LV-aortic junction or aorta at the level of the cusp commissures that is 30 mm or more in diameter, or an aortic root with dimensions that are 2 cm larger than those of the largest available allograft. Under these circumstances, the aortic root may be reduced in diameter (tailored) and an aortic root replacement used. The allograft aortic valve is less desirable than mechanical or biological prostheses when the ascending aorta is diffusely enlarged and thin walled and when severe and poorly controlled systemic hypertension is present.

Pulmonary Valve Autograft  A pulmonary valve autograft was considered by Ross and colleagues to be “an almost ideal means of aortic valve replacement in appropriate patients.” Hemodynamic performance of the pulmonary autograft in the aortic position is superior to any other replacement device. It is therefore possibly indicated in younger patients, usually younger than 50, when an active lifestyle or athletic performance requires superior hemodynamics. Warfarin anticoagulation is not required. The pulmonary autograft
Choice of Device for Replacing Aortic Valve and Ascending Aorta, En Bloc

The optimal device to replace the aortic valve and ascending aorta en bloc is controversial. Use of a composite mechanical prosthetic valve within a polyester cylinder probably offers the lowest early mortality (4.7%; CL 2.8%-7.5%) and the least risk of late postoperative complications, but it requires lifelong anticoagulation with warfarin and carries the usual risks of prosthetic valve thromboembolism.

Kouchoukos and colleagues reported early mortality of only 0.9% in patients with anuloaortic ectasia undergoing replacement of the aortic root and ascending aorta. This series was folded into a large multi-institutional study, and the results were reported by Gott and colleagues. Of the 675 patients studied, 604 had composite graft replacement, indicating that this was the treatment of choice from 1968 to 1996. Early mortality in this group was 1.5% (CL 1.0%-2.4%) among 455 patients having elective repair and 2.6% (CL 1.1%-5.1%) among 117 patients having operation performed urgently. Risk climbed to 12% (CL 8.3%-16%) among 103 patients having emergency operation.

Composite graft replacement is currently the procedure of choice in patients aged 55 to 70 who need replacement of the aortic valve because of demonstrated durability of the prosthetic valve. Operations that preserve the aortic valve are gaining more favor for these patients (see Special Situations and Controversies).

Use of an autograft pulmonary valve cylinder was once considered the ideal replacement device when the aortic valve and aortic root or ascending aorta are replaced en bloc, because the autograft is the patient’s own tissue. Even when the surgeon has specialized knowledge of the procedure, however, early mortality is 3.5% to 5.1% for this complex two-valve operation. With this initial risk and the high likelihood of late reoperation, the operation could be the procedure of choice in patients under about 30 years of age if the patient wishes to avoid anticoagulation and understands the likely need for reoperation. However, emerging data over the last decade have revealed an important risk of pulmonary artery dilatation and subsequent neoaortic valve regurgitation within the first 10 years following operation. In contrast to initial enthusiasm about the possibility that the pulmonary autograft may be a “permanent” normally functioning aortic valve, long-term follow-up indicates an actuarial freedom from autograft failure of 75% to 85% at 10 to 15 years in adults, with a progressively increasing probability of moderately severe or worse aortic regurgitation after 10 years (Fig. 12-58). Progressive aortic regurgitation can result from either dilation of the aortic anulus or aortic root (more common with the root replacement technique) or from SVD with progressive cusup prolapse (more common with the subcoronary technique). Longitudinal data from the German-Dutch Ross Registry indicate that both the root replacement technique with reinforcement of the autograft or the subcoronary technique are associated with greater freedom from autograft reoperation than is nonreinforced root replacement. Other reports support maintaining aortic diameter with reinforcement at least out to 6 years.

In pediatric patients, autograft reinforcement will likely impair autograft growth, which is a major disadvantage because autograft growth has been well documented in the nonreinforced root replacement technique. However, dilation of the aorta at the sinutubular junction in children is associated with progressive aortic regurgitation. Takkenberg and colleagues noted greater freedom from autograft reoperation in patients under age 16 years compared with older patients (93% at 10 years vs. 79%; P = .05). In infants undergoing the Ross procedure, late autograft failure appears to be low (≤5%), at least out to 10 years.

In both pediatric and adult patients, reoperations for replacement of the allograft in the pulmonary position are likely inevitable with sufficient follow-up. Among adults, freedom from conduit replacement is 85% to 95% at 10 to 15 years. Among pediatric patients, 10-year freedom from conduit replacement ranges from about 50% to 85%. Thus in pediatric patients, the Ross procedure seems to be the best option for aortic valve replacement. However, the family should be advised of the near certainty of reoperation and the real possibility of eventual autograft valve failure. For children with isolated valve replacement in whom a root enlargement procedure could allow an adult-sized mechanical prosthesis, the family would need to decide about the advantages of a single operation combined with lifelong anticoagulation (mechanical valve) vs. the absence of reoperation for the aortic valve.
of anticoagulation, but need for one or multiple additional operations over a lifetime (autograft).

Use of an allograft valve and ascending aortic cylinder is another option. The operation is less complex than when an autograft is used, but the replacement device is less durable, with a useful life of about 15 to 20 years. Early risk of the operation is low. O’Brien reported 30-day hospital mortality of 1.13% ± 1%.122 Yacoub and colleagues reported that of 67 patients who had complete aortic root replacement with an aortic allograft, 56% were free of tissue failure and 90% free of reoperation for valve replacement at 15 years.122 O’Brien reported only 7 valves removed for SVD over almost 15 years after full aortic root replacement in 350 patients using a cryopreserved allograft.122 The allograft is preferred when there is active native valve endocarditis with root abscess or infection from a previously placed prosthetic valve.122,214

SPECIAL SITUATIONS AND CONTROVERSIES

Low-Output, Low-Gradient Aortic Stenosis

In patients with low cardiac output, as in the presence of severe LV dysfunction, the calculated gradient and valve area may not reflect the severity of aortic stenosis, because the echo Doppler criteria are not sensitive to presence of low cardiac output (see Clinical Features and Diagnostic Criteria earlier in this section). In this circumstance, low-dose dobutamine may help distinguish true from “pseudo” aortic stenosis (Fig. 12-59). Although data support aortic valve replacement in patients with severe aortic stenosis and severe LV dysfunction,136,212 the major area of controversy relates to patients with a mean transvalvular gradient of 30 mmHg or less and an EF of 35% or less. Pai and colleagues reported a substantial survival benefit with aortic valve replacement in this group21 (Fig. 12-60).

Small Aortic Root and Small Prosthesis: Prosthesis/Patient Mismatch

Controversy surrounds whether a device used for aortic valve replacement can be too small for a patient and affect early, intermediate, and long-term outcomes. Foster and colleagues showed that prostheses as small as 17 mm in diameter can provide acceptable clinical results.29 Data from a multi-institutional meta-analysis of 13,258 patients having aortic valve replacement showed that small valve size increased operative mortality by less than 1% in the 10% of patients receiving a small valve relative to body size, and did not reduce midterm (6 months to 5 years) and late (5-15 years) survival.83 Similarly, Medalion and colleagues did not find that small aortic valve prostheses affected incidence of early or late mortality or cardiac events in patients, even when the prosthesis diameter was as much as four standard deviations below normal predicted for body size.220,221

Superior hemodynamics with a valve prosthesis, generally associated with a large orifice size and valve efficiency, should translate to a survival advantage. Such logic seems not to apply in this case, however, which may indicate that a marker other than survival should be analyzed when considering replacement of the aortic valve with a small aortic root. Although Izzat and colleagues argue that prosthesis/patient mismatch is not a problem of clinical significance,127 Pibarot and Dumesnil counter with a strong argument that when valve size and body size are used to calculate an indexed effective valve area, a strong relationship exists between small prosthetic valve size (19 or 21 mm) and pressure gradient across the valve during rest and exercise.116 This held for bileaflet mechanical and stent-mounted bioprosthetic valves. Del Rizzo and colleagues showed that indexed EOA less than 0.8 cm² · m⁻² affected the extent of LV mass regression after aortic valve replacement with stentless bioprostheses.127 Dumesnil and Yoganathan showed that indexed EOA predicts performance of prosthetic valves during exercise250 (Fig. 12-61). Indexed EOA greater than 0.85 cm² · m⁻² will keep pressure gradient from rising during exercise on the steep part of performance curves; indexed EOA less than that is considered to represent prosthesis/patient mismatch because of the

![Figure 12-59](https://example.com/fig59.png)  
**Figure 12-59** Algorithm for managing low-output, low-gradient aortic stenosis. Key: AS, Aortic stenosis; AVA, aortic valve area; DSE, dobutamine stress echocardiography; LV, left ventricular; LVOT, left ventricular outflow tract. (From Maganti and colleagues.22)

![Figure 12-60](https://example.com/fig60.png)  
**Figure 12-60** Effect of aortic valve replacement (AVR) on survival as a function of mean transaortic gradient (MG) in low ejection fraction (EF) patients (EF < 40%). (From Pai.21)**
Hemodynamic performance of prosthetic heart valves during rest and exercise. Indexed effective orifice area is compared with mean pressure gradient across prosthesis at rest and during increasing levels of exercise. Prosthetic heart valves show a steep rise in pressure gradient when indexed effective orifice is less than 0.85 cm\(^2\) m\(^{-2}\). From Dumesnil and Yoganathan.

Managing the Small Aortic Root

Some adult patients have a smaller-than-usual LV-aortic junction or a narrow aortic waist at the level of the commissural attachment of the cusps (see discussion of true congenital subvalvar or supravalvar aortic narrowing in Sections II and III of Chapter 47).

The simplest technique in patients with a small aortic annulus is placing the device partly in a supraanular position (Fig. 12-63, A). This takes advantage of the bulging of the noncoronary sinus of Valsalva. A replacement device one size larger than the aortic annulus can be used by suturing it to the annulus along the left and right sinuses and in the supraanular position along the noncoronary sinus. In that area, pledged mattress sutures are placed from outside in or on the ventricular side of the aortic annulus.

The freehand (subcoronary) aortic allograft is the best device in the small aortic root. Appropriately sized allografts are available in graft banks and can be inserted within the aortic root, resulting in minimal gradient. Subcoronary valve replacement using a stentless porcine bioprosthesis is also effective for the small aortic root. These devices are designed to be implanted in the intraanular position in the LVOT (Fig. 12-63, B). Absence of a supporting stent allows insertion of a valve with an effective orifice large enough to provide good hemodynamic function even in the small aortic root. Sintek and colleagues implanted 19- and 21-mm Freestyle bioprostheses and found the average LV-aortic gradient was 13 mmHg for 19-mm valves and 8 mmHg for 21-mm devices. Doty and colleagues noted similar results.

When a mechanical prosthesis is used, a size smaller than 23 mm often results in considerable obstruction, depending on the device and the patient’s BSA. Replacement device mismatch is a serious iatrogenic disease that produces persistent or increasing LV dysfunction, hemolysis, and a very difficult reoperation. Reoperation is difficult because, at the initial operation, the largest possible prosthesis has been inserted in a small passageway, which often results in erosion of anular support. Coronary ostia are usually drawn close to the sewing ring, increasing the possibility of coronary obstruction. Reoperation often requires full root reconstruction. All these increase difficulty and risk.

A 19-mm device may be obstructive but could be used cautiously, thoughtfully, and infrequently in some circumstances in small and sedentary patients. Modern mechanical prostheses may be less obstructive than stent-mounted bioprostheses of the same label size. Second- and third-generation bioprostheses and mechanical prostheses may provide adequate hemodynamic performance in small and sedentary patients, provided a 21-mm device can be implanted. Otherwise, aortic root enlargement by one of several methods to allow use of a larger prosthesis will provide better hemodynamics and reduce the chance of residual LVOT obstruction. A stentless bioprosthesis (autograft, allograft, or xenograft) implanted in the subcoronary position or as a full root replacement may also accomplish the desired hemodynamic performance.
When the narrowing is only at the supraanular level at the top of the sinuses of Valsalva, supraanular enlargement with a patch graft into the noncoronary sinus of Valsalva is used.\textsuperscript{N4} A patch of pericardium has the advantage of ease of handling and insertion, and the suture line is easily made hemostatic (Fig. 12-64, \textit{A} and \textit{B}). Piehler and colleagues followed patients nearly 20 years and showed that a pericardial patch in this position does not become aneurysmal.\textsuperscript{P18} Alternatively, a knitted or woven polyester velour or felt patch with pericardium on the inner surface may be used.

When the anulus is also involved supraanular and anular enlargement by patch graft enlargement in the noncoronary sinus is carried across the anulus and into the aortic-mitral anulus below it. Nicks and colleagues described this method, with a slight modification by Blank and colleagues.\textsuperscript{B38,N4}

Enlargement of both supraanular and anular areas can also be achieved by extending the aortotomy through the left coronary–noncoronary commissural area and into the underlying aortic-mitral anulus, as originally described by Manouguian and colleagues.\textsuperscript{N4,R10,S21} The valve is excised and the need for aortic root enlargement determined. The aortotomy is extended posteroinferiorly directly through the left coronary–noncoronary commissural area (see Fig. 12-64, \textit{A}), across the anulus, and into the base of the aortic-mitral anulus, where it adheres to the left atrial wall. The incision does not reach the hinge point of the mitral leaflet. The left atrium is first dissected away and may or may not be opened as the incision is made. A broad teardrop-shaped patch, generally about 4 cm wide, is created. Beginning at the midpoint of the bottom of the incision, interrupted felt pledget-supported horizontal mattress sutures of 3-0 polyester are placed through the aorta and patch. Special care is used because it is difficult to see this area again after the stitches are tied and aortic clamp removed. The valve is sewn into place using interrupted horizontal mattress sutures in the region of the patch, bringing these in from the outside to secure the valve against the patch (see Fig. 12-64, \textit{B}). The remainder of the circumference of the prosthetic valve is attached to the anulus of the aortic valve as usual with continuous or interrupted mattress stitches. The valve is seated in the LVOT in the intraanular position. The prosthetic patch is used to close all or part of the aortotomy using continuous stitches of 4-0 or 3-0 polypropylene.

When more diameter enlargement is required, the aortic incision is extended across the anulus of the mitral valve and into the midportion of its anterior leaflet (Fig. 12-64, \textit{C-E}). Degree of enlargement is related to depth of incision into the anterior leaflet. Diameter increase of up to 4 to 5 mm may be possible with aggressive incision to the free edge of the mitral valve. The roof of the left atrium is entered as the incision crosses the mitral anulus, creating a defect in the atrium. The defect in the mitral valve anterior leaflet is repaired with a prosthetic patch, which is extended across the aortic-mitral anulus into the aorta. Interrupted stitches of 3-0 braided suture are used to attach the patch to the mitral leaflet tissues. Continuous stitches are probably less desirable than simple interrupted ones in terms of strength and accuracy of repair. Interrupted mattress stitches of 2-0 braided suture with PTFE felt pledgets are used to approximate an appropriately sized prosthetic valve to the prosthetic patch. These stitches may be started in the rim of the left atrial defect if the atrial tissues are sufficiently flexible to allow approximation to the prosthetic patch without tension. Otherwise, the atrial defect

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure12-63}
\caption{Aortic valve replacement in small aortic root. \textbf{A}, Supraanular implant of stent-mounted xenograft. Contoured design of second-generation xenografts allows implanting device above aortic valve anulus, taking advantage of space in sinuses of Valsalva. A larger bioprosthesis may be implanted without obstructing coronary arteries for better hemodynamic function. \textbf{B}, Intraanular subcoronary implant of stentless porcine bioprosthesis. Improved hemodynamic performance provided by absence of support stent allows mounting of a stentless porcine xenograft even in small aortic root.}
\end{figure}
Figure 12-64  Aortic root enlargement.  

A, Incision is made through commissure between left and noncoronary sinuses and extended into intercusp triangle to level of mitral valve anulus. Loose connective tissues in triangle allow edges of aorta to separate. 

B, Teardrop-shaped patch of collagen-coated polyester is placed into defect in aortic wall. Pledget-reinforced mattress sutures placed from outside of patch through aorta and through sewing ring of a prosthesis create tight closure of widened left ventricular outflow tract (LVOT). 

C, Extending incision across mitral valve anulus into its anterior leaflet provides even greater separation of edges of aorta and further widens LVOT. Left atrium is also entered. A collagen-coated polyester patch is inserted to close defect in mitral valve and aorta. Interrupted stitches are used to attach patch to mitral valve leaflet tissues up to level of aortic valve anulus. 

D, Pledget-reinforced horizontal mattress sutures are placed through edge of defect in left atrium (if tissue is flexible and mobile), brought through polyester patch, then through sewing ring of prosthesis. A separate patch is used to close left atrium if there is any tension on closure. 

E, Patch is trimmed appropriately and used to fill defect in aorta.
is filled in with a separate patch of autologous pericardium. The prosthetic patch is tailored to a point and used to close all or part of the aortotomy.

An alternative to all these methods is replacing the aortic root and first part of the ascending aorta with a porcine aortic root bioprosthesis, an allograft aortic valve cylinder, or an autograft pulmonary valve cylinder. Excision of almost all the aortic root except for buttons of sinus aorta around the coronary arteries often opens up the narrow aortic anulus. Excision of the residual commissures to open into the intercusp triangles allows the more flexible tissues in the triangle to expand and enlarge the aortic root. The aortic root is then replaced with an appropriately sized porcine bioprosthesis, aortic allograft, or the patient’s own pulmonary trunk (autograft). In this technique, the conduit will represent an important “size up” compared with the original diameter of the aortic anulus and aortic root.

Associated subvalvar LVOT narrowing may be anatomic hypoplasia or acquired from excessive compensatory LV hypertrophy. In former practice, this was an indication for aortoventriculoplasty (Konno-Rastan operation; see Chapter 47). Clarke described a modification of this operation using an aortic allograft with its attached anterior mitral leaflet. An attractive alternative is the pulmonary autograft procedure in which the Konno-Rastan–type incision is less deep into the LV septum. The shallower incision virtually eliminates injury to the first septal branch of the left anterior descending coronary artery and resultant septal myocardial infarction and injury to the conduction system. The pulmonary autograft is implanted deeper into the LVOT below the aortic anulus for complete relief of the outflow tract obstruction.

Use of an LV apicoabdominal aortic valve conduit has nearly been abandoned. It should not be considered the primary approach to the problem of a small anulus or aortic root in patients requiring valve replacement. When the patient is facing a second or third replacement, however, and has no periprosthetic leakage, such a conduit might be considered as an alternative to aortic root enlargement.

Managing the Large Aortic Root

When the aortic root is large, it may be tailored to a size that will accommodate an allograft, pulmonary autograft, or stentless xenograft. Tailoring is accomplished by extending an incision in the noncoronary sinus across the base of the noncoronary cusp into the aortic-mitral anulus. The left atrium is dissected away as deeply as possible first, but whether this chamber is entered at the lowest point of the incision is not important. A second parallel incision is made posteriorly and tapered to remove an ellipse of aortic root with its widest point at anulus level. The amount of aortic wall to be removed to appropriately reduce the diameter can be calculated, but can also be judged visually, remembering that further reduction in circumference occurs when the sutures are placed several millimeters from the edge and tied down. The lowest part of the defect so created is closed using interrupted figure-of-eight or simple sutures through strong tissue, including the adjacent left atrial wall if it has been opened. This technique was used frequently in the past; residual aortic valve regurgitation afterward was common.

Current practice is full aortic root replacement in the presence of large dilated aortic root pathology. It may be necessary to reduce the diameter at the ventricular-aortic junction (anulus) so that an aortic root allograft or stentless porcine xenograft may fit perfectly into the LVOT. These methods are described earlier under “Repair of Aortic Valve Regurgitation due to Aortic Dilatation or Aneurysm.”

Repair of Aortic Valve Regurgitation

In the absence of dilatation of the aortic root at the anular or sinutubular level, the major causes of potentially repairable aortic regurgitation are forms of congenital aortic valve disease usually associated with a bicuspid aortic valve and floppy aortic valves resulting in cusp prolapse. Although use of reparative operations is not widespread, and the indications for and results of these procedures are not well defined, knowledge of reported techniques is useful for the cardiac surgeon’s armamentarium. Generally these procedures involve subcommissural anuloplasty, reefing up prolapsing tissue of one cusp at the commissural level using the Trussler technique (see Chapter 35), midcusp plication, (Fig. 12-65), partial cusp resection and pericardial cusp extension (Fig. 12-66), and free margin resuspension (Fig. 12-67). Applying these techniques in 122 patients with bicuspid aortic valve and isolated aortic valve regurgitation, Boodhwani and colleagues reported 83% freedom from aortic valve reoperation at 8 years.

Pettersson described a systematic morphology-directed repair of regurgitant bicuspid aortic valves, identifying repair at cusp, commissure, and root levels. A pliability and coaptation deficiency index was developed to evaluate reparable.

Aortic Regurgitation with Aneurysm of the Ascending Aorta

When aortic regurgitation is accompanied by aneurysms of the aortic root or ascending aorta, operation may be advisable for moderate or less aortic regurgitation when specific indications for operation are met regarding details of aortic enlargement. Prophylactic replacement of the ascending aorta to prevent rupture or (more likely) dissection is generally recommended when the aortic diameter exceeds about 5.5 cm. The precise diameter depends also on rate of enlargement and presence of other comorbidities that would increase operative risk.

In patients with Marfan syndrome, prophylactic aortic root replacement may have the greatest therapeutic benefit for patient survival. Elective aortic replacement is recommended in adults when the aortic root or ascending aortic diameter exceeds 5.0 cm or the aortic index (diameter of aorta-BSA) exceeds 4.25 cm · m⁻², or with slightly smaller aortic diameter if the progression of increase in aortic diameter exceeds 5 mm · year⁻¹. For women with Marfan syndrome who are contemplating pregnancy, prophylactic valve-sparing aortic root and ascending aorta replacement is generally advisable if the aortic diameter exceeds 4.0 cm by echocardiography. For shorter Marfan patients, dissection is likely at a smaller diameter, so operation may be considered if the maximal cross-sectional area in square centimeters of the ascending aorta or root divided by the patient’s height in meters exceeds a ratio of 10.
Other risk factors that push consideration for earlier operation include a family history of aortic dissection or rupture, and extension of dilatation beyond the sinuses of Valsalva. In pediatric patients, operation has been recommended when the aortic diameter increases by more than 10 mm · year⁻¹. In the absence of asymmetric cusp prolapse or multiple cusp perforations, valve-sparing root replacement is the preferred technique. The need for reoperation in Marfan patients appears to be lower with the reimplantation technique than with the remodeling operation. In patients with Loeys-Dietz syndrome or a confirmed TGFBR1 or TGFBR2 mutation, the threshold for aortic replacement should be lower than in Marfan syndrome patients because of the greater propensity for aortic dissection with an aortic diameter of less than 5.0 cm. Thus, surgical resection of the aortic root and ascending aorta with valve-sparing aortic root replacement is advisable with an aortic diameter of 4.2 cm or greater by TEE (internal diameter) or 4.4 to 4.6 cm or greater by CT scan or MRI (external diameter). Surgical procedures in this syndrome are not complicated by excessive tissue fragility.

In patients with Loeys-Dietz syndrome or a confirmed TGFBR1 or TGFBR2 mutation, the threshold for aortic replacement should be lower than in Marfan syndrome patients because of the greater propensity for aortic dissection with an aortic diameter of less than 5.0 cm. Thus, surgical resection of the aortic root and ascending aorta with valve-sparing aortic root replacement is advisable with an aortic diameter of 4.2 cm or greater by TEE (internal diameter) or 4.4 to 4.6 cm or greater by CT scan or MRI (external diameter). Surgical procedures in this syndrome are not complicated by excessive tissue fragility.

Reimplantation rather than remodeling appears preferable in the setting of adult connective tissue disorders such as Marfan, Loeys-Dietz, and Ehlers-Danlos syndromes, but each has its proponents for other forms of aortic root aneurysm and bicuspid or tricuspid aortic valves. The preferred procedure for infants and children has not been clarified.

**Bicuspid Aortic Valve and Ascending Aortic Aneurysm**

Because the natural history of ascending aortic aneurysm is more unfavorable in patients with a bicuspid aortic valve,
Figure 12-67  Leaflet prolapse resuspensions. A, Length differences between free margins can be easily appreciated by bringing together middle of free margins with a 7-0 polypropylene suture. B, A 7-0 polytetrafluoroethylene (PTFE) suture is passed twice in top of commissure. C, Successively, two running sutures are passed over and over around length of free margin. D, With gentle traction on each branch of PTFE sutures, applying opposite resistance with a forceps at the middle of free margin, first half of free margin is shortened by slightly wrinkling tissue until it reaches same length as adjacent normal free margin. E, Same maneuver is applied for second half of free margin. This two-step technique for free margin shortening allows symmetric and homogenous shortening. F, When appropriate shortening is achieved, the four suture ends are passed through aortic wall and tied externally.

Box 12-3  Bicuspid Aortic Valve with Dilated Ascending Aorta

1. Patients with bicuspid aortic valves and dilatation of the aortic root or ascending aorta (diameter > 4.0 cm) should undergo serial evaluation of aortic root/ascending aorta size and morphology by echocardiography, cardiac magnetic resonance imaging, or computed tomography on a yearly basis.

2. Surgery to repair the aortic root or replace the ascending aorta is indicated in patients with bicuspid aortic valves if the diameter of the aortic root or ascending aorta is greater than 5.0 cm or if the rate of increase in diameter is 0.5 cm per year or more.

3. In patients with bicuspid valves undergoing aortic valve replacement or repair because of severe aortic stenosis or aortic regurgitation, repair of the aortic root or replacement of the ascending aorta is indicated if the diameter of the aortic root or ascending aorta is greater than 4.5 cm.

*Consider lower threshold values for patients of small stature of either gender.

Percutaneous Balloon Aortic Valvotomy

Percutaneous balloon aortic valvotomy for aortic stenosis in adults was popularized in the late 1980s. One or more balloons are passed across the aortic valve and inflated. In elderly patients with calcific aortic stenosis, the balloon causes fracture of calcific deposits and separation of fused or calcified commissures. Reduction in gradient is usually moderate, but the resulting valve area rarely exceeds 1.0 cm². Embolization of calcific material and development of acute aortic regurgitation represent important risks. Furthermore, restenosis is common within 6 to 12 months. Despite these important limitations, percutaneous balloon valvotomy has an important role among patients who are elderly with multiple comorbidities and at high risk for surgical aortic valve replacement.

An additional important application is in patients with severe LV dysfunction who have likely severe aortic stenosis but without a high transvalvar gradient, and who are symptomatic with advanced heart failure. In this setting, especially with additional comorbidities, there may be uncertainty about whether the LV cardiomyopathy or aortic stenosis is the more important condition. If surgical risk is considered high, an initial balloon valvotomy may provide relief of the aortic stenosis and allow assessment of the patient’s heart failure symptoms and LV function. Improvement in one or both of these supports the role of aortic stenosis in the clinical setting, and aortic valve replacement can be undertaken with expectation of favorable outcome.

In addition, patients with refractory pulmonary edema or circulatory shock might be sufficiently improved and in stable...
condition for later operation to replace the aortic valve. Patients requiring urgent noncardiac surgery may also be considered candidates for balloon valvotomy, but they are usually successfully treated by other measures.07,113

Nonreplacement Valve Operations for Aortic Stenosis in Adults

Nonreplacement decalcification operations for aortic stenosis have given reasonably good results in selected patients.17,133 At a few centers, the procedure has been augmented by using ultrasonic decalcification. However, prevalence of immediate and delayed cusp rupture is sufficient to make the technique of doubtful value.28,113 In most patients, valve replacement operations yield better and more predictable overall results.

Silver-Coated Sewing Rings

Silver salts and colloids have a long history as antimicrobials. Silver has a broad spectrum of action against bacteria, although silver toxicity can be a problem if serum level is greater than 300 parts per billion (ppb).27 Ion beam–assisted deposition of silver as a coating on polyethylene terephthalate (polyester) fabric appears to be safe and is probably effective as an antimicrobial agent for use in the sewing cuffs of mechanical heart valves.116 Healing at the sewing rings in animal studies is not impaired, but pannus formation is thinner on the silver fiber.117

Silver coating (Silzone) was introduced onto the sewing rings of mechanical cardiac valves by St. Jude Medical to reduce infection on the device. More than 30,000 St. Jude Medical Silzone valves have been implanted. Some questions have been raised regarding reduced healing and increased thromboembolism. Ionescu and colleagues showed higher incidence of ischemic stroke and peripheral embolism when the Silzone sewing cuff was used (17.1% patient-year\(^{-1}\)) compared with the standard sewing cuff (0.85% patient-year\(^{-1}\)).11 The study groups were not randomized or even concurrent, but patient characteristics were similar.

A large randomized study comparing standard and silver-coated sewing rings (Artificial Valve Endocarditis Reduction Trial [AVERT]) enrolled patients to determine the effectiveness of preventing infective endocarditis. Enrollment in the study was suspended in January 2000 when audit of the data revealed 11 of 398 (2.8%) patients in the Silzone group had periprosthetic leakage, with 8 (2.01%) requiring reoperation for explant. Four of 394 (1.02%) patients in the conventional sewing cuff group had periprosthetic leakage, with one requiring explant (0.25%). The company voluntarily recalled all products with silver coating. Subsequent analysis of the data confirmed that the risk of explant for periprosthetic leakage was greater in the Silzone group (\(P < .02\)).22 Other studies independent of the AVERT trial, however, subsequently demonstrated no differences in prevalence of periprosthetic leakage between the silver-coated and standard St. Jude Medical prostheses.15,110,114 No differences were found in the incidence of thromboembolism or endocarditis. Continued follow-up of the patients may determine if there is any antimicrobial advantage of silver coating on the sewing ring of prosthetic cardiac valves.17

Aortic Valve Replacement Through Smaller Incisions

A number of reports have described a variety of incisions that are smaller than the standard median sternotomy for cardiac valve operations. Initial interest in performing cardiac valve operations through a minimal incision was stimulated by port access technology applied experimentally.13,114,120

The STS National Adult Cardiac Surgery Database has shown steady growth in the percentage of less invasive cardiac valve procedures, but they still represent a small fraction of all approaches.34 For isolated aortic valve replacement, 8.0% of operations were attempted by a minimally invasive approach. In the 2010 Cleveland Clinic experience, however, minimally invasive isolated aortic valve replacement reached 65%.114 The most popular incision for aortic valve procedures has evolved to a limited partial sternotomy. Reardon and colleagues studied the anatomy of partial sternotomy.86 Usually the incision is made vertically through the upper half or two thirds of the sternum for aortic valve operations, with a number of variations for the transverse section of the sternum, including T-, J-, C-, or even Z-shaped incisions.3,13,14,29,54

Parasternal and transverse sternal incisions have been tried and mostly abandoned because of limited exposure, injury to the internal thoracic arteries, and lung hernia.29,34,39 A lower-half sternotomy, however, provides a small incision that is so versatile that most if not all cardiac operations can be performed through this standard incision.14

To perform the partial lower half or lower two-thirds sternotomy, body habitus is studied after the patient is placed in supine position for operation. The angle of Louis (second rib) and the second and third intercostal spaces are located (Fig. 12-68). Length of the sternum is evaluated and shape of the thorax observed. It is desirable to make a large enough incision over the location of the cardiac valves to accommodate the surgeon’s hand, should direct palpation of the heart be required. When the sternum is long and the patient’s habitus slender, dividing the sternum in the third intercostal space is sufficient for most cardiac valve operations. When the patient’s sternum is short or body habitus

![Figure 12-68](image-url)
stocky or obese, a second intercostal transverse sternal incision will provide better access. Complex valve operations such as the Ross procedure are easier to perform through a second interspace incision. Third interspace incisions are shorter and cosmetically more appealing. The skin incision is made in the midline over the sternum, extending from the interspace selected to near the end of the sternum. The pectoralis major and intercostal muscles are dissected away from the sternum in the second or third intercostal space on each side of the sternum to free the internal thoracic vascular pedicle. The sternum is divided transversely at the second or third intercostal space and vertically from that point through the xiphoid process using an oscillating saw. The upper one third or half of the sternum, including the manubrium, remains intact.

CPB is established using a small (29F/37F) two-stage or three-stage (29F/29F) cannula for venous uptake, with oxygenated blood returned to a small (24F) cannula placed in the ascending aorta. Active venous uptake is used through a vacuum-assisted venous return system (see “Vacuum-Assisted Venous Return” in Section II of Chapter 2). The cannulae are brought through the primary incision. The aortic occlusion clamp is brought through a stab incision on the right side below the clavicle and passed through the open right pleural space into the pericardial sac to occlude the aorta. A small (12F) vent cannula is introduced through the right superior pulmonary vein. Cold blood cardioplegic solution is perfused into the coronary sinus through the usual cannula designed for this purpose. The aortic valve is exposed by dividing the aorta above the sinotubular junction. Retraction stitches are placed just above each of the commissures, which rotates the aortic root anteriorly and elevates it for optimum exposure.

Several reports suggest that smaller incisions lessen surgical morbidity as well as cost of the procedure. Aris and colleagues, however, found that reduced pulmonary function associated with aortic valve replacement was not prevented by a smaller incision. Szwercz and colleagues compared partial upper sternotomy with median sternotomy for aortic valve replacement and found similar results. They showed that partial sternotomy offered a cosmetic benefit but did not reduce pain, length of stay, or cost, although the Cleveland Clinic group has. They also noted that upper sternotomy does not provide access to the heart other than at the aorta and the base. This cardiac access problem is overcome by lower partial sternotomy, which centers the incision over the heart.

Arom and colleagues have compared port access to less invasive procedures in which a small incision is made, but the aorta and atria are cannulated directly. They found that port access procedures required more operating room time, longer operative and aortic clamp time, and more cost than the less invasive procedures. Their experience concurs with that of other surgeons. Therefore, the trend in cardiac valve operations is toward direct cannulation of the aorta and heart when small incisions are used. Byrne and colleagues have reported use of a partial upper hemisternotomy for reoperative aortic valve replacement. They found operative bleeding was reduced as well as operating time, compared with standard full sternotomy during reoperations.

In a diverse patient population, it seems that the approach at operation, age of the patient, and other comorbid factors are the major influences on outcomes, frequency of complications, and costs.

Percutaneous Transcatheter Aortic Valve Implantation

Despite the overall low mortality associated with aortic valve replacement, certain patient subsets carry a high risk of hospital mortality when exposed to a standard open aortic valve replacement using CPB. Such high-risk patients have been defined using the logistic EuroSCORE calculated risk of greater than 20%. Given the rather transient relief achieved with balloon valvuloplasty (see “Percutaneous Balloon Aortic Valvotomy” earlier in this chapter), major interest has developed in use of percutaneous or transapical valve implant systems for treating severe symptomatic aortic stenosis when both medical therapy alone and traditional aortic valve replacement carry a high expected mortality. As of 2011, two such devices have been approved for clinical use in Europe and are undergoing clinical trial in the United States: the SAPIEN valve (Edwards Lifesciences, Irvine, Calif.) and the CoreValve ReValving System (Medtronic Inc., Minneapolis, Minn.). The SAPIEN valve has been approved by the FDA for inoperable patients in the United States. Both systems can be delivered via transapical, femoral/iliac, or axillary/subclavian routes. In a recent review, Bande and colleagues noted that more than 4000 such implants occurred through early 2010. Thirty-day mortality is as low as 5% for a patient group considered surgically inoperable, with substantial survival advantage at 1 year over a similar group receiving medical therapy.

Relative advantages of one approach over another continue to be evaluated by multiple surgical and interventional multidisciplinary teams. Percutaneous approaches are less invasive but often limited by vascular access issues. Transapical approaches are more invasive but have no limitations with regard to access. The transapical approach is performed through a small left anterior thoracotomy centered over the LV apex in the fifth or sixth intercostal space. Apical deployment of transcatheter valves carries the additional advantages of avoiding the transverse aortic arch (a potential source of embolic strokes), and the short working distance may improve accuracy of valve deployment. Important LV apical bleeding and late pseudoaneurysms of the LV apical site have been reported in about 5% of patients. Intermediate and late outcomes of transcatheter valve implantation will be clarified in the coming years.

Functional Mitral Regurgitation Associated with Aortic Valve Disease

Important organic mitral regurgitation may coexist with severe aortic valve disease, and repair or replacement of both valves is the proper surgical procedure (see Chapter 13). However, mitral regurgitation of grade 1 or 2 (based on grades 1 to 4) may occur in the presence of aortic valve disease even when the mitral leaflets are normal, presumably because of annular dilatation. The mitral regurgitation is usually abolished or considerably reduced by aortic valve replacement.

When encountering this situation, the surgeon should evaluate the mitral valve by intraoperative TEE. If it seems structurally normal and regurgitation is no more than grade
2, the valve should not be repaired or replaced. In borderline cases, it is best to discontinue CPB after repair or replacement of the aortic valve and to reassess mitral valve function using TEE with the heart beating and ejecting. If mitral regurgitation continues to be important, CPB is recommenced, and the mitral valve is repaired with an anuloplasty band or ring.

REFERENCES

A


C


Chapter 12: Aortic Valve Disease


I


J


L


PART III Acquired Valvar Heart Disease


M


Chapter 12 Aortic Valve Disease

Y

Z
**DEFINITION**

Acquired diseases of both the aortic and mitral valves severe enough to require simultaneous surgery (replacement, repair, or valvotomy) are considered in this chapter. Because tricuspid valve disease may form part of this spectrum and require simultaneous surgery, it is also considered, although discussed in more detail in Chapter 14.

**HISTORICAL NOTE**

Surgical treatment of combined aortic and mitral valve disease began during the early 1950s by closed methods. In 1955, Likoff and colleagues reported 74 patients who had undergone simultaneous closed repair of aortic and mitral stenosis by Bailey and Glover in Philadelphia. In 1958, Lillehei and colleagues were the first to report simultaneous repairs of both valves by open techniques using cardiopulmonary bypass (CPB). In 1963, soon after introduction of durable mechanical prostheses, Cartwright and colleagues first reported simultaneous aortic and mitral valve replacement. In 1964, Starr and colleagues reported 13 patients who had undergone multiple valve replacements, including one who received mechanical aortic, mitral, and tricuspid prostheses.

**MORPHOLOGY**

Morphology of diseases involving mitral, aortic, and tricuspid valves is described in Chapters 11, 12, and 14. In most patients, multivalvar disease is rheumatic in origin, but each valve may manifest a separate pathologic condition—for example, rheumatic aortic valve disease and mitral regurgitation from infective endocarditis, idiopathic chordal rupture, or ischemic papillary muscle dysfunction.

The effect of combined disease on morphology of the left ventricle (LV) is of great importance. Thus, at the extremes, combined aortic and mitral regurgitation imposes a large volume overload on the LV, and LV volume and wall thickness increase severely; combined aortic and mitral stenosis results in a small, thick-walled, noncompliant LV.

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CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

In general, clinical criteria and noninvasive diagnostic tests are the same for mitral and aortic valve disease whether they are combined or isolated, but additional cardiac catheterization and angiography data are more frequently needed when they are combined. In patients older than 40 years of age, coronary angiography is indicated routinely, and the valve lesions are assessed at that time.

One lesion is usually dominant and may modify the clinical signs of the less dominant one. A frequent problem is assessing severity of the less dominant lesion; if it is mild or even mild to moderate, it may not require simultaneous correction. Historically, it was sometimes possible to obtain reliable information on the second lesion during operation by palpating an atrial chamber to detect systolic pulsation, by feeling the valve directly with the finger before beginning CPB, or by exposing the valve. Today, with two-dimensional (2D) and color Doppler echocardiography, the status of the aortic, mitral, and tricuspid valves is usually known before the patient enters the operating room. Intraoperative use of transesophageal echocardiography (TEE) verifies this status if necessary.

Dominant Aortic Stenosis

Dominant aortic stenosis is diagnosed by the same techniques used in isolated aortic stenosis (see Chapter 12). Dominant aortic stenosis may complicate diagnosing coexisting mitral stenosis by simple methods. The auscultatory signs of moderate mitral stenosis may be masked, and transmission of the aortic systolic murmur to the apex may confuse the assessment of mitral regurgitation. However, Doppler echocardiography can render as precise a diagnosis as in isolated mitral stenosis. Severity of pure mitral stenosis associated with aortic stenosis can be verified by pressure measurements (left atrium to LV) on the operating table, although varying cardiac output sometimes makes interpretation difficult. In questionable cases, the valve may be palpated on CPB or examined directly by opening the left atrium through the superior approach (see Chapter 11).

A convincing sign of important mitral regurgitation associated with aortic stenosis is a right parasternal systolic lift, especially if associated with an apical third heart sound when the venous and hepatic pulses do not indicate important tricuspid regurgitation. More than modest left atrial enlargement on the posteroanterior chest radiograph and also P mitrale in the electrocardiogram strongly suggest important associated mitral valve disease. Two-dimensional echocardiography with Doppler color flow interrogation is helpful in identifying mitral regurgitation, both preoperatively and intraoperatively.

Dominant Aortic Regurgitation

In dominant aortic regurgitation, as noted in Chapter 12, an Austin Flint murmur can mimic that of mitral stenosis, the absence of which can be confirmed by 2D echocardiography with Doppler color flow interrogation. If in addition to a mid-diastolic murmur there is an opening snap, left atrial enlargement above grade 2, and P mitrale, then important coexisting mitral stenosis is usually present.

With dominant aortic stenosis, severity of associated mitral regurgitation requires careful assessment by 2D echocardiography, particularly because it is frequently secondary to LV enlargement or dysfunction. If it is less than grade 2 in severity, it usually regresses after the aortic regurgitation is corrected. When the LV is severely enlarged, it is likely that both aortic and mitral regurgitation are severe.

Dominant Mitral Stenosis

Dominant mitral stenosis may minimize the usual signs and symptoms of coexisting aortic regurgitation. When aortic regurgitant flow is moderate or large, its presence and severity are readily assessed clinically by character of the arterial pulse and blood pressure. At times, however, what seems to be less than grade 2 aortic regurgitation becomes clearly moderate or severe after surgical relief of the mitral stenosis. Magnitude of aortic regurgitation cannot be assessed reliably at operation. Visual inspection of the aortic valve may provide information about extent of the rheumatic condition but not about magnitude of the leakage. Thus, evaluating the aortic valve preoperatively with 2D echocardiography Doppler color flow interrogation is important before undertaking mitral valve surgery. Intraoperative TEE can be of value as well. Size of the jet visualized by color Doppler echocardiography may not represent the degree of aortic regurgitation. It is possible to measure the vena contracta, which is the size of the regurgitant jet within the regurgitant aortic valve orifice. This measurement correlates well with effective regurgitant orifice. Width of the vena contracta is measured from the parasternal view long axis, just below the flow convergence. Vena contracta greater than or equal to 7 mm uniformly indicates severe aortic valve regurgitation, whereas measurements of 5 mm or less correspond to regurgitation that is moderate or less.

Moderate (grade 2) associated aortic stenosis can usually be identified clinically by characteristic physical findings (see Chapter 12), and LV-aortic gradient can be measured at operation, but flow may not be known. Therefore, an estimate of aortic valve orifice size by 2D echocardiography or cardiac catheterization (see Chapter 12) should be available when mitral valve surgery is undertaken.

Dominant Mitral Regurgitation

The same considerations discussed for dominant mitral stenosis apply to aortic valve disease associated with dominant mitral regurgitation.

Dominant Tricuspid Valve Disease

In uncommon cases of dominant tricuspid stenosis or regurgitation, accurate clinical assessment of downstream lesions in the mitral and aortic valves is seldom possible. Preoperative 2D echocardiographic study is required, and occasionally cardiac catheterization as well.

NATURAL HISTORY

The natural history of combined aortic and mitral valve disease is complicated by the same variability in dominance of one lesion over the other that makes diagnosis and decision making difficult. For example, in rheumatic aortic valve disease, the mitral valve is involved almost universally, although the lesions—either stenosis or regurgitation—may
be so mild that operation is not required until many years after replacement of the aortic valve. Double valve surgery in such patients is sequential. Patients with rheumatic mitral valve disease often have only mild rheumatic aortic valve disease at the time of their original mitral operation. The longer these patients survive, the more likely it is that a mild rheumatic aortic lesion will become important and require operation. Choudhary and colleagues followed 284 patients with rheumatic heart disease who had mild aortic valve involvement at the time of mitral valve surgery. After a mean interval of about 5 years, 35% of those with mild aortic valve stenosis had progressed to moderate or severe stenosis. Freedom from development of moderate or severe aortic valve stenosis was 75% ± 6%, 62% ± 9%, and 46% ± 11% at 5, 10, and 15 years, respectively. Mild aortic valve regurgitation at the time of mitral valve intervention, on the other hand, progressed slowly, with only 5% of patients developing moderate or severe aortic valve regurgitation after a mean interval of 12 years. Freedom from development of moderate or severe aortic valve regurgitation was 100%, 97% ± 2%, and 87% ± 5% at 5, 10, and 15 years, respectively.

Simultaneous development of important aortic and mitral valve disease usually results from a particularly severe and prolonged attack of rheumatic fever or from recurrent attacks, and there may be a florid myocarditis and pericarditis as well. Regurgitant combined valve lesions may mature particularly rapidly, requiring operation by the second decade of life.

When dominant aortic stenosis coexists with mitral steno-

sis, prognosis may be worse than that of isolated aortic stenosis. When dominant mitral stenosis coexists with important aortic stenosis, survival is shorter than for isolated mitral stenosis, with sudden death being a particular risk. When severe aortic and mitral regurgitation coexist, reduction of LV afterload by mitral regurgitation provides a protective effect (see Chapter 11), and patients with aortic regurgitation tend to remain asymptomatic despite advanced left ventricular dysfunction (see Chapter 12). Consequently, it is likely that patients with this combination will remain asymptomatic well beyond the stage when left ventricular dysfunction becomes irreversible.

**TECHNIQUE OF OPERATION**

After induction of general inhalation anesthesia and during appropriate preparation of the skin and draping of a sterile field, an echocardiography probe is inserted into the esophagus (see Chapter 4). Two-dimensional ultrasound imaging is used to evaluate valve morphology and color Doppler ultrasound to evaluate valvar hemodynamics. The plan for operation is then refined. The aortic valve is replaced in most circumstances, but it may be repaired if there is aortic valve regurgitation that is judged to be secondary to dilatation of the aortic root or to dilatation or aneurysm of the ascending aorta. The mitral valve may be repaired or replaced. The tricuspid valve may not need intervention or may be repaired. The crux of the operation usually involves the intervention judged necessary for the mitral valve; there are more options available for it than for the aortic valve, and the tricuspid valve is usually repairable.

A median sternotomy is performed. The cardiac valves lie in close proximity to each other, so an extensive incision is unnecessary. The pericardium is opened and suspended to provide optimal exposure of the heart. A systematic evaluation is made by assessing cardiac chamber size and palpating for thrills caused by turbulent blood flow. CPB is established using a single venous uptake cannula or two venous cannulae if the left atrium is small. Two venous cannulae and caval tapes with tourniquets are required for operations involving the tricuspid valve (see Chapter 2). Oxygenated blood is returned through a cannula placed in the ascending aorta. Multiple valve operations are enhanced by using small cannulae and vacuum-assisted venous return (see “Vacuum-Assisted Venous Return” in Chapter 2). The perfusate may be cooled to lower the body temperature to 28°C.

Operations involving more than one cardiac valve are most conveniently performed using intermittent retrograde administration of cardioplegic solution via the coronary sinus (see “Technique of Retrograde Infusion” in Chapter 3). A perfusion cannula is inserted into the coronary sinus through the right atrial wall for aortic and mitral valve operations, or directly after opening the right atrium for operations involving the tricuspid valve.

A vascular clamp occludes the ascending aorta. A vent catheter is inserted through the right superior pulmonary vein and advanced across the mitral valve into the LV. A transverse aortotomy is made and cold cardioplegia administered. For tricuspid valve operations, the right atrium is opened parallel to the atrioventricular groove, the coronary sinus cannula is inserted, and cold cardioplegia is administered.

The aortotomy is extended into the noncoronary sinus of Valsalva or extended to divide the aorta above the sinutubular junction. The aortic valve is inspected for the possibility of repair. If it is not reparable, it is excised. Calcific deposits are removed from the aortic anulus. Diameter of the LV outflow tract at the aortoventricular junction (aortic anulus) is measured.

The operation then focuses on the mitral valve. The left atrium is opened on the right side posterior to the interatrial groove at the junction of the right pulmonary vein, and the incision is extended superiorly behind the superior vena cava and inferiorly behind the inferior vena cava. Alternatively, the superior aspect of the left atrium is opened medial to the superior vena cava and behind the aortic anulus. This superior approach is particularly useful when the aorta has been divided. When operation on the tricuspid valve is required, a transeptal approach may be convenient, extending the right atrial incision superiorly medial to the superior vena cava and onto the superior aspect of the left atrium. The atrial septum is cut back inferiorly through the fossa ovalis to the inferior wall of the left atrium. A self-retaining retractor maintains exposure of the mitral valve.

The mitral valve is inspected for the possibility of repair. If repair is not feasible, the valve is usually replaced with a mechanical prosthesis, although second- or third-generation stent-mounted bioprostheses may be used in patients older than («)70 years of age. This influences the choice of replacement device for the aortic valve, because it is usually replaced with the same type of valve as the mitral valve (see “Choice of Device” in Chapter 12). The only exception to mixing rather than matching the type of prosthesis is in the case of a very small aortic root, when a stentless bioprosthesis (allograft or xenograft) may be chosen (see “Small Aortic Root and Small Prosthesis: Prosthesis-Patient Mismatch” in Chapter 12). If the mitral valve is reparable, more selection options are available for the aortic valve, with weight given to a bioprosthesis to avoid anticoagulation if the cardiac
rhythm is likely to be normal sinus after operation. The tricuspid valve is usually repaired regardless of choices made for the aortic and mitral positions. Occasionally the tricuspid valve is involved by rheumatic disease and requires replacement.

Coronary artery bypass grafting (CABG) may be required in combination with multiple valve procedures. It is usually performed after the valves are excised but before the prostheses are inserted, to reduce risk of atrioventricular groove disruption during cardiac retraction to expose the posterior wall of the LV. Proximal vein graft anastomoses to the aorta for left-sided grafts may be performed after completing distal anastomoses to the coronary arterics. For right-sided grafts, the proximal anastomosis is deferred until the atria and aorta are closed.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care of patients who have undergone combined aortic and mitral valve surgery is the same as that for other patients undergoing cardiac surgery with the aid of CPB (see Chapter 5). Anticoagulants are indicated in patients with atrial fibrillation or mechanical prostheses.

RESULTS

Survival

Early (Hospital) Death

Simultaneous aortic and mitral valve replacement is often accompanied by other procedures, so complexity of the operation partly explains higher hospital mortality after multiple valve operations than after single valve surgery. In the Society of Thoracic Surgeons National Adult Cardiac Surgery Database, operative mortality during the 1990s ranged from 6.9% to 9.9%. Hannan and colleagues reported hospital mortality of 9.6% in 1418 multiple valvuloplasty or replacement operations from 1995 to 1997 in the state of New York. John and colleagues reported 9.2% hospital mortality among 456 patients having aortic and mitral valve replacements, whereas Mueller and colleagues reported 5%. When CABG was added to the multiple valve operation, operative mortality doubled to 19% in the state of New York experience.

Time-Related Survival

Time-related survival of heterogeneous groups of patients undergoing simultaneous combined aortic and mitral valve replacement, including those undergoing concomitant tricuspid valve surgery and CABG, is lower than after single valve replacement. In the UAB group’s experience from an earlier era, it was 88%, 77%, 63%, 47%, and 23% at 1 month and 1, 5, 10, and 20 years after operation, respectively. The hazard function for death has a rapidly declining early phase of risk, giving way to a second slowly increasing hazard phase about 3 months postoperatively. The increasing phase of hazard may reflect an imperfect postoperative hemodynamic state dating from the time of operation.

Modes of Death

Most deaths early after primary combined aortic and mitral valve replacement are from acute or subacute cardiac failure. However, an unusually high prevalence of death with hemorrhage has occurred in this group of patients in the past. This is because of the ease with which left atrioventricular rupture can be produced at the time of double valve replacement. Currently, greater attention to this detail has considerably lessened the prevalence of this early postoperative complication.

Mode of death occurring after hospitalization discharge is most commonly due to chronic heart failure. Even when tricuspid valve regurgitation and right ventricular dysfunction have seemed to be absent before operation, a number of patients present late postoperatively with increasing evidence of tricuspid regurgitation, right atrial enlargement, and progressing hepatomegaly. The reason for the unusually high prevalence is not apparent. However, the primary feature appears to be right ventricular dysfunction, and tricuspid valve replacement at this stage generally does not improve the patient’s condition.

Incremental Risk Factors for Death

Double Valve Replacement

Double valve replacement itself is an incremental risk factor for death (9.4%) compared with isolated replacement of the mitral (5.7%) or aortic valve (3.5%). This is evident early after operation, and particularly in intermediate and long-term follow-up, when many deaths occur because of increasing tricuspid regurgitation progressing to right atrial enlargement, hepatomegaly, and finally cardiac cachexia. These types of death occur much less frequently after isolated mitral valve replacement and rarely after isolated aortic valve replacement. The relative roles of decreasing LV performance, increasing pulmonary vascular resistance, and decreasing right ventricular performance in this late deterioration after double valve replacement are uncertain.

Mitral Valve Replacement Rather than Repair

One-stage mitral and aortic valve operations may not involve replacement of both valves. When they do not, the early risks have generally been less, even when concomitant tricuspid valve surgery is performed, and the intermediate and long-term results are better. Gillinov and colleagues reported hospital mortality of 5.4% when the mitral valve was repaired and 7.0% when it was replaced. They also reported 15-year survival of 46% when the mitral valve was repaired compared with 34% when it was replaced (P < .01; Fig. 13-1).

The instantaneous risk of death was highest immediately postoperatively, decreased to its lowest level at 1 year, and increased slowly thereafter (Fig. 13-2). The late phase of hazard was consistently higher after mitral valve replacement than after repair.

Previous Operations

Approximately 15% of patients undergoing first-time simultaneous replacement of the aortic and mitral valves have had a previous valve operation. This has not, however, increased the risks of the double valve replacement.

Choice of Replacement Device

Choice of replacement device does not affect long-term survival. Caus and colleagues compared a matched population aged 60 ± 3 years having aortic and mitral valve replacement with either mechanical prostheses or bioprostheses. Survival at 5, 10, and 15 years was similar, although reoperation was
PART III Acquired Valvar Heart Disease

Left Ventricular Function and Preoperative Functional Status

The more advanced the heart failure, and thus the functional disability, the greater the early and late risks of death (Fig. 13-4). Patients whose condition necessitates an emergency operation can be expected to be particularly at risk early postoperatively. Even patients in New York Heart Association (NYHA) functional class II have reduced late survival. LV ejection fraction below 30% increased hospital mortality in multiple valve replacement in the New York State study to 13%, compared with 9.3% when it was higher. Mueller and colleagues found that LV ejection fraction below 50% increased risk of all deaths (P < .001). Moderate or severe LV dysfunction is a risk factor for death in the early and late hazard phases.

Age at Operation

Historically, age at operation has not been identified as an incremental risk factor for death during the first 30 days after operation (Table 13-1). However, more patients are now being operated on in their eighth and ninth decades of life, so older age is probably a risk factor for early postoperative death in the current era. It clearly is a risk factor for death late postoperatively, especially for patients older than 70 years at the time of operation (Fig. 13-3). Gillinov and colleagues demonstrated a 20% survival advantage for patients having operation at age 50 versus those having operation at age 65.

Left Ventricular Enlargement

Greater LV enlargement is a powerful risk factor for death late postoperatively. Because of the large volume overload, combined severe aortic and mitral regurgitation has a strong tendency to produce marked LV enlargement; the outcome after operation for patients with severe LV enlargement and this combination of valve lesions is particularly poor, with 5-, 10-, and 20-year survival of 64%, 37%, and 9%, respectively (Fig. 13-5).
Valve Pathology

Imperfect outcome after double valve replacement is well illustrated by survival of patients with the most favorable valve pathology—namely, important stenosis at one or both valves with only grade 2 LV enlargement (see Fig. 13-5). The combination of severe mitral regurgitation and severe aortic regurgitation has mildly increased the risk of death early after operation (see Fig. 13-5). Mueller and colleagues also found that aortic valve stenosis is a risk factor in the early hazard phase.

Patients having multiple valve operations for rheumatic valvar heart disease have greater survival benefit than those having operations for nonrheumatic disease. John and colleagues reported survival of 85% at 15 years and 82% at 24 years in patients with a mean age of 33 years having aortic and mitral valve replacement for rheumatic valve disease. Mueller and colleagues reported survival of 56% at 15 years and a linearized death rate of 2.3% per patient-year in a group of older patients (mean age 56 years) in whom 55% underwent operation for rheumatic disease. Gillinov and colleagues also reported that patients with rheumatic disease had greater predicted survival benefit than patients with nonrheumatic disease and that repair of the mitral valve further improved survival (Fig. 13-5). Nonrheumatic disease reduced survival in even the lowest-risk patients, and age at operation further reduced the chance of surviving for 16 years after aortic valve replacement and mitral valve repair or replacement (see Fig. 13-3, B).

Cardiac Comorbidity

Early mortality is increased by the presence of important tricuspid regurgitation, necessitating associated annuloplasty or, particularly, valve replacement, although this is not evident in all analyses. It is also increased by presence of ischemic heart disease requiring concomitant CABG, especially left main coronary artery stenosis. Pulmonary vascular resistance that is elevated before operation affects late survival. Mueller and colleagues also found that pulmonary systolic pressure of 60 mmHg or more is a risk factor for early death. Atrial fibrillation is a risk factor for death in the late
Noncardiac Comorbidity
Renal disease increases risk of death in the late hazard phase, and elevated blood urea nitrogen adds risk in the early phase after operation. Dialysis at the time of operation increases early relative risk ninefold. Diabetes mellitus also increases risk. Hepatic failure increased early risk of operation from 9.2% to 26% in the New York State series.

Functional Status
Most surviving patients are considerably improved by double valve replacement. However, by 10 years after operation, only 51% are in NYHA functional class I, and 34% are in class II (Fig. 13-7). The proportion of surviving patients who are in NYHA functional class I gradually declines as follow-up becomes longer, reaching only 35% by 20 years. Because only 47% of patients undergoing aortic and mitral valve replacement with or without concomitant procedures are alive 10 years after operation (see Fig. 13-1), only one fourth of patients operated on are alive and in NYHA functional class I 10 years after operation; at 20 years after operation, the percentage is only 8%. John and colleagues reported 72% in functional class I, 25% in class II, and 31% in class III at median 8.5 years of follow-up after aortic and mitral valve replacement for rheumatic disease. As noted earlier, this patient group was also young (mean age 33 years).

Freedom from Thromboembolism
Freedom from thromboembolism after primary combined aortic and mitral valve replacement (Fig. 13-8) is similar to that after isolated mitral valve replacement. The use of bioprostheses in both positions has not eliminated late postoperative thromboembolic episodes. Mueller and colleagues found similar results in a group of patients in which 82% had double valve replacement with bileaflet mechanical valves. Freedom from thromboembolism was 89% at 5 years, 74% at 10 years, and 66% at 15 years. Mitral valve repair did not reduce the risk compared with double valve replacement.

Just as after isolated mitral valve replacement or mitral commissurotomy, risk of a subsequent thromboembolic event is increased by more postoperative thromboembolic events (see Fig. 13-8) as well as those occurring prior to operation.

Complications of Anticoagulant Therapy
Prevalence of hemorrhage related to anticoagulant therapy is no different after double valve replacement than after single valve replacement (see “Complications of Long-Term Anticoagulation” under Mitral Valve Replacement in Section I of Chapter 11). In patients in whom mechanical prostheses were used (bileaflet in 82%), freedom from bleeding events was
89% at 5 years, 81% at 10 years, and 73% at 15 years. Linearized rates of valve-related thromboembolism and bleeding with bileaflet prostheses are listed in Table 13-2.

Hemolysis and Valve Thrombosis
With two mechanical prostheses, hemolysis and valve thrombosis are greater than with one. Both complications are rare.

Reoperation
As has been the experience with reoperations after valve replacement in general, the risk of yet another reoperation becomes greater after each (Fig. 13-9).

Need to reoperate is usually determined by the durability of the repair or replacement device applied in the mitral position (Fig. 13-10). Reoperation is done least frequently when mechanical prostheses are used. More than 90% of patients are free of reoperation at 15 years when a mechanical valve is used to replace the mitral valve in double valve operations; in contrast, that figure drops to 25% when a stented bioprosthesis is used.

The choice of replacement or repair of the mitral valve affects the procedure chosen for the aortic position. Patients requiring anticoagulant therapy for atrial fibrillation or recurrent deep vein thrombosis, for example, derive greatest benefit from the durability of mechanical prostheses. Extensive calcification of the mitral valve is usually best treated by mitral valve replacement. Severe mitral stenosis with thickening of the valve and subvalvar apparatus is usually treated by mitral valve replacement.

### Table 13-2  Linearized Rate of Thromboembolism and Bleeding after Double Valve Replacement with Bileaflet Prostheses

<table>
<thead>
<tr>
<th>Author and Year</th>
<th>Valve Type</th>
<th>Number of Patients</th>
<th>Embolism (% Patient-Year$^{-1}$)</th>
<th>Bleeding (% Patient-Year$^{-1}$)</th>
</tr>
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<tbody>
<tr>
<td>Kinsley et al., 1986$^{2}$</td>
<td>SJM</td>
<td>126</td>
<td>1.7</td>
<td>—</td>
</tr>
<tr>
<td>Armenti et al., 1987$^{a2}$</td>
<td>SJM</td>
<td>92</td>
<td>4.6</td>
<td>1.2</td>
</tr>
<tr>
<td>Burckhardt et al., 1988$^{b2}$</td>
<td>SJM</td>
<td>81</td>
<td>1.1</td>
<td>—</td>
</tr>
<tr>
<td>Arom et al., 1988$^{c}$</td>
<td>SJM</td>
<td>100</td>
<td>1.3</td>
<td>0</td>
</tr>
<tr>
<td>Czer et al., 1990$^{c}$</td>
<td>SJM</td>
<td>74</td>
<td>2.0</td>
<td>3.1</td>
</tr>
<tr>
<td>Smith et al., 1993$^{c1}$</td>
<td>SJM</td>
<td>64</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>de Luca et al., 1993$^{d1}$</td>
<td>CM</td>
<td>76</td>
<td>0.3</td>
<td>0.6</td>
</tr>
<tr>
<td>Nakano et al., 1994$^{c1}$</td>
<td>SJM</td>
<td>223</td>
<td>0.8</td>
<td>0.1</td>
</tr>
<tr>
<td>Ibrahim et al., 1994$^{c1}$</td>
<td>SJM</td>
<td>70</td>
<td>5.0</td>
<td>2.1</td>
</tr>
<tr>
<td>Baudet et al., 1995$^{c1}$</td>
<td>SJM</td>
<td>132</td>
<td>1.6</td>
<td>1.0</td>
</tr>
<tr>
<td>Copeland, 1995$^{c4}$</td>
<td>CM</td>
<td>144</td>
<td>3.1</td>
<td>1.2</td>
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<tr>
<td>Mueller et al., 1998$^{c4}$</td>
<td>SJM, CM, ATS</td>
<td>163</td>
<td>2.6</td>
<td>2.6</td>
</tr>
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Range 0.3-5.0
Median 1.6
Interquartile range 1.1-2.6

Key: ATS, Advancing the standard; CM, CarboMedics; SJM, St. Jude Medical.
Repair of both the mitral and aortic valves can be accomplished with acceptable early and late mortality and valve-related morbidity. Unfortunately, the durability of both mitral and aortic valve repairs is limited. Freedom from reoperation for valve dysfunction was 94%, 82%, and 65% at 1, 5, and 10 years, respectively. However, results of repair of rheumatic-type mitral valves decrease between 10 and 15 years.

### INDICATIONS FOR OPERATION

Remarkably few data exist to objectively guide management of multiple valve disease. Each case must be considered individually, and management must be based on hemodynamics and ventricular function as well as on the probable benefit of medical vs. surgical intervention. The most logical approach is to operate when valvar disease produces more than mild symptoms, or, in the case of dominant aortic valve stenosis, when patients have only mild symptoms. In regurgitant dominant lesions, surgery can be delayed until symptoms of LV dysfunction develop in asymptomatic patients. Use of vasodilators to delay surgery in mixed valve disease is untested.

Aortic and mitral valve operation is required when the patient’s symptoms are important (NYHA functional class III or greater) despite an appropriate and intensive medical regimen. Such an approach—more conservative than that with isolated mitral or aortic valve replacement—is indicated by the higher early and late risks of double valve replacement and the probably increased late morbidity when there are two rather than one artificial devices in situ. Despite these early and late risks, outcome after double valve replacement is surely superior to what can be accomplished with nonsurgical means. Because of the markedly increased risks with advanced heart disease, it is unwise to insist on severe limitation (NYHA class IV) before recommending double or triple valve surgery.

It is particularly unwise to keep deferring operation until it suddenly becomes necessary to perform an emergency operation on a class V patient, because then the early and late risks become high.

Exceptions to these general indications are cases of combined aortic and mitral regurgitation. These patients are advised to undergo operation when LV enlargement is grade 2 or higher (based on grades 1 to 6), even though symptoms are absent or mild. Otherwise, there is a strong tendency to develop extreme LV enlargement before symptoms become important, considerably lowering long-term survival and increasing the probability of developing ventricular arrhythmias and sudden death.

Patients with active rheumatic carditis, severe aortic and mitral regurgitation, and critical heart failure must be operated on when it is clear that the acute episode is not subsiding. Patients with severe aortic and mitral regurgitation and active bacterial endocarditis in whom neither infection nor heart failure can be controlled medically must also undergo operation without delay (see Chapter 15).

### SPECIAL SITUATIONS AND CONTROVERSIES

**Multiple Valve Replacement Through Small Incisions**

It has become possible to perform almost all cardiac valve operations through incisions smaller than standard median sternotomy. Experience and familiarity with smaller incisions have shown that exposure of cardiac valves is not compromised, and even though the smaller incision provides more confined dimensions within which the surgeon must work, results have been equivalent. The frequency with which the minimally invasive approach to cardiac valves is used has increased, but it is still a small fraction of the total.

A lower half partial sternotomy approach may be considered for any cardiac valve operation. This approach allows the minimally invasive operation not only in isolated single valve replacement but also in complex cardiac valve operations. The incision is centered over the location of the cardiac valves. Cadaveric dissections performed by Reardon and colleagues affirm the lower half sternotomy exposure. They found the pulmonary valve behind the third left costal cartilage, the aortic valve behind the sternum opposite the third intercostal space, and the mitral and tricuspid valves related to the fourth costal cartilage and fourth interspace.

Operations on the aortic valve are facilitated by dividing the ascending aorta above the sinutubular junction. The aortic root may then be positioned for direct visualization, allowing precise examination. The mitral valve approach through standard left atriotomy posterior to the intraatrial groove on the right side is comfortable and familiar to the surgeon. When aortic and mitral valve operations are combined, the mitral valve is easily accessible through the superior aspect of the left atrium, especially with the aorta divided and aortic root retracted inferiorly. A transatrial septal approach is used (1) when the mitral valve is repaired or replaced in conjunction with operations on the tricuspid valve, or (2) for triple valve operations.

Complex operations are easier when the transverse section of the sternum is through the second intercostal space. The longer the sternal incision, the less the incision qualifies as minimally invasive. Nevertheless, it is unwise to compromise exposure or needlessly confine the incision to the point that

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**Figure 13-10** Freedom from reoperation after mitral valve repair or replacement in combined aortic and mitral valve operations. Filled circles represent reoperation after replacement of the mitral valve with a mechanical prosthesis; triangles represent mitral valve replacement with a bioprosthesis; squares represent mitral valve repair in nonrheumatic etiologies; and circles represent mitral valve repair in rheumatic valve etiology. Parametric estimates are represented by solid lines; their confidence limits are suppressed for clarity. (From Gillinov and colleagues.)

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the operation becomes tedious and prolonged. When either the third or second interspace is used, the entire manubrium remains intact, along with the clavicular attachment. This should be of substantial benefit to the patient in terms of chest wall stability after operation and should eliminate the possibility of dehiscence of the sternal repair at the manubrium.

Small-diameter cannulae as used in vacuum-assisted venous return considerably aid placement of aortic and venous cannulae through the primary incision. Vacuum-assisted venous return has also been helpful in providing more reserve and safety in the venous drainage system to the reservoir of the oxygenator (see “Vacuum-Assisted Venous Return” in Chapter 2). The right heart remains empty and collapsed more consistently than with gravity drainage, and air entrainment with air lock, frequently seen with gravity drainage, is eliminated. This and other advances in cardiopulmonary technology have made operating through a small incision easier, and the technology is transferable to full sternotomy operations.

Dotty and colleagues studied the partial sternotomy (lower half) approach in 16 patients undergoing double valve operations.\textsuperscript{12} One patient died (6.3%). Triple valve operations were performed in five patients, none of whom died. They concluded that this approach provides a smaller, less invasive incision through which essentially all cardiac valve operations may be performed. It provides standard exposure to the cardiac valves, and standard instruments and retraction devices are employed. Maintaining the integrity of the manubrium and upper sternum should be beneficial for patient mobilization and rehabilitation after operation, and the smaller incision is appreciated by patients of all ages. Atik and colleagues studied hospital outcomes of 114 patients undergoing less invasive (upper sternotomy) combined valve surgery compared with 381 patients undergoing full sternotomy combined valve operations during 1995 through 2003.\textsuperscript{14} Among propensity-matched patients, mediastinal drainage was less and early pulmonary function better after less invasive surgery, but otherwise, complications, mortality, pain scores, and length of hospital stay were similar.

### 13A Survival and Related Matters

This appendix discusses survival and related matters in patients undergoing simultaneous combined aortic and mitral valve replacement, with or without concomitant cardiac procedures, and excluding only those patients with a previous aortic or mitral valve replacement operation (UAB group, 1967-1981, \( n = 569 \)). Follow-up extended to 22 years.

#### Parameter Estimates

Shaping parameter estimates, the risk factors retained in the analysis, their coefficients, standard deviations, and (in parentheses) \( P \) values were as follows:

**Early phase:** \( \delta = 0, \eta = 7.989, \nu = 1, m = -2.519, \) intercept 7.134, body surface area 0.9023 ± 0.41 \( (P = .03) \), preoperative NYHA functional class 0.8177 ± 0.139 \( (P < .0001) \), aortic and mitral regurgitation 0.6092 ± 0.21 \( (P = .004) \), use of cardioplegia −1.054 ± 0.28 \( (P = .0002) \), global myocardial ischemic time (using cardioplegia) 0.02138 ± 0.0080 \( (P = .007) \), surgeon \( X \) 0.9934 ± 0.46 \( (P = .03) \)

**Late phase:** \( \tau = 1, \gamma = 1, \alpha = 1, \eta = 1.458, \) intercept −10.64, age at operation 0.02698 ± 0.0060 \( (P < .0001) \), African-American 0.7758 ± 0.20 \( (P = .0001) \), preoperative NYHA functional class 0.2528 ± 0.124 \( (P = .04) \), pulmonary resistance index 0.04011 ± 0.020 \( (P = .05) \), left ventricular (LV) enlargement grade 0.2654 ± 0.072 \( (P = .0002) \), concomitant coronary artery bypass grafting (CABG) 0.7388 ± 0.26 \( (P = .005) \), Bjork-Shiley prostheses used in aortic and mitral position −0.6490 ± 0.156 \( (P < .0001) \)

#### Specific Solutions of the Multivariable Equation

**Figure 13-4:** Age was entered as 65 years, African-American 15\%, body surface area as 1.7 \( \text{m}^2 \), pulmonary vascular resistance as 4.3 units · \( \text{m}^2 \), important aortic and mitral regurgitation = no, LV enlargement grade 3, CABG = no, and global myocardial ischemic time as 80 minutes, with cardioplegia.

**Figure 13-5:** The entries were similar, and NYHA was entered as class III.
13B

**Ordinal Logistic Equation for NYHA Functional Class**

The NYHA functional class on the date of latest follow-up (November-December 1988) in living patients was analyzed using the ordinal logistic model for an ordered categorical response variable. The intercepts and regression coefficient, its standard deviation, and $P$ value are as follows: intercept 1, $-0.7283$; intercept 2, $-2.417$; intercept 3, $-4.389$; interval (months) from operation to last follow-up $0.005665 \pm 0.0030$ ($P = 0.06$).

**REFERENCES**

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DEFINITION

This chapter discusses regurgitation and stenosis of the tricuspid valve in those uncommon situations in which it occurs as an isolated lesion, as well as tricuspid valve disease associated with mitral or combined mitral and aortic valve disease. Mitral valve surgery with coexisting tricuspid valve disease is also discussed in Chapter 11.

Tricuspid valve abnormalities or disease may be associated with various conditions discussed in other chapters, including atrioventricular septal defect (Chapter 34), ventricular septal defect with straddling tricuspid valve (Chapter 35), pulmonary atresia and intact ventricular septum (Chapter 40), Ebstein anomaly (Chapter 42), and right atrial myxoma (Chapter 18). Rarely, isolated tricuspid valve disease is secondary to chronic cor pulmonale, inferior myocardial infarction, administration of methysergide, scleroderma, lupus erythematosus, primary phospholipid syndrome, and hypercosinophilic syndrome.

MORPHOLOGY

Functional (Secondary) Tricuspid Regurgitation

The multitude of chordal attachments of the tricuspid valve, described in Chapter 1, may impair proper leaflet coaptation and promote tricuspid regurgitation (TR) in the presence of right ventricular (RV) dysfunction and dilatation. The tricuspid anulus shortens during systole when the tricuspid valve is competent. When right ventricular (RV) dilatation develops, usually as a consequence of important disease of the left-sided heart valves in association with pulmonary arterial hypertension, the tricuspid anulus also dilates (lengthens) and fails to shorten during systole. The leaflets and chordae remain normal in appearance.
Experimental work by Tsakiris and colleagues has shown that perfect systolic tricuspid leaflet closure depends on proper systolic shortening in the circumference of the tricuspid anulus. In support of this finding, Simon and colleagues have demonstrated a considerable increase in systolic shortening postoperatively in patients whose TR lessens after mitral valve surgery and no change in those in whom it persists or worsens. An increased diastolic diameter of the tricuspid anulus results in TR; diastolic diameter is increased by pulmonary artery hypertension, RV myocardial failure, and increased diastolic volume secondary to left-sided heart pathology.

The pathogenesis of functional TR in mitral valve disease is summarized in Fig. 14-3. The final common pathway is RV dysfunction and dilatation and tricuspid anular dilation. The process becomes self-propagating, because worsening TR exacerbates RV volume overload with further RV dysfunction and enlargement. In addition, because of ventricular interdependence, worsening RV dysfunction increases interventricular shift toward the left, causing restricted left ventricular filling, further elevation of left atrial pressure, pulmonary hypertension, and greater RV afterload, which further affects the RV.

It is these mechanisms that may produce TR late after isolated mitral valve operations or after combined aortic and mitral valve operations (see Chapters 11 and 13).

**Rheumatic Tricuspid Stenosis and Regurgitation**

Rheumatic tricuspid valve disease occurs in association with rheumatic involvement of the mitral valve, the mitral and aortic valves combined, or rarely, the aortic valve alone. It is not seen as an isolated lesion.

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Rheumatic tricuspid disease usually results in a regurgitant valve with variable amounts of stenosis, but in rare cases there

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**Figure 14-1** Dilatation of the tricuspid valve anulus, indicated by a sequence of overlaid annulae. Tricuspid anular dilatation due to increased right ventricular and pulmonary artery pressures secondary to left-sided heart valve disease occurs predominantly in the septal-lateral direction, as indicated by arrows.

**Figure 14-2** Correlation between tricuspid anulus diameter (TAD) and tricuspid regurgitant volume ($V_{TR}$) in patients with valvar heart disease (open circles) and those with atrial septal defect (closed circles). Correlation with the former is .87 and with the latter, .88. Correlation lines cross the horizontal axis at a tricuspid anulus diameter of 33 to 34 mm, which is the threshold for tricuspid regurgitation in adult patients. Key: ASD, Atrial septal defect; VHD, valvar heart disease.

**Figure 14-3** Pathogenesis of tricuspid regurgitation in mitral valve disease. Key: DCM, Dilated cardiomyopathy; MR, mitral regurgitation; MS, mitral stenosis; RHD, rheumatic heart disease; RV, right ventricle; TV, tricuspid valve. (Redrawn from Shiran and Sagie.)
may be pure stenosis. In tricuspid stenosis, the orifice is larger than in mitral stenosis, even when hemodynamically there is severe obstruction. Therefore, the hemodynamic effects of anatomically moderate tricuspid stenosis are the equivalent of tight mitral stenosis. A mean diastolic gradient of even 4 to 5 mmHg across the tricuspid valve indicates important stenosis. Borders of the stenotic tricuspid orifice are usually fibrous and thickened, although peripheral portions of the leaflets remain thin.

The hallmark of organic tricuspid stenosis is commissural fusion. All commissures are usually equally fused, but occasionally fusion is limited to the anteroseptal commissure. Chordal thickening and fusion are usually mild, and calcification is usually absent.

Tricuspid Valve Endocarditis

Acute tricuspid valve endocarditis is rare and usually associated with habitual intravenous self-administration of drugs. The most common etiologic organism is Pseudomonas aeruginosa, followed by Staphylococcus aureus. A variety of gram-negative bacilli may be involved. Rarely, Candida albicans is the infective organism. The organisms may form masses on the valve leaflets, or simply erode and destroy large portions of leaflets and chordae (see Chapter 15).

Traumatic Injury of Tricuspid Valve

TR is an uncommon result of severe, nonpenetrating chest injury, and in this setting is due to rupture of one or more papillary muscles or chordae (see “Atrioventricular Valve Rupture” in Section II of Chapter 17). Usually it is the anterior tricuspid leaflet that becomes failed. Rarely, the ventricular septum may rupture. Occasionally a transvenous ventricular pacing lead is associated with important TR. This may be due to perforation, laceration, or scarring. Apical electric activation may also contribute. Rarely, pacemaker leads can cause tricuspid stenosis secondary to leaflet scarring and adhesions. Similar scarring of the septal and posterior leaflets following cryothermic or radiofrequency ablative procedures rarely can produce severe tricuspid regurgitation. Following cardiac transplantation, many years of repeated transvenous endomyocardial biopsies may induce severe TR secondary to inadvertent severing of chordae during biopsy.

Carcinoid Tricuspid Valve Disease

Carcinoid tumors originate from Kulchitsky cells in the gastrointestinal tract, which produce serotonin (5-hydroxytryptamine), a substance inactivated in the liver. However, carcinoid tumors that metastasize to the liver produce serotonin there, and this powerful substance passes into the pulmonary and, to a lesser extent, systemic circulation (because a good deal of it is inactivated in the lungs). Thereby, the carcinoid syndrome may be produced, with a good deal of it inactivated in the lungs. Thereby, the carcinoid syndrome may be produced, with a good deal of it inactivated in the lungs.

The chest radiograph shows right atrial enlargement, and the electrocardiogram shows a prominent P wave, followed by a sharp, deep y descent. The murmur maximal over the lower left sternal edge, which increases on inspiration; there may be a tricuspid opening snap. The jugular venous pulse shows a dominant a wave, followed by a sharp, deep y descent. The murmur, maximal over the lower left sternal edge, which increases on inspiration; there may be a tricuspid opening snap. The jugular venous pulse shows a dominant a wave, followed by a sharp, deep y descent. The murmur, maximal over the lower left sternal edge, which increases on inspiration; there may be a tricuspid opening snap.

Other signs include a mid-diastolic, often high-pitched murmur maximal over the lower left sternal edge, which increases on inspiration; there may be a tricuspid opening snap. The murmur can be confused with an aortic early diastolic murmur (because its timing may be relatively early) or with a mitral diastolic murmur. The liver is enlarged but not pulsatile (unless from forceful atrial contraction that produces a presystolic pulse).

The chest radiograph shows right atrial enlargement, and the electrocardiogram shows a prominent P wave unless atrial fibrillation is present. Two-dimensional (2D) echocardiography is helpful in establishing the presence of leaflet thickening. Cardiac catheterization with simultaneous measurement of right atrial and RV pressures identifies a diastolic gradient (>4 mm) across the valve.

Tricuspid Regurgitation

History and physical signs are sufficient to suggest diagnosis of important TR. The jugular venous pulse shows a dominant fused e and v wave, followed by a sharp, deep y descent. The murmur, maximal over the lower left sternal edge, is pansystolic, is often high pitched, and increases on inspiration. The enlarged liver shows systolic pulsation. However, when TR is severe, such as after excision of the tricuspid valve, a murmur may be absent. In advanced cases, there are other signs of right heart failure, including peripheral edema and ascites. Mitral or aortic valve disease signs can dominate the findings, and severe right heart failure may occur under such conditions without TR.

The symptomatic state of severe TR is generally manifested by progressive fatigue and weakness, related to reduction in cardiac output and the unpleasant sensation of ascites, congestive hepatosplenomegaly, and peripheral edema. The symptomatic state of right heart failure and volume overload can be palliated with aggressive diuretic therapy, but in the chronic stages, symptoms become refractory. In late stages, cachexia and jaundice may complicate the clinical complex.
Quantification of the degree of TR is important when surgical treatment of valvar heart disease is being considered, but preoperative assessment is often difficult because of the confounding effect of severe cardiac failure. In this regard, 2D echocardiography is particularly useful, because presence of the cardiac catheter across the tricuspid valve interferes with angiographic assessment. Both contrast and Doppler echocardiography have been useful, but the increasing precision of color flow mapping and Doppler color flow map-guided interrogation have made them the favored methods for estimating tricuspid regurgitant flow.\(^4\) The vena contracta, as determined by color flow Doppler, indirectly reflects effective regurgitant orifice area, which if greater than 0.7 cm indicates severe TR.\(^8\) Quantitative assessment of TR can also be accomplished with the proximal isovelocity surface area (PISA) method.\(^4\) Dilatation of the inferior vena cava and flow reversal in the inferior vena cava and hepatic veins provide supporting evidence. Echocardiography can also detect paradoxical ventricular septal motion and shift of the atrial septum toward the left atrium in isolated TR. Maximum circumference of the tricuspid anulus is larger in patients with TR than in normal adults (14 ± 0.7 cm and 11.9 ± 0.9 cm, respectively), and its reduction during systole is less (10% ± 2% vs. 19% ± 4%).\(^6\)\(^,\)\(^7\)

Despite these refinements in diagnosis, the presence and severity of TR need to be assessed in the operating room. The patient’s hemodynamic state must be optimized by the anesthesiologist for any form of assessment to have validity. The surgeon’s finger, inserted through the right atrial appendage, can appreciate a TR jet. Severe TR correlates reasonably well with a jet of greater intensity, greater width, and increased propagation from the valve orifice. If TR is severe, however, there may not be a jet with sufficient velocity to be identified in this manner.\(^3\) In the current era, rigorous assessment of TR and tricuspid anular circumference by transeosophageal echocardiography in the operating room has largely supplanted finger palpation.\(^6\)\(^,\)\(^13\),\(^3\)

In the special setting of tricuspid valve endocarditis in drug addicts, the valve is usually rapidly destroyed, and classic signs and symptoms of severe TR develop. The illness is usually only 1 to 3 weeks in duration before the patient presents for medical care. Frequently, pulmonary symptoms and signs secondary to septic pulmonary emboli are marked.\(^8\)\(^,\)\(^2\) The diagnosis can be strongly suspected from a history of drug abuse, evidence of pulmonary infection, elevated jugular venous pressure, pulsatile neck veins, and pulsatile liver. These features, combined with positive blood cultures (in samples withdrawn from the RV or pulmonary artery) and echocardiography, are usually sufficient to establish the diagnosis.\(^1\)^\(^4\)

Diagnosis of traumatic TR is usually easily established by signs of severe TR and a history of a blow to the chest (see Chapter 17). Occasionally, however, the relationship of these signs to a history of injury is not obvious. In patients with traumatic TR, right-to-left shunting may occur across a patent foramen ovale, which can lead to the mistaken diagnosis of Ebstein anomaly.

**NATURAL HISTORY**

The natural history of patients with dominantly stenotic tricuspid valve disease is usually determined primarily by the associated rheumatic mitral or aortic valve disease. No doubt, however, the increased systemic venous pressure, hepatomegaly, and peripheral edema accelerate deterioration of patients with rheumatic tricuspid stenosis.

Primary TR has an inherent tendency to progress, just as do other types of valvar regurgitation. However, the deleterious effects of ventricular volume overload on the right side of the heart are slower to develop than on the left. For example, in patients with traumatic TR who survive the initial trauma, regurgitation may be well tolerated for many months or years.\(^5\)\(^,\)\(^3\)\(^2\) Ultimately, however, symptoms develop as regurgitation increases; by 5 to 10 years after trauma, they are usually severe and incapacitating. In patients with acute tricuspid endocarditis caused by *S. aureus*, tricuspid vegetations greater than 1 cm in diameter (visualized by 2D echocardiography) worsen the natural history of TR.\(^5\) In a study of 60 patients with severe TR secondary to trauma, myxomatous change, or endocarditis, those who did not undergo operation had an increased risk of heart failure, atrial fibrillation, and death (Fig. 14-4). Functional (secondary) TR of severe degree is present in about 30% of patients with severe mitral regurgitation. If not surgically treated, the TR tends to progress, even after adequate treatment of the left-sided valvar lesion.\(^7\) The tendency for progression of TR related to anular size and other risk factors is also discussed in Chapter 11.

There is now increasing awareness of the potential deleterious effects of even moderate TR if left uncorrected at the first operation for mitral valve disease, especially if the tricuspid anulus is dilated. King and colleagues reported that 66% of patients returning for tricuspid valve procedures late after mitral valve replacement had only mild TR at the time of the initial valve operation.\(^3\)\(^7\) In this regard, preoperative echocardiography at initial operation is advisable to detect not only morphology and severity of TR, but also tricuspid anular size. Once the anulus dilates, its diameter does not spontaneously normalize. Typically, tricuspid anular dilatation is a progressive process that eventually leads to severe TR. The importance of a dilated tricuspid anulus in the genesis of severe TR is underscored by the study of Dreyfus and colleagues; they reported a dramatic reduction in late progression of TR by routinely performing tricuspid anuloplasty during surgery for...
left-sided valve lesions if the tricuspid anulus was greater than twice normal size. Thus, preoperative tricuspid anular dilatation is a predictor of late TR. Among patients with heart failure, approximately one third have moderate or severe TR, which is a predictor of reduced long-term survival (hazard ratio 1.3), and even more so when pulmonary hypertension is present.

### TECHNIQUE OF OPERATION

**Tricuspid Valve Anuloplasty**

**Anuloplasty Ring Technique**

Because isolated tricuspid valve disease is rare, the technique of operation is given for TR accompanying left-sided valve disease. When evaluation before cardiopulmonary bypass (CPB) indicates important TR, two venous cannulae are used. The tricuspid procedure may be performed in the beating, perfused heart during rewarming of the patient, with suction on the aortic vent needle after the left heart has been carefully de­aired, or during continuing antegrade/retrograde cold cardioplegia with addition of external cardiac cooling.

After the mitral procedure is completed, the right atrium is opened with the usual oblique incision (Fig. 14-5). When an anuloplasty is performed using a ring, length of the base of the tricuspid septal leaflet is measured with calipers, or area of the anterior leaflet with a sizer, and on this basis the proper­sized ring is selected. The Carpentier-Edwards anuloplasty ring, for example, is a modified oval corresponding to configuration of the tricuspid anulus, with a gap in the portion designed to overlie the atrioventricular (AV) node so that the conduction tissue is not compromised. It is unwise to select too small a ring in the belief that it will be more effective, because it distorts and narrows the orifice and may subsequently detach. Because tissues around the tricuspid valve are usually tenuous, sutures must take adequate bites, beginning in the atrial wall and passing into the deeper part of the anulus itself, carefully avoiding leaflet tissue. The surgeon must also be cognizant of the location and course of the right coronary artery, as its inadvertent suture ligation has been reported.

After discontinuing CPB and before decannulation, competence of the valve is assessed by 2D echocardiography, using either a handheld or esophageal probe. Presence of moderate or severe TR is an indication for valve replacement or repair. If the heart is beating and normothermic, a reasonable assessment of competence of the repair is possible as soon as it is completed. With the atrium still open, the RV is allowed to fill with blood, and the tricuspid leaflet apposition is assessed. If apposition is obviously inadequate, the valve is replaced or repaired. If it appears adequate, the right atrium is closed, air is aspirated from the RV and pulmonary artery, and the operation is completed in the usual manner (see “Completing Operation” in Section III of Chapter 2).

**Figure 14-5** Tricuspid ring anuloplasty. A, Exposure is through the usual oblique right atriotomy. Venous cannulae are inserted directly into superior and inferior venae cavae (for alternatives, see Chapter 2). B, Stay sutures provide excellent exposure (alternatively, a Cooley retractor may be used). The surgeon identifies anteroseptal tricuspid valve commissure, membranous part of atrioventricular septum, and coronary sinus orifice and can then mentally visualize location of the atrioventricular (AV) node and penetrating portion of the bundle of His. Using appropriate sizers, notched at points corresponding to the anteroseptal and posteroseptal commissures at both ends of the septal tricuspid leaflet, a proper­sized tricuspid anuloplasty ring is selected.
Chapter 14 Tricuspid Valve Disease

Figure 14-5, cont’d  C. The first stitch, of No. 2-0 or 3-0 polyester, is positioned exactly at the midpoint of the septal leaflet anulus, and only two further mattress stitches are needed for the septal portion of the ring. Small pledgets may be used on these mattress sutures. These and all other sutures are passed first through host tissue and then through the cloth of the undersurface of the ring, just as in suturing the ring for mitral anuloplasty (see Chapter 11). D, Five or six mattress stitches are needed in the portion of the anulus to be plicated, which is adjacent to the posterior leaflet, and these are passed through the cloth of the ring close together (marking stitches are present on the ring cloth to guide the surgeon). The remainder of the ring, corresponding to about half its circumference, is attached to the anulus at the base of the anterior cusp with, at most, four fairly widely spaced mattress sutures. The ring is lowered into position along the sutures and the sutures tied, with great care taken not to pull upward strongly on them, lest they tear out. In some cases the anuloplasty ring can be secured in place with three or four interrupted mattress sutures along the septal leaflet and then with continuous sutures for the remainder.

Bicuspidization Technique

An alternative technique is to shorten the circumference of the tricuspid anulus by simply excluding that part to which the posterior leaflet is attached. To accomplish this, a No. 2-0 or 3-0 polyester suture is passed through the anulus at the anteroposterior commissure, then at the center of the posterior leaflet, and then through the anulus at the posteroseptal commissure. The suture is tied snugly, and a second one is placed for reinforcement. Pledgeted mattress sutures also may be used. A further modification that incorporates a flexible strip into the posterior leaflet anuloplasty has been reported to be useful. The repaired tricuspid valve should have about a normal diameter (see “Dimensions of Normal Cardiac and Great Artery Pathways” in Chapter 1.)

De Vega Technique

The De Vega technique is used in patients with no more than moderate TR from anular dilatation, where it is anticipated that good long-term function is not dependent on integrity of the repair. This technique has the advantages of simplicity and low cost. A No. 2-0 polyester suture (not monofilament polypropylene) is passed in a counterclockwise direction as a circular stitch deeply into the junction of the anulus and right ventricular wall from 1 or 2 cm medial to the anteroseptal commissure to the base of the anterior leaflet 2 to 4 cm medial to the anteroseptal commissure (Fig. 14-6). The same suture is then reversed and passed in clockwise direction slightly peripherally to the first stitch back to the starting point. Separate pledgets of polyester felt are incorporated in the suture at each end to prevent its pulling through the tissues. The suture is tightened until the orifice will admit an appropriate sizer (24 to 30 mm) and is then tied.

Other Supplemental Techniques

Many of the techniques of mitral valve reconstruction have been applied to repair of TR, particularly in the setting of congenital heart disease. Partial or complete closure of accessory commissures, implanting artificial chordae, Alfieri edge-to-edge technique, and pericardial leaflet augmentation have all been described.

Tricuspid Valve Replacement

When tricuspid valve replacement is elected, the leaflets are excised, and a 2- to 3-mm fringe of leaflet tissue is left on the anulus (Fig. 14-7). Alternatively, the septal leaflet may be left in situ. Interrupted pledgeted mattress sutures are placed in the fringe of leaflet tissue along the area occupied by the
septal leaflet, to avoid damaging the AV node and bundle of His. Either a continuous polypropylene suture or interrupted pledgeted mattress sutures may be used for the remainder of the insertion. Alternatively, simple interrupted sutures may be used throughout. Infrequently, to avoid heart block, the suture line for valve insertion can be placed on the atrial aspect above the coronary sinus and base of the septal defect.

Tricuspid Valve Excision

In drug addicts with active tricuspid valve endocarditis, the three leaflets and their chordae tendineae can simply be excised, using the general techniques described earlier. However, postoperative convalescence and late cardiac performance are compromised by the resulting severe TR. In addition, later valve replacement is more difficult.

Stern and colleagues suggest that primary bioprosthetic valve replacement is preferable to valve excision and is not followed by recurrent endocarditis unless intravenous drug abuse continues.

Partial Tricuspid Valve Replacement with Cryopreserved Tricuspid Valve Allograft

Partial replacement of the tricuspid valve with a cryopreserved allograft is an attractive option for severe TR caused by endocarditis, because allografts are known to demonstrate greater freedom from reinfection compared with xenografts or mechanical valves in the aortic position (see Chapter 15). Shrestha and colleagues from Brisbane, Australia, reported favorable outcomes in 13 patients (three late reoperations) using tricuspid valve allografts for tricuspid endocarditis.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Long-term anticoagulation is needed when a mechanical valve has been used or if there is an additional mechanical prosthesis in either the mitral or aortic position. Warfarin
Figure 14-7  Tricuspid valve replacement. A, Exposure is as for repair. All three leaflets of the tricuspid valve are excised, leaving a cuff at the base of the septal leaflet 5 to 8 mm wide. Alternatively, the septal leaflet may be left in situ. B, Starting at the midpoint of the septal leaflet cuff, interrupted horizontal mattress sutures buttressed with felt pledgets are placed first into remaining valve tissue and then through the sewing ring of the replacement device. C, After placing four to five interrupted mattress sutures, remainder of the insertion is completed using a continuous suture technique. Bites may be through the anulus, mindful that the right coronary artery lies deep to the anulus anteriorly. Alternatively, interrupted sutures can be used circumferentially. Key: AV, Atrioventricular.
administration is begun on the evening of postoperative day 1 (see “Special Features of Postoperative Care” in Chapter 11). If a bioprosthesis is used and has also been used for all other valves replaced, long-term anticoagulation is controversial.

Because of the risk of complete heart block in the latter part of the hospital stay, electrocardiographic monitoring should be continued until a stable rhythm is established at an adequate heart rate.

Fluid retention is prominent among patients with tricuspid valve disease. Characteristically, their postoperative care requires aggressive use of diuretic agents.

RESULTS
Tricuspid Valve Anuloplasty

Symptom Relief
Assessing the clinical benefit of tricuspid anuloplasty in the setting of concomitant mitral valve surgery is confounded by the favorable impact of relieving mitral valve stenosis or regurgitation. The symptomatic benefit can be more directly evaluated in patients undergoing isolated tricuspid valve surgery. In a study of 60 patients with flail tricuspid valve leaflets, symptomatic improvement occurred in 88% of those who underwent tricuspid valve repair or replacement.\(^{15}\)

Survival
Because tricuspid anuloplasty is rarely performed as an isolated procedure, its effect on early and late survival is difficult to assess directly. In patients with isolated TR from trauma or endocarditis, reported surgical mortality is low.\(^{15}\) In combined operations including tricuspid anuloplasty, early mortality can be similar to that of operations in which tricuspid anuloplasty was not required.\(^{15}\) However, end-organ damage from long-standing right heart failure increases the risk of operation. When right heart failure is severe enough to cause liver damage, the Model for End-Stage Liver Disease (MELD) score has been applied as a predictive model for operative mortality in combined procedures that include tricuspid anuloplasty.\(^{14}\) By multivariable analysis, a MELD score of 15 or greater was strongly predictive of increased mortality (hospital mortality of 19% with MELD score of \(\geq 15\) vs. 6% with score <15). Intermediate-term survival may be compromised by persistence of important RV dysfunction that often accompanies severe TR (see “Mitra Valve Surgery with Coexisting Tricuspid Valve Disease” in Chapter 11). An analysis by Singh and colleagues\(^{11,12}\) indicates that anuloplasty is an independent predictor of better 10-year survival compared with tricuspid valve replacement for organic disease.

Tricuspid Valve Competence
Anuloplasty of the tricuspid valve results in valvar competence in most patients. Freedom from moderate or severe recurrent TR in 98 patients receiving anuloplasty (mostly Carpentier rings) was 85% at 6 years.\(^{15}\) Carpentier and colleagues found that with use of the Carpentier ring, mild or less TR was present late postoperatively in more than 90% of patients with preoperative moderate or severe regurgitation.\(^{15}\) Long-term relief of TR by use of anuloplasty rings has been confirmed by postoperative 2D echocardiography with Doppler color flow mapping.\(^{13}\)

Kay and colleagues have also reported satisfactory results in a sizable group of patients after suture bicuspidization anuloplasty.\(^{14,15}\) Experience with the De Vega anuloplasty has also provided good results, confirmed in larger series by echocardiography.\(^{11,12,15}\)

However, there are established risk factors for persisting TR after repair. Recurrence is more likely when mitral disease progresses or severe pulmonary hypertension persists\(^{11}\) (see “Mitral Valve Surgery with Coexisting Tricuspid Valve Disease” in Chapter 11). Duran and colleagues found that when functional TR was repaired, 31 of 35 patients (89%; CL 80%-94%) with low late postoperative pulmonary vascular resistance (<6 units · m\(^{-2}\)) had no regurgitation, whereas this was true of only 6 of 14 patients (43%; CL 27%-60%) with high pulmonary vascular resistance \((P = .001).\(^{12}\)

Tethering of the tricuspid valve leaflets is a risk factor for early recurrent TR, and depressed right or left ventricular function predict later TR recurrence.\(^{12,13}\) Other factors increasing the risk of late TR recurrence include higher preoperative TR grade, depressed left ventricular function, and permanent pacing leads through the tricuspid valve. In a study of pacemaker leads remaining across the tricuspid valve following anuloplasty repair, 42% of patients had severe TR at 5 years, twice the prevalence of those without such leads.\(^{11,14}\) The relationship between anuloplasty technique and outcome is discussed in text that follows (see “Techniques of Operation, “Selection of Anuloplasty Technique and Choice of Device”).

Reoperation
Reoperation for tricuspid valve dysfunction is infrequent following Carpentier ring anuloplasty, with 97% of this group being free of reoperation 3 years postoperatively.\(^{15}\) Nakano and colleagues reported that after suture anuloplasty for important functional tricuspid regurgitation, 94% of patients were free of reoperation 10 years later, as were 70% 17 years later.\(^{15}\) Usually, redeveloped TR is associated with persisting or developed pulmonary hypertension. Because persisting severe TR appears to be a marker for underlying advanced myocardial and valvar heart disease, reoperations for recurrent TR are generally high-risk procedures, with hospital mortality of up to 35%.\(^{12}\)

Functional Status
Functional status as assessed by New York Heart Association (NYHA) functional class is usually improved by tricuspid anuloplasty.\(^{11}\)

Tricuspid Valve Replacement

Survival
Early mortality for tricuspid valve replacement with or without double or triple valve surgery is currently about 2% to 10%,\(^{13,20}\) less than in earlier years (see “Risk Factors for Premature Death after Tricuspid Valve Surgery” later in this chapter); however, mortality may exceed 25% in patients in NYHA class III or IV, those having repeat operations, or those with complex congenital heart disease.\(^{13}\) Of importance, a propensity analysis indicated no important differences in early and late survival among patients undergoing tricuspid valve repair versus replacement.\(^{11}\) Thus, the surgeon should not hesitate to consider valve replacement...
Mode of Premature Late Death
Following tricuspid valve surgery, most late deaths are related to advanced RV dysfunction or arrhythmias. Endocarditis and stroke are uncommon modes of death, as are recurrent moderate or severe tricuspid stenosis or regurgitation resulting from malfunction of the replacement devices or failed anuloplasty. Thus, among 284 patients followed over nearly 10 years (combined GLH-UAB), prevalence of these complications was similar after either tricuspid valve repair or replacement and accounted for 9 (11%; CL 8%-16%) of the late deaths, or 3.2% of the entire group (CL 2%-5%).

Complete Heart Block
Complete heart block occasionally develops late after tricuspid valve replacement, usually with associated mitral valve replacement. This association is undoubtedly related to the position of the AV node between the two replacement devices. In all, approximately 10% of patients undergoing both tricuspid and mitral valve replacement require insertion of a pacemaker late postoperatively because of heart block, and up to 10 years postoperatively the prevalence is 25%. Late heart block is rare among patients undergoing tricuspid valve replacement as an isolated procedure. Late development of complete heart block is also uncommon after tricuspid anuloplasty.

Thromboembolism
Pulmonary embolization is a rare complication of tricuspid valve surgery. Only 1 of 103 patients had probable large pulmonary emboli on follow-up (UAB), and the origin of that embolus was uncertain.

Thrombosis
After tricuspid valve replacement, thrombosis may occur, more often of mechanical devices than of bioprostheses. The older types of mechanical prostheses (Smelloff-Cutter, Bjork-Shiley) apparently had a greater risk than present bileaflet valves. The linearized thrombosis rate in Van Nooten’s series of 146 tricuspid replacements was approximately 1% per patient-year. In an Italian study of 43 patients undergoing tricuspid valve replacement with a variety of mechanical prostheses, actuarial freedom from valve thrombosis was greater than 80% at 10 years. Initial thrombolytic treatment using streptokinase may relieve obstruction in many cases. Hurrell and colleagues have reviewed the efficacy of thrombolytic therapy for all valve positions, and this approach seems particularly effective for prostheses in the tricuspid position (Table 14-1). Currently, thrombolysis is considered the first line of therapy for tricuspid valve thrombosis, in contrast to left-sided valve thrombosis, in which risk of systemic and cerebral emboli is increased.

Streptokinase is administered as in treatment of acute myocardial infarction: 1 million units over 45 to 60 minutes optionally followed by 150,000 units · h⁻¹ for 4 to 6 hours. Alternatively, urokinase may be infused intravenously at 50,000 to 150,000 units · h⁻¹ for up to 24 hours. Allergy to streptokinase is manifested by hypotension and fever. An unusual reaction to urokinase is severe rigor.

Functional Status
Late functional status of patients undergoing tricuspid valve surgery is influenced more by the multivalvar nature of most of the procedures than by the tricuspid repair or replacement itself. Nonetheless, most patients are considerably improved by the surgical procedure. Thus, in the GLH-UAB follow-up group, 42% of 103 patients were in NYHA class I late postoperatively. This is more impressive when it is realized that of these, 34 were preoperatively in class IV, 62 in class IV, and 6 in class III. In both series, less than 15% were in class IV late postoperatively.

Symptoms of Systemic Venous Hypertension
Most patients remain free of systemic venous hypertension late postoperatively. However, peripheral edema and hepatomegaly, with or without ascites, are common at follow-up. These symptoms could be the result of functional or organic obstruction of the tricuspid replacement device, residual left-sided cardiac failure with or without left-sided valvar disease, or important residual pulmonary hypertension (high pulmonary vascular resistance) or residual RV dysfunction. In this regard, Silver and colleagues reported higher right atrial pressures after tricuspid valve replacement than before in patients with Ebstein anomaly, but they also noted marked symptomatic improvement in cardiac function.

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<th>Table 14-1 Efficacy of Thrombolytic Therapy and Recurrence of Valve Obstruction, Stratified by Valve Position</th>
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Overall success of thrombolytic therapy was 84%. Success for right-sided valves (88%) was similar to that for left-sided valves (83%; p = .4). From Hurrell and colleagues.

*bBased on patients (n) with reported follow-up.

When anatomic substrate is suboptimal for repair. No survival difference has been demonstrated between mechanical and bioprosthetic tricuspid valves. Survival at 10 years is approximately 55% to 60%, including hospital deaths. Most of these patients have multivalvar disease, and tricuspid valve failure is seldom the dominant factor in late death. Predictors of late mortality after tricuspid valve replacement include older age at operation, poor left or right ventricular function, endocarditis, preoperative stroke or renal failure, and concomitant mitral valve surgery.

*Class V is cardiogenic shock or hemodynamic instability requiring emergency operation. This class augments the usual NYHA class IV, based on the observation of the UAB group that this subgroup of class IV was generally at higher risk than patients simply confined to bed. The Society of Thoracic Surgeons National Cardiac Database classifies this as emergency salvage.
Performance of Replacement Devices

Both porcine and pericardial bioprostheses have performed well in the tricuspid position. Small gradients of 4 to 10 mmHg exist across stent-mounted xenografts in the tricuspid position (Table 14-2). In general, however, prostheses with an internal diameter of at least 27 mm do not exhibit clinically important gradients. Bioprosthetic valves seem to degenerate at about the same rate and with the same age-related occurrence in the tricuspid position as they do in the mitral and aortic positions (see “Reoperation” under Mitral Valve Replacement and Results in Section I of Chapter 11; see also “Central Leakage” under Replacement Device Regurgitation in Chapter 12), although studies by Cohen and colleagues and Ohata and colleagues suggest that freedom from degeneration may be somewhat greater in the tricuspid position than in the mitral position. Although Nakano reported 100% freedom from structural degeneration at 9 years, pannus formation on the ventricular side of the cusps was a frequent finding by echocardiographic analysis in patients with at least 5 years of follow-up.

The Starr-Edwards ball valve mechanical prosthesis and the Bjork-Shiley mechanical prosthesis have performed well in the tricuspid position. The St. Jude Medical valve (and other bileaflet valves) appears also to exhibit good hemodynamic performance in the tricuspid position; Singh and colleagues reported diastolic gradients of 2 mmHg or less in seven patients.

Reoperation

Most patients who have undergone tricuspid valve replacement are free of reoperation up to 10 years later. Of those receiving mechanical or xenograft valves at UAB, 96% were free from tricuspid reoperation at 5 years, and 89% at 9 years. In McGrath’s series of 530 patients having a procedure involving the tricuspid valve, freedom from reoperation was 26% at 15 years. However, because of the competing risk of 81 late deaths, cumulative incidence of reoperation was 59% at 15 years (see “Competing Risks” under Time-Related Events in Chapter 6).

Tricuspid Valve Excision

Survival

An early mortality of 12% was reported among drug addicts after excision without replacement of the tricuspid valve. Late survival in such patients exceeded 60% at 15 years, with death due to return to drug addiction and not to right-sided endocarditis.

Hemodynamic Status

After excision of the tricuspid valve, the expected hemodynamic state develops. Cardiac murmurs are usually absent, but hepatomegaly with systolic pulsation is often present. Jugular venous pulsations with prominent v waves are universal as a result of the dramatic increase in right atrial pressure during systole.

The volumes of the right atrium and RV are considerably increased within a few months of tricuspid valve removal. The atrial septum shifts to the left with each ventricular systole, and the left atrium is compressed. The deleterious effects of RV remodeling are generally progressive, but the point of irreversibility has not been defined. Tricuspid valve replacement has induced substantial reverse remodeling of the RV as long as 21 years after tricuspid valve excision.

Functional Status

Most young patients are in NYHA functional class II for at least several years. Ankle edema and mild exercise intolerance are noted in about half the patients. Hemodynamic and functional states begin to deteriorate progressively after about 5 years, often in association with troublesome substernal fullness, which is worse in the recumbent position.

Risk Factors for Premature Death after Tricuspid Valve Surgery

A general understanding of the results of tricuspid valve surgery per se, especially of the risk factors for surgical failure, is difficult to obtain because of the relative infrequency of these operations, variety of operations, numerous concomitant procedures, and heterogeneity of the patient population. It is possible to have low hospital mortality across all components of this heterogeneity, but this has not been the experience universally.

Tricuspid valve excision without replacement is clearly a risk factor for a poor early and long-term result. The need for tricuspid anuloplasty and replacement, particularly the latter, has been associated with an increased risk of early death in multivalvar disease (see “Mitrail Valve Surgery with Coexisting Tricuspid Valve Disease” in Chapter 11). However, early mortality after these combined procedures need not necessarily be determined by the tricuspid procedure.
Multivariable analysis of risk factors for both early and late deaths indicates that neither repair nor replacement is associated with a greater risk than the other; type of replacement device (allograft, mechanical, bioprosthetic) was not a risk factor.\textsuperscript{M7}

Older age has been a risk factor for death early and late after operation,\textsuperscript{B1} as has preoperative functional disability, as reflected in NYHA class, particularly when the disability was severe\textsuperscript{T5} and associated with cardiomegaly.\textsuperscript{B3,B4} Prior valve surgery was also a risk factor for premature late death.

**INDICATIONS FOR OPERATION**

Selection of Anuloplasty Technique and Choice of Device

*Tricuspid Regurgitation*

When isolated severe TR is present, operation is indicated. This should be anuloplasty rather than replacement unless competence cannot be achieved. In intravenous drug users with endocarditis, simple valve excision may suffice, but tricuspid valve replacement is preferred over total excision; partial valve excision and reconstruction can be considered for less extreme valvar destruction.\textsuperscript{N5} (Indications for operation in functional tricuspid regurgitation associated with mitral valve disease are discussed in detail under “Mitral Valve Surgery with Coexisting Tricuspid Valve Disease” in Chapter 11.) Because most tricuspid procedures are performed to accompany left-sided valve operations, the left-sided hemodynamics usually determines indications for operation. However, because NYHA class IV, severe heart failure, high mean pulmonary artery pressure, and icterus are incremental risks for mortality when a tricuspid procedure is done, intervention early rather than late in multiple valve disease is prudent.\textsuperscript{P4,V1} The general American College of Cardiology/American Heart Association Guidelines for surgical management of TR are listed in Box 14-1. In patients with severe TR secondary to pulmonary hypertension, the current standard treatment is vasodilator therapy and diuretics.

When important TR occurs late after mitral valve replacement, the outlook after tricuspid valve surgery is less optimistic. Five-year survival after subsequent operation is only 44%, and most patients who fail to survive have little or no symptomatic improvement from the tricuspid valve procedure.\textsuperscript{E7} Despite an early mortality of about 9% and important symptomatic improvement in most patients, Staab and colleagues reported event-free survival of only 42% at 5 years.\textsuperscript{S15} This suggests the frequent presence of severe and irreversible RV failure in such patients. Thus, TR after previously adequate mitral valve operation is an uncommon indication for tricuspid valve operation.

*Choice of Anuloplasty Technique*

Several longitudinal studies indicate that severe TR is more likely to return after the De Vega and suture plication techniques than after use of anuloplasty rings. The impact of anuloplasty technique on freedom from reoperation was analyzed by McCarthy and colleagues.\textsuperscript{M5} “Non-ring” anuloplasties (De Vega and Peri-Guard) were less effective than anuloplasty rings in preventing late TR after mitral valve repair for degenerative disease. The same advantage of prosthetic ring anuloplasty over non-ring techniques was demonstrated in rheumatic mitral and tricuspid valve surgery.\textsuperscript{B6}

Similar findings were reported by Tang and colleagues\textsuperscript{T3} and Navia and colleagues.\textsuperscript{N6} Although some surgeons have reported good results with bicuspidization or modified De Vega techniques,\textsuperscript{N5} a ring anuloplasty clearly provides more durable protection against recurrent or progressive TR. The durability of bands\textsuperscript{M6} or pericardial strips\textsuperscript{S5} is probably intermediate between these two techniques.

In a longitudinal study by Tang and colleagues, use of an anuloplasty ring (vs. a DeVega suture anuloplasty) was an independent predictor of better survival (hazard ratio 0.7) and event-free survival at 6 years.\textsuperscript{T2}

Thus, suture plication techniques should probably be reserved for mild anular reductions in the setting of moderate TR in which repair of the left-sided valve lesions is expected to favorably impact functional TR. Rigid or flexible rings or bands are preferable to bicuspidization or De Vega techniques if major anular reduction and durability are required.

In view of the high risk of recurrent TR if pacemaker leads are left across the tricuspid valve, consideration should be given to replacing such leads with an epicardial lead at the time of tricuspid valve repair.

*Choice of Replacement Device*

In no other valve position is the choice between durability of a mechanical prosthesis and lack of thrombogenicity of a xenograft more apparent. It can be argued that younger patients with a better prognosis should receive a low-profile mechanical device, and older patients a xenograft.\textsuperscript{V1} Nakano and colleagues report satisfactory valve performance using an inverted Carpentier-Edwards pericardial valve (Fig. 14-8).\textsuperscript{N1}
Others prefer porcine xenografts for all patients despite a 10% to 40% prevalence of structural deterioration within 7 to 10 years. In all cases a large device (27 mm or larger) should be implanted. There is no evidence favoring use of a xenograft in the tricuspid area when mechanical prostheses are implanted on the left side, and vice versa.

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DEFINITION

Infective endocarditis includes conditions in which structures of the heart, most frequently the valves, harbor an infective process that leads to valvar dysfunction, localized or generalized sepsis, or sites for embolism (Box 15-1). The term infective endocarditis (IE) includes acute, subacute, and chronic processes; infection of bacterial, viral, rickettsial, or fungal etiology; and involvement of either native or prosthetic valves. As such, the term has no implication as to duration of the processes, infecting agent, or site of infection and thus supplants previously used terms such as “subacute bacterial endocarditis.”

HISTORICAL NOTE

In 1806, Corvisart described mitral valve vegetations found at autopsy in a 39-year-old man. In their 1824 book on heart disease, Bertin and Bouillaud discuss induration and vegetations on the valves of patients dying with endocarditis. The term endocarditis was introduced by Bouillard in 1841 when he described clinical and pathologic features of the disease. Earlier, Morgagni, Lancisi, and Sandifort had described hearts with probable endocardial vegetations. Weinstein and Bruschi reported that in 1886, Wyssokowitch and Orth designed an experimental model for endocarditis in which aortic valve cusps of animals were traumatized and the animals subsequently injected with bacterial suspensions from patients with endocarditis. The animals developed murmurs, embolic complications, and valve lesions at autopsy.

At the 1885 Gulstonian Lecture, Osler described the classic features of endocarditis. By 1909, he had refined his understanding of the pathologic anatomy (“proliferative vegetations”) and introduced the clinical finding of changing murmurs. Along with Horder, Osler emphasized the role of blood cultures for diagnosis.

Successful treatment of endocarditis lagged behind pathologic and clinical descriptions. In the 1940s, the era of sulfas, cure was achieved in about 5% of patients. By 1950, however, principles of antibiotic therapy had been established, including high-dose penicillin, long duration of treatment, and antibiotic suppression. It was also recognized at that time that delay in treatment, heart failure, advanced age, and preexisting rheumatic valvulitis were adverse prognostic factors. In 1940, Tauroff and Vessell successfully ligated a patent ductus arteriosus in treating a 2-year-old female with endocarditis. In 1957, Bahnon and colleagues reported occurrence of staphylococcal infection on silk sutures used for great vessel and intracardiac repairs.

Direct surgical treatment of IE began in 1961, when Kay and colleagues reported successful treatment of Candida endocarditis of the tricuspid valve. The native valve was debrided and an accompanying ventricular septal defect (VSD) closed. The first report of replacing a cardiac valve for native IE was published in 1965 by Wallace and colleagues. Their patient was a 45-year-old man who had severe aortic regurgitation with heavy Klebsiella vegetations on each cusp. He was treated intensively with antibiotics over 3 weeks, but there was resistant active infection and heart failure. Valve replacement was successful, eradicating the infection and restoring satisfactory hemodynamics.

In 1972, Merendino’s group from the University of Washington reported the collective results of cardiac operations for endocarditis in 139 patients, 24 of whom were treated by mitral valve repair, mechanical prosthetic mitral replacement, and replacement of the aortic valve with...
β-propiolactone–sterilized allografts; 17 of 24 patients survived. The report emphasized continuing sepsis and heart failure as indications for operation, compared native (“primary”) to prosthetic (“secondary”) valve endocarditis, and differentiated between active and healed lesions.

Most of the modern concepts of surgical treatment of IE were articulated by the late 1970s and reviewed in publications by Stinson and by Richardson and colleagues. 

### Pathogenesis and Morphology

#### Pathogenesis

The most common site of cardiac involvement is on the line of closure of a valve surface, typically on the atrial side of atrioventricular valves and on the ventricular surface of semilunar valves. Once bacteria become attached to the surface, the vegetation matures through bacterial proliferation and fibrin deposition. The preponderance of bacteria below the surface of the vegetation provides protection from phagocytes and high antibiotic concentration.

Several predisposing factors have been identified that may contribute to or be responsible for development of IE. Despite Osler’s initial observations, valvulitis of rheumatic fever was often confused histologically with IE. However, unlike rheumatic valvulitis, IE is not characterized in its early stages by global neovascularization or global inflammation of valve cusps. In most cases, the valvar endocardial surface must be altered to allow deposition of fibrin and platelets and subsequent attachment of bacteria. This injury may result from preexisting valvar lesions such as rheumatic valvulitis, anular or valvar calcification, or catheter trauma. Hemodynamic factors may contribute, such as the jet effect of blood flow through a patent ductus arteriosus or restrictive VSD, mitral valve prolapse, or bicuspid aortic valve. Bacteremia must occur in bacterial-based IE. Frequent transient bacteremias are found in 60% to 80% of normal individuals, but the number of organisms is small, and without the presence of one or more of the above factors, infection and vegetations do not result.

Several lines of evidence have demonstrated the importance of a compromised or altered immune system in the pathogenesis of IE. Histopathologic analysis of kidney tissue in patients with IE may reveal diffuse proliferative glomerulonephritis, with evidence of deposition of immunoglobulin (Ig)G and IgM. Circulating immune complexes (CICs) may be found in the glomerular basement membrane, retina, and peripheral lesions (Roth spots and Janeway lesions). Various manifestations of complement activation have been found in IE. Hooper and colleagues identified CICs in patients with prosthetic valve endocarditis (PVE). Kauffmann and colleagues found a positive correlation between CIC levels and duration of illness, and several investigators have noted a decline in CIC levels with successful treatment.

Staphylococcus aureus binds to porcine valvar endothelial cells by a mechanism that is specific and receptor mediated. This characteristic most likely represents a specific physicochemical interaction between microbial adhesins and a host-cell receptor that involves fibronectin lipoteichoic acid. IE involving a previously normal valve is often caused by S. aureus.

In several studies, one quarter of IE cases occurred on normal valves. Likely organisms are those that have increased adhesion molecules noted on dextran polymerization, namely Staphylococcus, Streptococcus viridans, and Enterococcus. Common risk factors are presence of overwhelming sepsis, resuscitation from shock, use of long-term indwelling catheters, intravenous (IV) drug abuse, and fungemia associated with prolonged antibiotic therapy. Only about 5% of patients with catheter sepsis are found to have IE, and this is generally due to staphylococcal organisms. Intravenous IE most often occurs in patients undergoing

### Definitions

**Endocarditis**: Exudative and proliferative inflammatory alterations of the endocardium, characterized by vegetations on the endocardial surface or within the endocardium. It may occur as a primary disorder (infective endocarditis) or as a complication of or in association with another disease (e.g., lupus erythematosus, rheumatic heart disease). **Infective endocarditis**: Invasion and multiplication of microorganisms on the endocardial surface, within the endocardium, within the myocardium, or on prosthetic materials within and around cardiac structures. It includes conditions in which structures of the heart, most frequently the valves, harbor an infective process that leads to valvar dysfunction, localized or generalized sepsis, or sites for embolism. The term covers:

- Acute, subacute, and chronic processes
- Infection of bacterial, viral, rickettsial, or fungal etiology
- Involvement of either native or prosthetic valves (or other prosthetic material)

**Acute endocarditis**: A severe form of infective endocarditis caused by virulent pyogenic microorganisms such as hemolytic streptococci or staphylococci. It can become life threatening within days.

**Subacute endocarditis**: A form of infective endocarditis that develops subtly over a period of weeks to several months. It may produce symptoms for months before heart valve damage or emboli make the diagnosis clear. It is usually caused by *Streptococcus viridans* or *Streptococcus fecalis*.

**Active endocarditis**: A surgical term indicating an operation carried out in the presence of obvious local cardiac infection manifested by inflammation, active vegetations, abscesses, burrowing sinuses, or fistulae. If such an operation is carried out while a patient is being treated with antibiotics for active infection, or has been treated within 2 weeks of operation, the disease is considered active.

**Healed endocarditis**: A surgical term indicating an operation carried out in the absence of obvious local cardiac infection and inflammation, generally following treatment and supposed eradication of microorganisms. It is characterized by lack of local inflammation; vegetations may be present but are generally endothelialized, and abscesses have resulted in well-defined and stable cavities, including sinuses and fistulae.

**Native valve endocarditis**: Infectious endocarditis involving a patient’s own (native) heart valve.

**Prosthetic valve endocarditis**: Infectious endocarditis involving a surgically implanted prosthetic heart valve. Prosthetic valve endocarditis and its abbreviation PVE are familiar, standard, and historical designations for infective endocarditis on any heart valve substitute, but “prosthetic” is at times a misnomer (e.g., infection of a pulmonary autograft). A more appropriate term is replacement device endocarditis, but in this chapter the historical term is maintained for the sake of familiarity.

**Iatrogenic IE**: Complications of, or in association with, another disease (e.g., overgrowth of indwelling catheters, intravenous [IV] drug abuse, and fungemia associated with prolonged antibiotic therapy).

**Enterococcus**: Common risk factors are presence of overwhelming sepsis, resuscitation from shock, use of long-term indwelling catheters, intravenous [IV] drug abuse, and fungemia associated with prolonged antibiotic therapy. Only about 5% of patients with catheter sepsis are found to have IE, and this is generally due to staphylococcal organisms.

**Intravenous IE**: Most often occurs in patients undergoing
chronic hemodialysis who have frequent staphylococcal bacteremias and also may have sclerotic aortic or mitral valves. It has long been acknowledged that usual bacterial vegetations of IE can result from seeding of a platelet-thrombin nidus after mechanical trauma. Garrison and Freedman produced endocarditis in rabbits by inserting a catheter into the endocardium and injecting bacterial isolates from humans with endocarditis. \(^{61}\) This model remains the principal experimental paradigm for the mechanical basis of IE.

Perhaps the most persuasive hypothesis for the pathogenesis of IE has been put forward by Rodbard.\(^{64}\) Basically, high-velocity jets of blood from a high-pressure source form at an orifice and enter a low-pressure sink. Venturi currents deposit bacteria immediately beyond the orifice to form vena contracta and result in mechanical erosion and deposition of platelets and thrombin (Fig. 15-1). These mechanical conditions exist beyond stenotic valves, on the pulmonary artery opposite a patent ductus arteriosus (Fig. 15-2), and on the left atrial aspect of a regurgitant mitral valve. Because most IE lesions of the aortic valve begin on the ventricular aspect, however, this suggests a role for valvar regurgitation in the pathogenesis of these lesions, and the Venturi effect would also apply (Table 15-1).

The abnormal endocardial and endothelial surfaces and increased turbulence imparted by numerous cardiac malformations create a substrate that is vulnerable to infection. The risk of infection associated with various cardiac abnormalities is reflected in the American Heart Association recommendations for prophylactic antibiotics in patients with such malformations.

**Morphology**

Usual sites for IE found at operation in patients with native valve endocarditis (NVE) not related to IV drug use are shown in Fig. 15-3. Vegetations and erosive cavities are on the ventricular aspect of the aortic valve cusps and at the base of the atrial aspect of the mitral valve leaflets, often resulting in separation or discontinuity at the ventriculoarterial or atrioventricular junction. Less often, discrete perforations caused by isolated vegetations are located on the aortic cusps themselves. Occasionally, “drop lesions” from the aortic valve occur on the anterior mitral leaflet or the tensor apparatus of the mitral valve.

In the vast majority of non–drug-related cases of NVE, valve deposits are left-sided. In IV drug–related IE, the tricuspid valve is involved in about half the cases and aortic or mitral valves in the remainder.\(^{64}\) Perianular pseudoaneurysms (abscesses) are more frequently associated with aortic than with mitral vena contracta endocarditis and occur in about one third of cases studied by transesophageal echocardiography (TEE); *S. aureus* is the predominant organism.\(^{79}\) Clinically, presence of pericarditis, rapid progression of symptoms, and a high degree of atrioventricular block are associated with perianular abscess.\(^{85}\)

In PVE, all or most vegetations are on the ventricular aspect of the prosthesis. Only a small area of sewing-ring detachment may be apparent and may appear sterile. At operation, therefore, a thorough search must be made beneath the prosthesis for the bulk of the pathologic process. As noted in some series, there may be important detachment without apparent vegetations; this may occur in either the presence or absence of positive blood cultures.\(^{11}\) This represents PVE and requires replacement of the prosthesis.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Infective endocarditis is present when defined in accordance with New York Heart Association (NYHA) criteria\(^{82}\): positive blood cultures associated with either new or changing murmurs or embolic phenomena; or new or changing murmurs in a patient with a congenital cardiac anomaly or prior valve damage, associated with either embolic phenomena or sustained fever, anemia, and splenomegaly. Most authorities accept a modification of that definition to include progressive heart failure in the presence of positive blood cultures. In an effort to improve specificity and sensitivity for the diagnosis of IE, investigators at Duke University have
The most common clinical manifestation of IE is fever, which is present in 95% to 100% of patients. This applies to both NVE and PVE. The fever may be low grade or spiking and generally follows peaks of bacteremia by about 2 hours. Patients at risk for IE who develop unexplained fever for more than 48 hours should have two or more sets of blood cultures drawn from different sites. Because of the importance of proper identification of the offending organism, administration of antibiotics should be delayed until blood cultures have been obtained.

Positive blood cultures are obtained in about 95% of patients even when right-sided endocarditis, endocarditis caused by fungus, endocarditis in addicts, and endocarditis caused by fastidious organisms are included.

In IE cases confirmed by echocardiographic, autopsy, or operation, positive blood cultures are obtained in 95% of cases with two blood specimens and in 98% with four specimens. However, occurrence of negative-culture endocarditis rises to about 10% in most surgical series, and PVE predominates in this group of patients.

Culture-negative IE is more likely with intracellular or fastidious organisms, or with previous antibiotic therapy. A history of antibiotic therapy or serologic evidence of Mycoplasma or Chlamydia species is likely responsible for negative-culture IE. Other causes include Candida, Aspergillus, and fastidious slow-growing organisms such as Q-fever (Coxiella burnetii) and Bartonella organisms.

A heart murmur is found in about 85% to 95% of IE patients. Changing murmurs occur much less frequently (≈15% to 20%). Although the concept of changing murmurs has been classically associated with IE since Osler’s Gulstonian Lecture in 1885, clinically changing murmurs are not often appreciated. Ten percent of IE patients lack murmurs, particularly those with tricuspid involvement. Infection involving the aortic valve and root is often characterized by a relatively short diastolic murmur. There may be a murmur only in early systole or mid-systole, although murmurs are often obscured by tachycardia. The murmur of mitral regurgitation caused by IE is similar to that of other mitral regurgitation murmurs and may exhibit a typical radiation posteriorly when the anterior leaflet is perforated. There also may be signs of mitral stenosis secondary to obstruction by large vegetations, in which case the murmur may be diastolic.

Pulse pressure may be normal or even narrowed in aortic regurgitation if IE is acute or important heart failure exists. Narrowed pulse pressure is caused by high left ventricular end-diastolic pressure with low cardiac output. There is frequently a gallop rhythm.

Infection of the mitral valve and its supporting structures is considered to be less frequent than aortic valve endocarditis, but may be more indolent in its course. The mitral valve is most commonly involved (~40% of cases), followed by the aortic valve in about 36%, when S. aureus is the infecting organism. Right-sided endocarditis is almost uniquely related to the tricuspid valve. Right-sided IE accounts for about 10% of IE cases and usually occurs in the setting of IV drug abuse. Affected patients tend to be younger and have fewer comorbidities and less structural heart disease than patients with left-sided IE. Right-sided lesions are associated with fever, but often a cardiac murmur is initially absent.

Anemia frequently occurs in IE patients and has multifactorial causes, but primarily it results from marrow suppression secondary to chronic disease. Arthritis and arthralgias are infrequently seen today, generally because endocarditis is diagnosed earlier. Myalgias are common and may be associated with bacteremia or occasionally may result from myocardial microabscesses, generally occurring in staphylococcal bacteremia.

Severity of heart failure in a hospitalized IE patient is not appropriately classified by NYHA functional class. In general, heart failure can be termed mild when only small doses of diuretic or digitalis are necessary; moderate when large doses

Table 15-1  Loci of Infective Endocarditic Lesions

<table>
<thead>
<tr>
<th>Condition</th>
<th>High-Pressure Source</th>
<th>Orifice</th>
<th>Low-Pressure Sink</th>
<th>Location of Lesions</th>
<th>Satellite Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coarctation of aorta</td>
<td>Central aorta</td>
<td>Coarctation</td>
<td>Distal aorta</td>
<td>Downstream wall of aorta</td>
<td>Lateral wall peripheral to stenotic lesion</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>Aorta</td>
<td>Ductus</td>
<td>Pulmonary artery</td>
<td>Pulmonary artery</td>
<td>Pulmonary artery</td>
</tr>
<tr>
<td>Arteriovenous fistula</td>
<td>Artery</td>
<td>Fistula</td>
<td>Vein</td>
<td>Communications and veins</td>
<td>Tricuspid leaflets</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>Left ventricle</td>
<td>Defect</td>
<td>Right ventricle</td>
<td>Right ventricular surface of defect</td>
<td>Pulmonary artery</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>Aorta</td>
<td>Closed aortic cusps</td>
<td>Left ventricle</td>
<td>Ventricular surface of aortic valves</td>
<td>Mitral chordae</td>
</tr>
<tr>
<td>Mitral regurgitation</td>
<td>Left ventricle</td>
<td>Closed mitral leaflets</td>
<td>Left atrium</td>
<td>Atrial surface of mitral valves</td>
<td>Atrium</td>
</tr>
<tr>
<td>Pulmonary regurgitation</td>
<td>Pulmonary artery</td>
<td>Closed pulmonary cusps</td>
<td>Right ventricle</td>
<td>Ventricular surface Pulmonary cusps</td>
<td></td>
</tr>
<tr>
<td>Tricuspid regurgitation</td>
<td>Right ventricle</td>
<td>Closed tricuspid leaflets</td>
<td>Right atrium</td>
<td>Atrial surface Tricuspid leaflets</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Rodbard; in Weinstein and Schlesinger.

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P3 A51 M10

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of diuretic, afterload-reducing medications and bed rest are necessary; and severe when cardiogenic shock is present and inotropic agents are needed.

Embolization is the presenting manifestation in about 10% to 15% of patients with left-sided IE, and about half of patients with IE have evidence of embolic phenomena on physical exam or via diagnostic imaging. These emboli seem about evenly distributed between cerebral and peripheral sites. Classic peripheral signs of endocarditis—Osler nodes, Janeway lesions, Roth spots, petechiae, and clubbing—are late manifestations and are infrequently seen in a surgical practice. The one exception may be Janeway lesions, and when noted, the infecting organism is almost always Staphylococcus.

In practice, diagnosis of IE is primarily based on two tests: blood cultures and echocardiography. The diagnosis is made most often by the presence of positive blood cultures and a cardiac lesion characterized by new stenosis, new regurgitation, or echocardiographic evidence for a vegetation. There are many more individuals with sepsis and positive blood cultures but without cardiac manifestations, and they are not considered to have IE.
An excellent microbiology laboratory is essential for accurate and prompt diagnosis. With current techniques, ability to culture fastidious organisms (e.g., Q-fever [Coxiella burnetii], Mycoplasma) is high. Thus, diagnosis of IE involving cardiac valves or congenital malformations is made on a constellation of findings, usually fever, positive blood cultures, and hemodynamic derangement within the cardiac structures that is best assessed and followed by echocardiography.

Echocardiography has become a standard modality for diagnosis and continuing observation of patients with IE. In all situations, TEE has greater sensitivity and specificity than transthoracic echocardiography (TTE). Specificity for TEE is approximately 90% and sensitivity 95%. For TTE, accuracy ranges from 40% to 80%. These figures apply equally to NVE and PVE. Perivalvar or perianular cavities associated with prosthetic valves are more easily delineated with TEE, and in the view of some authorities, these represent pseudoaneurysms rather than abscess cavities in most patients. Box 15-3 summarizes the echocardiographic and clinical findings in IE that indicate the potential need for operation.

An algorithm for diagnosis of IE begins with fever, requires positive blood cultures, includes some sign or symptom referable to the heart, and receives anatomic corroboration with TEE. From TEE, vegetation size, mobility, and position can be documented; degree of stenosis and regurgitation associated with the valve lesion can be assessed; and in PVE the presence of prosthetic leakage or perianular cavities can be determined.

The decision to use cardiac catheterization and angiography has varied over the years and continues to be made on a case-by-case basis. In few cases have vegetations been disturbed by intraarterial or venous catheters, and a reasonable policy is that if coronary artery disease or coronary embolization is suspected, coronary angiography should be undertaken before operation.

Neurologic abnormalities may have occurred in as many as 25% to 30% of IE patients at initial presentation. They are protean in nature and include stroke, transient ischemic attack, toxic encephalopathy, meningitis, brain abscess, loss of vision, seizures, headache, backache, and acute mononeuropathy. Funduscopic examination (Roth spots or flame hemorrhages), cerebrospinal fluid examination, and computed tomography (CT) scanning or magnetic resonance imaging are recommended in every case. 

### Box 15-2 Diagnostic Criteria for Infective Endocarditis

#### Major Criteria

**Positive Blood Culture**
- Typical microorganisms for infective endocarditis (IE) from two separate blood cultures (viridans streptococci, *Streptococcus bovis*, HACEK group, or community-acquired *Staphylococcus aureus* or enterococci) in absence of a primary focus, or
- Persistently positive blood culture, defined as recovery of a microorganism consistent with IE from:
  - Blood cultures drawn more than 12 hours apart, or
  - All of three or majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart

**Evidence of Endocardial Involvement**
- Positive echocardiogram for infective endocarditis:
  - Oscillating intracardiac mass on valve or supporting structures, or in path of regurgitant jets, or on implanted material, in absence of an alternative anatomic explanation, or
  - Abscess, or
  - New partial dehiscence of prosthetic valve or new valvar regurgitation (increase or change in preexisting murmur not sufficient for diagnosis)

**Minor Criteria**

**Predisposition**
- Predisposing heart condition or IV drug use
- Fever ≥38°C

**Vascular Phenomena**
- Major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions

**Immunologic Phenomena**
- Glomerulonephritis, Osler nodes, Roth spots, rheumatoid factor

**Microbiological Evidence**
- Positive blood culture but not meeting major criterion, or serologic evidence of active infection with organism consistent with infective endocarditis

**Echocardiogram**
- Consistent with infective endocarditis but not meeting major criterion

### Box 15-3 Echocardiographic and Clinical Features Suggesting Potential Need for Surgical Intervention in Patients with Infective Endocarditis

**Vegetation**
- Persistent vegetation after systemic embolization
- Anterior mitral valve leaflet vegetation, particularly with size ≥10 mm
- One or more embolic events during first 2 weeks of antimicrobial therapy
- Two or more embolic events during or after antimicrobial therapy
- Increase in vegetation size after 4 weeks of antimicrobial therapy

**Valvar Dysfunction**
- Acute aortic or mitral regurgitation with signs of ventricular dilatation
- Heart failure unresponsive to medical therapy
- Valve perforation or rupture

**Perivalvar Extension**
- Valvar dehiscence, rupture, or fistula
- New heart block
- Large abscess or extension of abscess despite appropriate antimicrobial therapy

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*°Surgery may be required because of risk of embolization.
°Surgery may be required because of heart failure or failure of medical therapy.*
imaging (MRI) of the brain are performed as indicated, and results may alter timing of surgical therapy (see following discussion). MRI may be particularly effective in detecting cerebral embolic lesions in IE patients without neurologic symptoms.316

Embolic events are reported frequently in IE patients (24%-67%).46 Prevalence is probably higher in IV drug-related endocarditis and perhaps slightly lower in PVE. The brain is the most frequently identified site of emboli.54

**NATURAL HISTORY**

**Epidemiology**

The incidence of IE in the United States is reported to be 1.7 to as high as 11.6 episodes per 100,000 persons per year with variance due in great part to varying diagnostic and reporting criteria. Approximately 10,000 to 20,000 new cases of IE are diagnosed each year in the United States, accounting for about 1 in 1000 hospital admissions.31 The IE profile has changed over the past several decades; in the current era, IE is more frequently associated with invasive medical procedures and old age and less frequently associated with rheumatic heart disease and poor dentition.47 In the elderly, it is more often linked to a prosthetic valve and bacteria from the gastrointestinal tract.515

Terpenning and colleagues found that indwelling catheters were implicated as the source of bacteremia in half the cases of nosocomial IE.72

Prosthetic heart valves represent a strong risk factor for IE.56 In a large study of adult patients, occurrence of PVE was 4.1% at 48 months after valve replacement in 1465 consecutive hospital survivors, and 64% of these patients died.11 Occurrence of PVE after valve replacement appears to be much lower in the current era, with overall risk about 1% to 5% in the first year after valve replacement and about 1% per year thereafter.511 Other studies report an annual incidence of PVE ranging from 0.12% to 0.4% per patient-year.197 The hazard for developing PVE is greater in patients operated on for NVE than in those undergoing valve replacement for other reasons313,11 (Fig. 15-4). In addition to NVE as a risk factor for PVE, placement of a mechanical prosthesis (vs. a tissue valve), black race, male gender, and longer cardiopulmonary bypass time are incremental risk factors for subsequent development of PVE. Finally, prosthetic valve reoperation is a greater hazard for development of PVE than primary valve replacement (Fig. 15-5).

It is difficult to identify a precise causative factor for PVE. However, intraoperative surface contamination, introduction of contaminated blood or blood substitute, bacterial colonization of a member of the surgical team, bacterial aerosolization in ventilators, nasal colonization of the patient, and preexisting urosepsis have all been implicated. In contrast to prosthetic heart valves, implanted anuloplasty rings and indwelling pacemaker leads are infrequently disposed to IE.56,45

Among the pediatric population, IE most often occurs in patients with VSDs and valvar aortic stenosis. Incidence is low (14.5 per 10,000 person-years) but 35 times that of the normal population.43 Incidence of IE in patients with VSD is reduced by about 50% after surgical closure. Postoperative IE in children most often occurs after aortic valvotomy, valve replacement, or use of a right ventricular–pulmonary artery conduit.56 In both pediatric and adult populations, mitral valve prolapse has emerged as a frequent preexisting malformation in the spectrum of IE (29% of patients in McKinsey and colleagues’ series).38

**Causative Organisms**

Approximately 80% of endocarditis cases are caused by streptococcal or staphylococcal species. S. aureus predominates as the infecting organism in the majority of hospital-acquired and drug-related cases of IE. S. aureus involves the mitral valve more than the aortic valve and results in higher occurrence of embolism compared with other organisms.510 Streptococcal IE accounts for about 30% of IE cases, and viridans streptococci are the most common causative organisms. Enterococci are the third leading cause of IE, implicated in about 10% of cases.55 Enterococcal IE typically occurs in elderly males with multiple comorbidities, results less commonly in embolic events, and disproportionately affects the aortic valve. Gram-negative bacilli account for about 5% of
cases. Distribution of infecting organisms in the usual NVE population, however, may vary among institutions and temporally.\textsuperscript{26-30,32,34-36} In PVE occurring within 2 months of operation, \textit{Staphylococcus epidermidis} is the major offending organism. Late-onset PVE has the same general spectrum of causative organisms as NVE. Enterococcal PVE (usually caused by \textit{Enterococcus faecalis} or \textit{Enterococcus faecium}) is usually associated with manipulation of the gastrointestinal or genitourinary tract or with malignancy.

Complications

The most frequent cardiac complication of NVE is heart failure, primarily caused by valvar regurgitation. However, NVE occasionally results in mitral or tricuspid valve stenosis and infrequently in aortic valve stenosis. Perianular leakage and abscess and occasionally stenosis are the major causes of heart failure in PVE, with perianular extension occurring in over 50% of cases.\textsuperscript{36} It occurs in 10% to 40% of NVE cases and is more common with aortic valve involvement.\textsuperscript{38} This dangerous complication can lead to abscess formation, pseudoaneurysms, and aortocavitary fistula formation (which can develop from any aortic sinus).\textsuperscript{32} Myocardial abscesses (most commonly related to \textit{S. aureus} infection) complicate IE in 20% to 40% of cases and are particularly common with PVE and aortic valve involvement.\textsuperscript{39} Patients with a bicuspid aortic valve and IE carry a high risk of abscess formation.\textsuperscript{112} Development of conduction abnormalities should prompt further TEE evaluation for abscess formation or extension. If left untreated, abscess cavities may progress to fistula formation and intracardiac shunting from myocar-dial perforation. Once these complications develop, mortality may exceed 40% despite surgical intervention.\textsuperscript{32} If the rare patient with a small abscess cavity (≤1 cm), clinically controlled infection, and multiple comorbidities is treated medically, close follow-up with serial echocardiography during prolonged antibiotic therapy is mandatory.\textsuperscript{75} Pericarditis typically occurs in association with anular abscess or myocardial perforation.

Renal complications of IE take at least four forms: prerenal failure secondary to low cardiac output, microabscess formation caused by septic emboli, glomerular dysfunction resulting from circulating immune complexes, and renal failure caused by antibiotic toxicity.

Embolic events are common in IE patients (Fig. 15-6), with a reported prevalence of 43% in NVE, 67% in IV drug–associated IE, and 25% in PVE.\textsuperscript{34} Ting and colleagues report a 19% occurrence of splenic emboli in their series of patients with IV drug–related endocarditis.\textsuperscript{17} Occurrence is about 5% in the usual type of left-sided NVE. Metastatic infection of viscera is typically caused by \textit{Staphylococcus}. Other classic peripheral manifestations of IE (e.g., petechiae, Osler nodes, splinter hemorrhages) are infrequently seen now, probably because of earlier intervention in the disease process. Multiple coronary emboli may result in myocardial infarction and ventricular dysfunction; the highest risk of embolic complications occurs with \textit{S. aureus}, Candida, and HACEK (\textit{Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, and Kingella}) species.\textsuperscript{75}

About half the embolic complications of IE are associated with neurologic manifestations, and one fourth to one third of patients with NVE or PVE at some time have neurologic complications, 90% of which are related to emboli in the distribution of the middle cerebral artery.\textsuperscript{14,32} Presence of \textit{S. aureus} increases risk of neurologic complications.\textsuperscript{36,74} Stroke is the most common neurologic event. Vegetations are seen on echocardiography in about 40% of patients with neurologic complications and in about 80% of patients without neurologic sequelae.\textsuperscript{32} Some characteristics of vegetations visualized on TTE or TEE (e.g., density, mobility) may not be helpful in defining emboli risk.\textsuperscript{126} Cerebral embolism generally occurs before the start of antibiotic therapy, with risk of stroke falling rapidly after initiation of effective antibiotics.\textsuperscript{110} A European multicenter study estimated the prevalence of acute ischemic stroke at 12% (CI 10%-14%) on hospital admission, but only 3.7% (2.7%-4.9%) after start of appropriate antibiotic therapy.\textsuperscript{113} Data from the International Collaboration on Endocarditis indicated a stroke incidence of 4.8 per 1000 patient-days during the first week of antibiotic therapy, which decreased to 1.7 per 1000 patient-days in the second week and fell further thereafter.\textsuperscript{112} After instituting antibiotic therapy, however, both absolute vegetation size and observed increase in vegetation size are associated with increased embolic risk\textsuperscript{74} (Fig. 15-7). Large vegetations are commonly caused by the HACEK group of organisms and fungi.

The most devastating neurologic complication is intra-cerebral hemorrhage, which complicates about 5% of IE cases.
and carries a mortality exceeding 50%. The pathophysiology may involve septic arteritis with erosion of the vessel wall during uncontrolled infection, hemorrhage following cerebral infarction, or rupture of a mycotic aneurysm. For patients on chronic anticoagulation who develop neurologic symptoms, anticoagulation should be discontinued (or maintained at low therapeutic levels in patients with a mechanical prosthetic valve) until intracranial hemorrhage can be excluded by CT scanning or MRI.

Medical treatment alone (vs. operative) increases risk of embolism. However, delaying repair of the cardiac lesion is usually advised in the presence of central nervous system (CNS) complications. Morbidity is less when repair is done in the presence of cerebral infarction versus cerebral hemorrhage (see Indications for Operation). Evidence indicates that cerebral mycotic emboli will regress after extirpation of the valvar septic lesion, so early cardiac operation in patients with mycotic aneurysm and cerebral abscess may be advisable.

Mortality

Mortality associated with IE is reported at 15% to 20% during the initial hospitalization and 20% to 30% during the first year. Early mortality is similar between NVE and PVE and between mitral and aortic valve IE. Gram-negative bacillus and fungal IE carry a mortality exceeding 50%. Development of heart failure, intracardiac abscess, embolism, a large mobile vegetation, hemodynamic instability, altered mental status, immunocompromise, and advanced age have also been identified as risk factors for mortality.

THERAPY

Antibiotics

Several blood cultures should routinely be obtained before initiating antibiotic therapy. Over half of cases can be managed solely with antibiotics. Because antibiotic penetration of vegetations is difficult, prolonged parenteral antibiotic administration is advisable. Once antibiotics are started, blood cultures should be drawn every 1 to 2 days until they become negative. Total duration of antibiotic therapy is counted from the time of the first negative culture.

Vancomycin and aminoglycoside therapy should be guided by blood levels to ensure adequate dosing while minimizing toxicity. Aminoglycosides are often used in combination with a cell wall–active agent (β-lactam or vancomycin) to effect synergy (by increasing aminoglycoside entry into bacteria) in treating staphylococci, streptococci, and enterococci. Standard antibiotic recommendations are listed in Table 15-2 for NVE and Table 15-3 for PVE. Detailed recommendations about antibiotic therapy for IE are available from the American Heart Association.

Surgery

About 40% to 45% of all patients with IE undergo surgical therapy. Goals of operative therapy are to (1) remove infected tissue and drain abscesses, (2) restore or reconstruct atrioventricular or ventriculoarterial continuity, and (3) reverse the hemodynamic abnormality. Drainage of abscesses, débridement of areas of necrosis, and improvement of mechanical function by repair or replacement of infected valves are done as required. Operation is also aimed at closing acquired defects (e.g., VSD, ring abscess, fistula, aneurysm) and in children may include repairing the underlying malformation.

All operations for IE are done through a partial or full median sternotomy. Presence of adhesive or suppurative pericarditis is strong evidence of previous perforation at the aortic or mitral ring or ring abscess. It is prudent to use bicaval cannulation to allow flexibility in the presence of burrowing abscesses, acquired septal perforation, unexpected right-sided valve involvement, and complex aortic root reconstruction. Intraoperative TEE is extremely useful to diagnose and plan treatment of the various manifestations of the infectious process. In left-sided IE, minimal manipulation of the heart

<table>
<thead>
<tr>
<th>Table 15-2</th>
<th>Selected Native Valve Endocarditis Treatment Regimens (All Doses Based on Normal Renal Function)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organism</strong></td>
<td><strong>Drug</strong></td>
</tr>
<tr>
<td>Oxacillin-sensitive <em>Staphylococcus</em></td>
<td>Oxacillin/nafcillin 2 g IV q 4 h&lt;br&gt;<strong>With or without:</strong> Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h⁻¹</td>
</tr>
<tr>
<td>Oxacillin-resistant <em>Staphylococcus</em></td>
<td>Vancomycin 15 mg · kg⁻¹ IV q 12 h⁻¹</td>
</tr>
<tr>
<td>Viridans streptococci/Streptococcus bovis with penicillin MIC ≤0.12 µg · mL⁻¹</td>
<td>Penicillin G 12-18 million units IV per 24 h&lt;br&gt;<strong>Or:</strong> Ceftriaxone 2 g IV/IM q 24 h</td>
</tr>
<tr>
<td>Viridans streptococci/S. bovis with penicillin MIC ≤0.12 µg · mL⁻¹ to ≤0.5 µg · mL⁻¹</td>
<td>Penicillin G 24 million units IV per 24 h&lt;br&gt;<strong>Plus:</strong> Gentamicin 3 mg · kg⁻¹ IV/IM q 24 h&lt;br&gt;<strong>Or:</strong> Ceftriaxone 2 g IV/IM q 24 h&lt;br&gt;<strong>Plus:</strong> Gentamicin 3 mg · kg⁻¹ IV/IM q 24 h</td>
</tr>
</tbody>
</table>
Table 15-2  Selected Native Valve Endocarditis Treatment Regimens (All Doses Based on Normal Renal Function)—cont’d

<table>
<thead>
<tr>
<th>Organism</th>
<th>Drug</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viridans streptococci/S. bovis or nutritionally-variant streptococci with penicillin MIC ≥0.5 µg · mL⁻¹</td>
<td>See treatment regimen for penicillin/ampicillin-resistant enterococcal endocarditis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterococcus spp. susceptible to penicillin, ampicillin, gentamicin, and vancomycin</td>
<td>Ampicillin 2 g IV q 4 h &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h &lt;br&gt;Or: Penicillin G 18-30 million units IV per 24 h &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h</td>
<td>4-6 weeks</td>
<td>For penicillin/ampicillin allergy, vancomycin 15 mg · kg⁻¹ IV q 12 h for 6 weeks &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h for 6 weeks</td>
</tr>
<tr>
<td>Enterococcus spp. resistant to penicillin/ampicillin, susceptible to vancomycin and gentamicin</td>
<td>Vancomycin 15 mg · kg⁻¹ IV q 12 h &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h</td>
<td>6 weeks</td>
<td>If β-lactamase production, ampicillin-sulbactam 3 g IV q 6 h</td>
</tr>
</tbody>
</table>

Adapted with permission from Baddour and colleagues.⁹⁰

Table 15-3  Selected Prosthetic Valve Endocarditis Treatment Regimens (All Doses Based on Normal Renal Function)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Drug</th>
<th>Duration</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxacillin-sensitive S. epidermidis</td>
<td>Oxacillin/nafcillin 2 g IV q 4 h &lt;br&gt;Plus: Rifampin 300 mg IV/PO q 8 h &lt;br&gt;Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h</td>
<td>≥6 weeks</td>
<td>For non-anaphylactoid penicillin allergy, substitute cefazolin 2 g IV q 8 h for oxacillin/nafcillin</td>
</tr>
<tr>
<td>Oxacillin-resistant S. epidermidis</td>
<td>Vancomycin 15 mg · kg⁻¹ IV q 12 h &lt;br&gt;Plus: Rifampin 300 mg IV/PO q 8 h &lt;br&gt;Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h</td>
<td>≥6 weeks</td>
<td>For anaphylactoid penicillin allergy, substitute vancomycin 15 mg · kg⁻¹ IV q 12 h for oxacillin/nafcillin</td>
</tr>
<tr>
<td>Viridans streptococci/ Streptococcus bovis with penicillin MIC ≤0.12 µg · mL⁻¹</td>
<td>Penicillin G 24 million units IV per 24 h &lt;br&gt;With or without: Gentamicin 3 mg · kg⁻¹ IV/IM q 24 h &lt;br&gt;Or: Ceftriaxone 2 g IV/IM q 24 h &lt;br&gt;With or without: Gentamicin 3 mg · kg⁻¹ IV/IM q 24 h</td>
<td>6 weeks</td>
<td>For penicillin/ceftriaxone allergy, vancomycin 15 mg · kg⁻¹ IV q 12 h for 6 weeks without gentamicin</td>
</tr>
<tr>
<td>Viridans streptococci/ S. bovis with penicillin MIC &gt;0</td>
<td>Penicillin G 24 million units IV per 24 h &lt;br&gt;With or without: Gentamicin 3 mg · kg⁻¹ IV/IM q 24 h &lt;br&gt;Or: Ceftriaxone 2 g IV/IM q 24 h &lt;br&gt;With or without: Gentamicin 3 mg · kg⁻¹ IV/IM q 24 h</td>
<td>6 weeks</td>
<td>For penicillin/ceftriaxone allergy, vancomycin 15 mg · kg⁻¹ IV q 12 h for 6 weeks without gentamicin</td>
</tr>
<tr>
<td>Enterococcus spp. susceptible to penicillin, ampicillin, gentamicin, and vancomycin</td>
<td>Ampicillin 2 g IV q 4 h &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h &lt;br&gt;Or: Penicillin G 18-30 million units IV per 24 h &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h</td>
<td>4-6 weeks</td>
<td>For penicillin/ampicillin allergy, vancomycin 15 mg · kg⁻¹ IV q 12 h for 6 weeks &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h for 6 weeks</td>
</tr>
<tr>
<td>Enterococcus spp. resistant to penicillin/ampicillin, susceptible to vancomycin and gentamicin</td>
<td>Vancomycin 15 mg · kg⁻¹ IV q 12 h &lt;br&gt;Plus: Gentamicin 1 mg · kg⁻¹ IV/IM q 8 h</td>
<td>6 weeks</td>
<td>If β-lactamase production, ampicillin-sulbactam 3 g IV q 6 h</td>
</tr>
</tbody>
</table>

Adapted with permission from Baddour and colleagues.⁹⁰

¹Target gentamicin peak 3-4 µg · mL⁻¹; target trough <1 µg · mL⁻¹.
²Target vancomycin peak 30-45 µg · mL⁻¹; target trough 10-15 µg · mL⁻¹.
³Penicillin dosing can be by continuous infusion or dosed every 4 to 6 hours in equal divided doses.

Key: MIC, Minimum inhibitory concentration; NVE, native valve endocarditis; PO, by mouth; PVE, prosthetic valve endocarditis.
should be the rule to avoid dislodging infected thrombotic material or vegetations. As in other valvar procedures, myocardial management is accomplished with antegrade and retrograde cardioplegia supplemented with moderate systemic hypothermia (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). Thorough excision of infected tissue is performed with drainage of abscesses and closure of defects.

Operation for aortic IE should involve examining the anterior leaflet of the mitral valve and its chordae for drop lesions. It is sometimes necessary to open the left atrium to examine the posterior leaflet apparatus. Similarly, when mitral endocarditis is present, the possibility of concomitant aortic vegetations should be considered. However, absence of a murmur or thrill, presence of a competent aortic valve, and no echocardiographic evidence of vegetations at the aortic area argue against aortic involvement and preclude need for inspecting the valve.

Reparative procedures may be done on the mitral valve when the vegetation is healed, small, or discrete and does not involve a major portion of the tensor apparatus. It may include closing small perforations of the posterior or anterior leaflet using autologous or bovine pericardium or direct suturing (Fig. 15-8). Small vegetations may be stripped from chordae tendineae. Major destruction of the mitral leaflets by active infection presents a unique challenge if reconstruction is considered. Although one approach is valve replacement for all but small vegetations, the increased risk of early PVE in the setting of active infection (particularly in the setting of ongoing positive blood cultures) argues for concerted efforts at valve reconstruction. After débridement of infected tissue, a sliding anuloplasty technique (see Chapter 11) may be applicable to reconstruct commissural areas. Partial leaflet resection, pericardial patch replacement of mid-leaflet areas, or both may be needed. The remaining orifice size following reconstruction must be large enough (generally 25 mm in the average adult or a z value of −2 or greater in children) to prevent important mitral stenosis. Suture anuloplasty may be preferable to a prosthetic ring in an actively infected anulus, but a biodegradable anuloplasty ring has been suggested by Pektok and colleagues.³²

In the absence of active IE, as defined by positive blood cultures and overt inflammation at the site of vegetation, mitral repair of the classic type can be accomplished. Triangular resection of a portion of the anterior leaflet or quadrangular resection of a portion of the posterior leaflet may be performed, supplemented by inserting a partial or complete anular ring. Partial leaflet resection and anuloplasty procedures for tricuspid valve endocarditis can be applied on a more liberal basis (Fig. 15-9).

At the time of mitral valve resection, the posteroinferior portion of the mitral anulus should be inspected because the usual myocardial ring abscess occurs in this location. In infection of the aortic root, the abscess is usually found just posterior to the membranous portion of the ventricular septum or at the posterior portion of the septum just anterior to the orifice of the left coronary artery. When found, abscesses should be totally evacuated and surrounding tissue débrided. The concept of atrioventricular or ventriculoarterial discontinuity must be kept in mind. The infecting process often erodes those junctions, with potential or actual separation. In mitral valve IE with left atrioventricular discontinuity, the defect can be handled in several ways. Often a simple variation of the usual valve replacement technique is appropriate; interrupted horizontal mattress sutures anchored with felt or pericardial pledgets are placed on the ventricular aspect of the mitral anulus, brought up through the left atrial aspect, and then through the prosthetic sewing ring. Deep bites are necessary. This can be done only after thorough débridement of the infected tissue within the mitral ring (Fig. 15-10).

In more extensive ring abscess or often in PVE with abscess, a different type of reconstruction is necessary. The atrioventricular discontinuity is bridged by a patch fashioned from a sheet of autologous or bovine pericardium. The ventricular aspect is anchored to the endocardium and myocardium using deep bites of continuous 3-0 or 4-0 polypropylene suture. The superior aspect of this tissue reconstruction is anchored to the atrial endocardium with a similar suture.
The new prosthesis is anchored to the composite suture line on the ventricular aspect of the suture line using interrupted horizontal mattress sutures buttressed with felt pledgets. Various maneuvers have been suggested for seating valves in the aortic position in the presence of frank abscesses of the aortic root. The advantage of tissue valves over mechanical valves in preventing reinfection has not been conclusively demonstrated. In the aortic area, however, stentless tissue valves, either allografts or xenografts, have some advantage in that their pliability allows some flexibility in reconstructing continuity between the ventricle and aorta. When stent-mounted valves—either mechanical or tissue—are used, a technique using felt or bovine pericardial buttressed horizontal mattress sutures is advised. The mattress is placed on the ventricular aspect of the aortic anulus or from outside the aortic wall, dissecting the aortic root upstream in its noncoronary and posterior left coronary aspects and occasionally opening the right ventricular outflow tract to place pledged sutures from the infundibular septum through the aortic anulus.

When a simple small abscess lies under the left coronary ostium, evacuation, débridement, and patch closure of the defect can be accomplished. The stent-mounted or stentless tissue prosthesis is then placed in its usual orthotopic position using techniques similar to those required in noninfected cases (see Chapter 12). In many patients with important aortic valve IE, full root replacement offers the most satisfactory solution (Fig. 15-11). Infected tissue is first débrided, and formal root replacement is done in the usual way, with particular emphasis on locating the upstream (proximal) suture line within the left ventricular outflow tract, thus appropriately bridging the left ventricular–aortic discontinuity. All infected tissue is thus exteriorized.

Ancillary procedures during valve replacement may be helpful. Some authorities suggest soaking the prosthetic device in an appropriate antibiotic, and others have irrigated

**Figure 15-9** Repair of tricuspid valve infective endocarditis in which vegetation is localized to a portion of septal leaflet. A, Line of leaflet resection. B, Repair of defect using fine interrupted sutures. C, Completed repair supported by an anuloplasty ring.
Figure 15-10 Infective endocarditis producing a ring abscess involving base of posterior leaflet of mitral valve. A, Abscess is evacuated and débrided. B, Defect is covered by a pericardial patch anchored within left ventricle and extending up across base of portion of posterior leaflet, then sewn to left atrial wall. C, Prosthesis is sutured into place, siting posterior suture line either on patch (in this case) or occasionally below patch on ventricular wall.
or swabbed the local area with antiseptic solution such as povidone-iodine or antibiotics specific for the infecting organism. In fungal endocarditis, irrigation of the local area with amphotericin or other antifungal agents may be efficacious.

When both the aortic and mitral valves are involved but infection is limited to the cusps, usual sequencing of operation is followed: aortotomy, then aortic valve resection, followed by left atriotomy and mitral valve resection. The mitral anulus is then sized and an appropriate mechanical device or
bioprosthetic valve inserted. The aortic annulus is then sized and an appropriate mechanical or tissue prosthesis inserted. When infection is not limited to the leaflets, there may be destruction of aortomitral continuity with absence of the aortomitral curtain. In this case, seating of the mitral prosthesis is modified because much of the anterior lateral suture attachment of the sewing ring will be absent. As much of the mitral prosthesis as possible is inserted in the usual way. Attention is then redirected to the aortic exposure, and a new synthetic aortomitral curtain is formed with polyester or pericardium. Upstream or proximal anchoring is done with sutures to the sewing ring of the mitral prosthesis, and downstream aortoventricular continuity is established by suturing this curtain to the root of the aorta. Thereafter, the aortic prosthesis is inserted as usual, attaching the prosthesis in its right lateral aspect (noncoronary sinus aspect) to the reconstructed mitral curtain. Alternatively, the sewing ring of the aortic prosthesis can be attached where it interfaces directly to the sewing ring of the mitral prosthesis.124

Treatment of associated infection, particularly peripheral mycotic aneurysm; brain, spleen, or liver abscess; and renal parenchymal infection, usually takes second priority to the intracardiac operation. Use of cardiopulmonary bypass does not generally exacerbate associated neurologic deficits except in the specific case of cerebral hemorrhage (see Special Situations and Controversies). Persisting infection after valve replacement should alert the surgeon to splenic and liver abscesses. Similarly, continued renal decompensation suggests the presence of renal parenchymal disease.

SPECIAL FEATURES OF POSTOPERATIVE CARE

In general, patients undergoing operations for complications of IE are subject to the same early postoperative monitoring and intervention algorithms as non-IE patients undergoing similar operations for valve replacement or repair (see Chapter 5). Hemodynamic state is assessed by measuring or estimating cardiac output and measuring left atrial, right atrial, or pulmonary artery pressures, combined with assessing blood pressure and peripheral perfusion.

Occasionally, patients with an acute septic syndrome manifest decreased peripheral resistance with low, normal, or high cardiac output early postoperatively. Appropriate treatment may include use of phenylephrine, levarterenol, or arginine vasopressin to increase peripheral resistance. Mobilizing extravascular lung water may be important to facilitate extubation. Adequate diuretic therapy and positive end-expiratory pressure ventilation early postoperatively are then indicated.

In all patients, tissue should be obtained for Gram stain and subsequent culture and histologic analysis. Results of these studies are integrated into the postoperative care plan, with appropriate changes in antibiotic regimen. Because renal function often is compromised, antibiotic levels must be closely monitored during the initial stages of therapy to allow adjustment in dosing interval if renal function is changing.

Patients with compromised renal function often have increased blood urea nitrogen and creatinine levels early postoperatively, followed by a decline to near-normal levels over the next 3 to 7 days. Monitoring renal function is therefore important, and pharmacologic therapy with large doses of diuretics is often indicated. In some patients, temporary renal dialysis is necessary. Some surgeons may want to follow white blood cell counts or phase reactants over the postoperative period to monitor resolution of sepsis. If a septic picture continues, possible involvement of peripheral sites should be investigated.

Protocols for anticoagulation are the same in IE patients as in those having similar devices without IE.

Antibiotic treatment, most often administered IV, is continued for 4 to 6 weeks based on the type of organism and its sensitivity to antimicrobials. In the case of fungal endocarditis, oral treatment with ketoconazole or fluconazole may be appropriate for 3 to 6 months.

RESULTS

Early (Hospital) Death

Native Valve Endocarditis

Hospital mortality for valve operations (and associated procedures) in patients with IE varies between 4% and 30%.84,91,92,114,115,116,117,118,119,120,121 The variation can be ascribed to several factors, most notably the difference in risk between operation in the acute vs. healed stages of endocarditis (see Box 15-1 for definitions). In general, operations for healed IE are performed after a full course of antibiotic therapy.

Other factors affecting the variation in reported hospital mortality reflect the incremental risks for an operation, as discussed later.

Operative treatment of IE is in reality a combined medical-surgical treatment, and timing of the operation is an important factor in patient survival. However, it is convenient to compare strictly medical (nonoperative) treatment of IE with results of operative treatment. In general, the more urgent the surgical indication and the more severe the heart failure, the better the surgical results compared with medical therapy. However, no prospective or randomized studies have been done, so patients in the nonoperative medical group may not be strictly comparable with those in the surgical group. Richardson and colleagues reported that operative treatment in 81 patients with NVE resulted in 11 deaths (14%; CL 10%-19%), compared with 24 deaths (44%; CL 37%-52%) in 54 patients treated medically.82 Operative mortality was affected by urgency of operation. For elective operations (next convenient operative date), mortality was 5%, for urgent operations (next day) 16%, and for emergency operations in patients with severe heart failure and low cardiac output (immediate operation) 33%.

Operations in IE patients often demand complex procedures that may affect hospital mortality after valve repair or replacement.913,115 Complexity of the procedure is frequently dictated by duration of the illness and particularly by the infecting organism. Tissue destruction is characteristic of staphylococcal and some gram-negative organisms and is much less likely to occur in streptococcal or pneumococcal endocarditis. In reports from Bauernschmitt and Middlemost and their colleagues, however, early results of valve replacement did not seem to be adversely affected by excessive complexity of the procedure.94,131 Rather, preoperative complications and severity indices have a more profound influence on mortality.

Often, IE can be successfully treated without operative intervention in children. Nomura and colleagues reported on 98 patients seen over 13 years, 30 of whom were treated operatively, with a hospital mortality of 6.7%.124
remaining patients were treated medically, with a 10% hospital mortality. Tolan and colleagues reviewed 132 published reports in which children underwent operative intervention during active endocarditis.\textsuperscript{7,11} Hospital survival was 77%. Only 67% of patients had preoperative conditions thought to predispose them to IE, and about one quarter of those were operated on for infection associated with patent ductus arteriosus.

**Prosthetic Valve Endocarditis**

PVE is an incremental risk factor for operative mortality in the domain of all IE.\textsuperscript{2,52} Again, overall survival for patients with PVE is improved in those treated operatively compared with those treated medically. Although results may not be strictly comparable, most series report a difference in outcome when operative treatment of NVE is compared with PVE. In the Brigham and Women’s Hospital experience, mortality was 22% in 49 PVE patients vs. 6% in 109 NVE patients.\textsuperscript{1,3} Several factors more prevalent in the PVE group are likely responsible for this difference, including reoperation, prevalence of abscess, anular erosion and peri-anular aneurysm, insidious onset of infection, and fastidious or fungal organisms. However, Sabik and colleagues at the Cleveland Clinic report a 3.9% (CL 2%-7%) hospital mortality among 103 patients managed with radical débridement of infected tissue and aortic root replacement with a cryopreserved allograft.\textsuperscript{51}

**Time-Related Survival**

Late survival after valve replacement for NVE is good, but not as good as with similar operations done in the absence of endocarditis (Fig. 15-12). Death and other events late after operation often are not related to IE or recurrent IE but rather to other conditions associated with heart disease, such as the valve replacement device and associated complications, myocardial dysfunction, and coronary artery disease. Using mechanical valves exclusively, Bauernschmitt and colleagues reported 81% survival among 138 patients after 8 years.\textsuperscript{54}

There is an early, high-peaking hazard for death after operation, and then a constant later phase (Fig. 15-13). Survival is lower in patients who have PVE than in those with NVE (Fig. 15-14). Recurrent IE, nonstreptococcal organisms, and heart failure are associated with late death after valve replacement.

Data for long-term survival after heart valve replacement in IE patients are typified by those reported by d’Udekem and colleagues from Toronto; survival at 10 years was 61% ± 6%.\textsuperscript{D13} Aranki and colleagues, in two separate publications from Brigham and Women’s Hospital, reported 81% to 83% 5-year survival and 61% to 68% 10-year survival for both mitral and aortic valve replacement.\textsuperscript{A3, A4}

**Incremental Risk Factors**

Several factors portend higher mortality with operative treatment for IE. A strong risk is hemodynamic deterioration,\textsuperscript{B4, D3, H3} characterized as preoperative shock, advanced heart failure, or advanced NYHA functional class. Some have also found a relationship with low preoperative cardiac index.\textsuperscript{1,5} A second important risk factor is the infecting organism. Nonstreptococcal organisms, primarily staphylococci, increase operative risk. Staphylococcal infection is generally associated with abscesses, and abscesses independently may also increase risk.\textsuperscript{B4, D3, L3, A1, L3} Likewise, most studies report that PVE is associated with a lower early postoperative survival than NVE.\textsuperscript{B4, D3, M7} Additional incremental risk factors are older age, renal dysfunction, longer cardiopulmonary bypass time, acute vs. healed IE, insidious onset of infection, and associated procedures (Fig. 15-15). A 20-year analysis from Berlin identified preoperative ventilation, mitral valve abscess, and age older than 60 years as risk factors for early mortality following operation for mitral valve endocarditis.\textsuperscript{M21}

David and colleagues identified preoperative cardiogenic or septic shock and abscess formation in both mitral and aortic anuli as risk factors for hospital mortality in patients with periannular extension.\textsuperscript{B25} Anguera and colleagues found moderate or severe heart failure, PVE, and urgent or emergency operation to be major risk factors for mortality.\textsuperscript{A2}
Figure 15-14  Survival according to initial native valve endocarditis (NVE) or prosthetic valve endocarditis (PVE) in 108 patients undergoing aortic valve replacement ($P = .03$). (From Haydock and colleagues.$^{11}$)

**Figure 15-15**  Factors influencing operative mortality after surgical treatment of patients with infective endocarditis. Data are presented as relative risk (see Chapter 6 for definition) for each factor plus 95% confidence limits, as determined by meta-analysis of 30 major studies. Key: AV, Aortic valve; MV, mitral valve; NVE, native valve endocarditis; PVE, prosthetic valve endocarditis; Staph, Staphylococcus aureus or Staphylococcus epidermidis. (From Moon and colleagues.$^{13}$)

In-Hospital Morbidity

A few IE patients have continuing episodes of sepsis despite an apparently adequate cardiac operation. Almost uniformly, the source of this sepsis is not the heart; however, an overlooked valvar lesion must be sought, generally by repeat TEE. There is a high prevalence of splenic and other visceral infarcts, emboli, or abscesses,$^{13}$ but usually these do not cause continuing sepsis and are amenable to continued antibiotic therapy. Renal parenchymatous disease as a cause of sepsis is rare, as are cerebral mycotic aneurysms. Peripheral mycotic aneurysms are a potential source of continuing sepsis.

New or evolving conduction abnormalities preoperatively reflect evolution of the cardiac sepsis or may result from coronary emboli. Postoperatively, heart block occurs more often than in patients without endocarditis. In most situations, this is a predictable occurrence resulting from the radical débridement necessary to eradicate infections around the aortic root, mitral valve apparatus, and ventricular septum.

Most observers have noticed increased postoperative bleeding. Inflamed tissue, inflammatory pericarditis, complex reconstructions, renal dysfunction, and platelet dysfunction may play a role in excessive bleeding.

A devastating complication is a new or deepening neurologic deficit after valve replacement. Even with meticulous surgical technique, friable vegetations may dislodge to cause new CNS deficits. More frequently, however, an existing CNS finding is aggravated by operation. Ting and colleagues found evidence of cerebral septic emboli in 45 (42%) of 106 patients who underwent valve replacement for IE.$^{18}$ Neurologic complications after valve replacement included postoperative strokes in 6%, cerebral abscesses in 2%, and seizures in 1%. Presence of a hemorrhagic infarct preoperatively predisposes patients to perioperative stroke (see further discussion under Special Situations and Controversies).

Recurrent Infection

Some institutions report few cases of subsequent reinfection even when operation is done early in the course of NVE. Despite 20% of patients requiring valve replacement in the UAB series having uncontrolled infection at operation, no cases of subsequent PVE occurred.$^{82}$ This finding is similar to the experience of Utley and Mills and of Okies and colleagues, who reported that reinfections were rare in such patients and emphasized the importance of adequate débridement of infected areas.$^{32,11}$ In each of the studies, however, follow-up was short. Indeed, recurrent infection after valve replacement (or repair) does occur. In Larbalestier and colleagues’ report, 18 of 109 patients surviving surgery for NVE underwent reoperation.$^{13}$ Eight had developed recurrent endocarditis. Recurrent IE is more common when the initial organism is nonstreptococcal and when there has been major destruction of the anulus or surrounding valve structures. This finding is reflected in Aranki’s report, in which freedom from recurrent endocarditis in acute aortic IE surgical patients...
was 89% ± 3% at 5 years and 83% ± 4% at 10 years, vs. 96% ± 3% at 5 years and 86% ± 6% at 10 years in patients with healed aortic valve IE.\footnote{34}

Freedom from reoperation is higher when the mitral valve is involved (compared with the aortic valve), reflecting less anular destruction. In a series reporting results of operation for mitral valve IE at Brigham and Women’s Hospital, freedom from reoperation at 5 and 10 years was 92% ± 4% and 62% ± 13% for acute endocarditis and 94% ± 4% and 84% ± 10% for healed endocarditis (\(P = .7\)), respectively.\footnote{34} There was little difference in recurrent IE at 10 years for patients operated on for NVE (85%) vs. PVE (82%), although long-term survival was better for those with NVE. Reinfection with the same or different organism is common in drug abusers, and late mortality is greater in that group. In Hiramta’s experience, late mortality was 39% in drug abusers vs. 7% for non–drug users.\footnote{16}

There is some controversy as to whether a tissue valve, particularly a cryopreserved allograft, is preferable for use in aortic NVE. In 108 patients, Haydock and colleagues reported a small but statistically significant difference in incidence of recurrent IE in patients having allografts vs. prosthetic valves\footnote{13} (Fig. 15-16). Hazard functions were qualitatively different for allografts; there was a constant phase of hazard when an allograft was used, but an early peaking hazard phase and late rising phase when a prosthetic device was used (Fig. 15-17). In a similar study, McGiffin and colleagues noted that allografts in the aortic position had a higher freedom from \textit{recurrent endocarditis} than mechanical or xenograft valves\footnote{47} (Fig. 15-18). Thus, if there is an advantage among valve substitutes, it is conferred uniquely by allografts. In both Haydock’s and McGiffin’s series, where aortic valve replacement was done with allograft valves, freedom from recurrent endocarditis was about 80%.

Not all institutional experience supports this view, however.\footnote{11,13,14,15} In 138 patients who received only mechanical valves, \textit{reoperation-free survival} was similar (77%), suggesting that mechanical prostheses may perform as well as...
allografts when operation is done for aortic NVE. However, reoperation-free survival does not comparably address differences in early hazard for recurrent infection. Lytle and colleagues reoperated on 146 patients with PVE, with 19 (13%) in-hospital deaths. Subsequent reoperation was performed in 15% of hospital survivors, and in those who had aortic valve replacement, reoperation-free survival was similar among those who received biological, mechanical, or allograft valves (Fig. 15-19). Similar findings were reported by Nguyen and colleagues.

Thus, for aortic NVE, some evidence suggests that an allograft is the preferable replacement device. For all aortic PVE, mitral NVE, or mitral PVE operations, there is no evidence indicating the superiority of xenografts over mechanical devices.

INDICATIONS FOR OPERATION

In healed NVE, indications for operation are related primarily to hemodynamic severity of the valvar lesion or defect. It follows that, in general, results of operation in healed endocarditis are identical to those in patients with endocarditis having the same hemodynamic disturbance (see Indications for Operation in Chapters 11 to 14).

In the setting of active NVE, consensus is lacking about some of the specific indications for surgical intervention. Nevertheless, consensus has emerged from both the European and North American medical communities with regard to specific indications for operation (Box 15-4). Specific recommendations regarding timing of operation are listed in Box 15-5. Minor variations exist in the recommendations from the American College of Cardiology/American Heart Association Guidelines and European Society of Cardiology (Table 15-4).

Among the indications for operation for IE, surgery for acute heart failure provides the greatest survival benefit. Operation is best performed within about 1 week of presentation of heart failure symptoms, urgently in the presence of subtle deterioration, and emergently with rapid or marked hemodynamic compromise. Heart failure is usually secondary to valve regurgitation but occasionally results from valve obstruction or intracardiac shunting. Acute, severe aortic regurgitation is poorly tolerated and often requires emergency operation. Patients with reasonably compensated heart failure may benefit from several days of medical therapy with diuretics and afterload reduction prior to surgery. However, extended delay is not recommended because of the tendency for insidious progression with a marked increase in operative risk.

Early surgical treatment of staphylococcal NVE, regardless of hemodynamic compromise, is usually advocated. However, there are isolated cases of successful medical treatment. Development of new-onset atrioventricular block is highly predictive of abscess formation; after verification by TEE, prompt operation should be performed.

Because recidivism is common in drug abusers, surgical treatment of right-sided endocarditis is occasionally inappropriate despite or abandoned in favor of nonsurgical treatment. This approach may be particularly appropriate when replacement is more likely to be done than repair, because reinfection often follows tricuspid valve replacement. Tricuspid valve resection without replacement is an option, although hemodynamic sequelae are important limitations to this approach (see Chapter 14). Recurrent pulmonary emboli are not an indication for operation unless fever persists despite 3 weeks of antibiotic therapy in the absence of a pulmonary abscess.

Right-sided endocarditis in IV drug abusers is caused by Staphylococcus aureus in 80% of patients. Tricuspid valve replacement has been advocated in IE patients who have large vegetations and fever that persist for more than 3 weeks despite appropriate antibiotic therapy. Bayer and colleagues, however, correlating echocardiographic findings with clinical outcome in 53 patients with tricuspid NVE secondary to S. aureus, found that 50 patients were cured with antibiotics; only 3 required surgery. Of 38 vegetations detected, 21 were 10 mm or greater in diameter. Similarly, recurrent pulmonary emboli were not correlated with demonstrable vegetations or with size of the vegetation.

Surgical intervention in early PVE usually is recommended, particularly when the offending organism is Staphylococcus or a fastidious organism. In the complete absence of heart failure, emboli, or a large vegetation, however, nonsurgical treatment may suffice.

The clinical presentation and natural history of late PVE (>2 months after initial operation) are similar to those of active NVE. Therefore, inducations for valve replacement in late PVE—advanced degree of heart failure, emboli, continuing sepsis, and staphylococcal organism—are similar to those for NVE. Timing of operation for either NVE or PVE should be based on clinical considerations, not on duration of antibiotic treatment.

Echocardiography has become an integral part of the algorithm for diagnosing and treating endocarditis. Vegetation size as the sole indication for surgery remains controversial. However, the presence of mobile vegetations, vegetations larger than 10 mm, and obstructing vegetations warrant consideration for operative therapy. In left-sided NVE, Sanfilippo and colleagues found that vegetation size, extent, mobility, and consistency were univariable predictors of complications (Fig. 15-20). Patients with a vegetation greater than 10 mm in diameter on echocardiography have a substantially higher risk of embolic phenomena than those with small or no vegetations (47% vs. 19%). It must be stressed that...
**Box 15-4 Indications for Surgery for Infective Endocarditis**

<table>
<thead>
<tr>
<th>Category</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Congestive Heart Failure</strong></td>
<td>Congestive heart failure caused by severe aortic or mitral regurgitation, more rarely by valve obstruction caused by vegetations.</td>
</tr>
<tr>
<td></td>
<td>Severe acute aortic or mitral regurgitation with echocardiographic signs of elevated left ventricular end-diastolic pressure or significant pulmonary hypertension.</td>
</tr>
<tr>
<td></td>
<td>Congestive heart failure as a result of prosthetic dehiscence or obstruction.</td>
</tr>
<tr>
<td><strong>Perianular Extension</strong></td>
<td>Most patients with abscess formation or fistulous tract formation.</td>
</tr>
<tr>
<td><strong>Systemic Embolism</strong></td>
<td>Recurrent emboli despite appropriate antibiotic therapy.</td>
</tr>
<tr>
<td></td>
<td>Large vegetations (&gt;10 mm) after one or more clinical or silent embolic events after initiation of antibiotic therapy.</td>
</tr>
<tr>
<td></td>
<td>Large vegetations and other predictors of a complicated course.</td>
</tr>
<tr>
<td></td>
<td>Very large vegetations (&gt;15 mm) without embolic complications, especially if valve-sparing surgery is likely (remains controversial).</td>
</tr>
<tr>
<td><strong>Cerebrovascular Complications</strong></td>
<td>Silent neurologic complication or transient ischemic attack and other surgical indications.</td>
</tr>
<tr>
<td></td>
<td>Ischemic stroke and other surgical indications, provided that cerebral hemorrhage has been excluded and neurologic complications are not severe (e.g., coma).</td>
</tr>
</tbody>
</table>

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**Modified from ACC/AHA 2006 Guidelines.**

*Surgery should be performed immediately, irrespective of antibiotic therapy, in patients with persistent pulmonary edema or cardiogenic shock. If congestive heart failure disappears with medical therapy and there are no other surgical indications, intervention can be postponed to allow a period of days or weeks of antibiotic treatment under careful clinical and echocardiographic observation. In patients with well-tolerated severe valvar regurgitation or prosthetic dehiscence and no other reasons for surgery, conservative therapy under careful clinical and echocardiographic observation is recommended, with consideration of deferred surgery after resolution of the infection, depending upon tolerance of the valve lesion.*

*In all cases, surgery for preventing embolism must be performed very early because embolic risk is highest during the first days of antibiotic therapy.*

*Surgery is contraindicated for at least 1 month after intracranial hemorrhage unless neurosurgical or endovascular intervention can be performed to reduce bleeding risk.*

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**Box 15-5 Timing of Surgery**

<table>
<thead>
<tr>
<th>Type</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Emergency Surgery (Within 24 Hours)</strong></td>
<td>Native (aortic or mitral) or prosthetic valve endocarditis and severe congestive heart failure or cardiogenic shock.</td>
</tr>
<tr>
<td></td>
<td>Acute valvar regurgitation.</td>
</tr>
<tr>
<td></td>
<td>Severe prosthetic dysfunction (dehiscence or obstruction).</td>
</tr>
<tr>
<td></td>
<td>Fistula into a cardiac chamber or the pericardial space.</td>
</tr>
<tr>
<td><strong>Urgent Surgery (Within Days)</strong></td>
<td>Native valve endocarditis with persisting congestive heart failure, signs of poor hemodynamic tolerance, or abscess.</td>
</tr>
<tr>
<td></td>
<td>Prosthetic valve endocarditis with persisting congestive heart failure, signs of poor hemodynamic tolerance, or abscess.</td>
</tr>
<tr>
<td></td>
<td>Prosthetic valve endocarditis caused by staphylococci or gram-negative organisms.</td>
</tr>
<tr>
<td></td>
<td>Large vegetation (&gt;10 mm) with an embolic event.</td>
</tr>
<tr>
<td><strong>Large vegetation (&gt;10 mm) with other predictors of a complicated course</strong></td>
<td>Very large vegetation (&gt;15 mm), especially if conservative surgery is available.</td>
</tr>
<tr>
<td></td>
<td>Large abscess and/or perianular involvement with uncontrolled infection.</td>
</tr>
<tr>
<td><strong>Early Elective Surgery (During In-Hospital Stay)</strong></td>
<td>Severe aortic or mitral regurgitation with congestive heart failure and good response to medical therapy.</td>
</tr>
<tr>
<td></td>
<td>Prosthetic valve endocarditis with valvar dehiscence or congestive heart failure and good response to medical therapy.</td>
</tr>
<tr>
<td></td>
<td>Presence of abscess or perianular extension.</td>
</tr>
<tr>
<td></td>
<td>Persisting infection when extracardiac focus has been excluded.</td>
</tr>
<tr>
<td></td>
<td>Fungal or other infections resistant to medical care.</td>
</tr>
</tbody>
</table>

Adapted from Prendergast and colleagues.®
Table 15-4  Indications and Timing of Surgery in Native and Prosthetic Valve Infective Endocarditis

<table>
<thead>
<tr>
<th>Indications</th>
<th>Timing of Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart Failure</strong></td>
<td></td>
</tr>
<tr>
<td>Aortic or mitral IE or PVE with severe acute regurgitation or valve obstruction or fistula causing refractory pulmonary edema or cardiogenic shock</td>
<td>Emergency</td>
</tr>
<tr>
<td>Aortic or mitral IE with severe acute regurgitation or valve obstruction and persisting heart failure or echocardiographic signs of poor hemodynamic tolerance (early mitral closure or pulmonary hypertension)</td>
<td>Urgent</td>
</tr>
<tr>
<td>Aortic or mitral IE or severe prosthetic dehiscence with severe regurgitation and no heart failure</td>
<td>Elective</td>
</tr>
<tr>
<td>Right heart failure secondary to severe tricuspid regurgitation with poor response to diuretic therapy</td>
<td>Urgent/elective</td>
</tr>
<tr>
<td><strong>Uncontrolled Infection</strong></td>
<td></td>
</tr>
<tr>
<td>Locally uncontrolled infection (abscess, false aneurysm, fistula, enlarging vegetation)</td>
<td>Urgent</td>
</tr>
<tr>
<td>Persisting fever and positive blood cultures for more than 7 to 10 days and not related to an extracardiac cause</td>
<td>Urgent</td>
</tr>
<tr>
<td>Infection caused by fungi or multi-resistant organisms</td>
<td>Urgent/elective</td>
</tr>
<tr>
<td>PVE caused by staphylococci or gram-negative bacteria (most cases of early PVE)</td>
<td>Urgent/elective</td>
</tr>
<tr>
<td><strong>Prevention of Embolism</strong></td>
<td></td>
</tr>
<tr>
<td>Aortic or mitral IE or PVE with large vegetations (&gt;10 mm) following one or more embolic episodes despite appropriate antibiotic therapy</td>
<td>Urgent</td>
</tr>
<tr>
<td>Aortic or mitral IE or PVE with large vegetations (&gt;10 mm) and other predictors of complicated course (heart failure, persistent infection, abscess)</td>
<td>Urgent</td>
</tr>
<tr>
<td>Aortic or mitral or PVE with isolated very large vegetations (&gt;15 mm³)</td>
<td>Urgent</td>
</tr>
<tr>
<td>Persistent tricuspid valve vegetations &gt;20 mm after recurrent pulmonary emboli</td>
<td>Urgent/elective</td>
</tr>
</tbody>
</table>

Adapted from the 2009 guidelines of the European Society of Cardiology.  
*Emergency surgery: Surgery performed within 24 hours; urgent surgery, within a few days; elective surgery, after at least 1 or 2 weeks of antibiotic treatment.  
†Surgery may be preferred if procedure preserving the native valve is feasible.  
Key: IE, infective endocarditis; PVE, prosthetic valve endocarditis.

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*Emergency surgery: Surgery performed within 24 hours; urgent surgery, within a few days; elective surgery, after at least 1 or 2 weeks of antibiotic treatment.  
†Surgery may be preferred if procedure preserving the native valve is feasible.  
Key: IE, infective endocarditis; PVE, prosthetic valve endocarditis.

vegetation size is only one of several criteria recognized as indications for surgical intervention. However, the combination of a recent nonhemorrhagic CNS event, a highly mobile (prolapsed vegetations crossing the plane of valve leaflet coaptation during the cardiac cycle) vegetation, and vegetation size greater than 10 mm while a patient is on effective antibiotic therapy should mandate serious consideration for operation.  

Indications for surgical intervention in children are much the same as those in adults: heart failure, continuing sepsis, and embolization. In children, however, large masses associated with chronic right-sided indwelling catheters are often indications for surgical extirpation. Small right-sided masses associated with indwelling catheters in both children and adults can be treated with antibiotics, heparinization, and nonsurgical removal of the catheter.

**SPECIAL SITUATIONS AND CONTROVERSIES**

Timing of Operation in Patients with Central Nervous System Events

The risk of urgent operation for IE complicated by stroke remains controversial. There is general agreement that if at all possible, operation should be delayed at least 4 weeks following an intracerebral hemorrhage, because the risk of deepening stroke or death resulting from a neurologic complication is particularly serious in patients with demonstrable cerebral hemorrhage (as opposed to infarction) as diagnosed with brain CT or MRI. On the other hand, a number of studies have shown that cardiopulmonary bypass is not particularly dangerous (risk of worsening neurologic event 3%-6%[36]) in patients with cerebral infarction without hemorrhage[31,32,33] or in those with cerebral mycotic aneurysm. In fact, mycotic aneurysms have been shown to regress in the presence of an adequate cardiac operation and continued antibiotic therapy.[34] Eishi and colleagues reviewed 2523 surgical cases of IE and found that 10% of patients had associated cerebral complications.[1] In-hospital mortality of those patients was 11%; cerebral infarction occurred in 65%, cerebral bleeding in 32%, and abscess in 3%. Exacerbation of cerebral complications (including death), according to interval from onset of cerebral infarction to cardiac operation, occurred in 46% of patients operated on within 24 hours, 44% of those operated on days 2 through 7, 17% of those operated on days 8 through 14, 10% of those operated on days 15 through 28, and just 2% of those operated on after 4 weeks (Figure 15-21). Thus, an important correlation existed between the interval from onset of cerebral complications to operation and exacerbation of cerebral complications (P = .008). Preoperative risk factors affecting exacerbation of cerebral complications were severity of cerebral complication, interval...
Exacerbation of cerebral damage, including death related to cerebral infarction until cardiac operation. Key: CI, Cerebral infarction. (From Eishi and colleagues.)

Figure 15-21 Exacerbation of cerebral damage, including death related to cerebral injury, according to interval from onset of cerebral infarction until cardiac operation. Key: CI, Cerebral infarction. (From Eishi and colleagues.)

between complication and surgery, and uncontrolled heart failure.

Postoperative exacerbation of cerebral complications is more likely in patients with more severe preoperative manifestation of brain infarction. In the Eishi study of 51 patients without exacerbation of their cerebral complication, operation occurred on average of 15 days after diagnosis, compared with 8 days among 17 patients having exacerbation (P = .01). Thus, exacerbation is inversely related to interval between diagnosis and operation. If cerebral infarction is not associated with hemorrhage, however, earlier operation is usually well tolerated.

In a large cohort of patients undergoing valve surgery after a neurologic complication of IE, Ruffman and colleagues found the risk of neurologic deterioration following brain infarction to be about 20% within 3 days, 20% to 50% between day 4 and 14, less than 10% after 14 days, and less than 1% after 4 weeks. On the basis of these data, Angstwurm and colleagues recommended valve surgery within 72 hours if a patient with brain infarction (but without hemorrhage) has severe heart failure, and after 4 weeks if the patient remains stable on antibiotic therapy. Urgent operation should be considered reasonably safe in patients with transient ischemic episodes or “silent” cerebral embolism.

Preferred Device for Operation

Choice of valve replacement device depends on several factors, including likelihood of PVE, durability, need for anticoagulation, availability, and ease of insertion. However, factors such as adequate eradication of foci of infection and “best fit” also apply. For that reason, a number of choices may be available for patients with aortic IE. Although good results have been reported with mechanical or stented bioprosthetic valves, the preponderance of data suggests better outcome with an aortic allograft. When abscess cavities can be excluded by a pliable allograft, this device is preferable. On the other hand, when aortic root replacement is necessary, insufficient evidence exists to indicate that a tissue valve is superior to a mechanical valved conduit (although indirect evidence would support the use of an allograft root).

Because tricuspid valve endocarditis frequently accompanies IV drug abuse, repair is preferred over replacement. If replacement is necessary, choice of device depends on the usual factors associated with tricuspid valve replacement (see Chapter 14). Tricuspid valve allografts have provided encouraging outcomes (see Chapter 14).

Repair is occasionally successful in mitral valve endocarditis, but most repairs are done when IE is healed rather than acute. In the acute stage, a mechanical valve is a suitable option if satisfactory reconstruction is not possible following effective débridement.

In cases of extreme recurrent PVE despite multiple reoperations, cardiac transplantation may be considered if systemic foci of infection are absent.

Guidelines for Antibiotic Prophylaxis

The important morbidity and mortality of IE despite its relative rarity has prompted development of national and international guidelines for prophylactic antibiotics, beginning in 1955. Periodic revision of existing guidelines has been driven by emerging information about shifting patterns of disease. A rise in the prevalence of staphylococcal skin flora has been noted as the causative organism for community-acquired as well as iatrogenic nosocomial IE. Treatment of IE has been complicated by emergence of multidrug resistance for streptococci, staphylococci, and enterococci. Lack of complete concordance among various guidelines stems from the preponderance of case-control studies, animal data, and expert opinion in guiding the recommendations.

Patients considered at high or moderate risk have an increased risk of contracting IE from a transient bacteremia. High-risk groups include patients with a previous history of IE, prosthetic heart valves, surgically created conduits, and complex cyanotic congenital anomalies. Moderate-risk groups include persons with acquired valvar heart disease, noncyanotic congenital heart disease, hypertrophic cardiomyopathy, and mitral valve prolapse with regurgitation or severe valve thickening. The risk of IE in patients with mitral valve prolapse and important mitral regurgitation is estimated to be five times that of the normal adult population. Use of antibiotic prophylaxis for anyone with a systolic murmur has been deemed cost-effective in the British guidelines. IE has been reported following colonoscopy, but transient bacteremia is not associated with CT colonography.
Table 15-5  Antibiotic Prophylaxis Regimen for Dental Procedures

<table>
<thead>
<tr>
<th>Situation</th>
<th>Agent</th>
<th>Adults</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral</td>
<td>Amoxicillin</td>
<td>2 g IM or IV</td>
<td>50 mg · kg⁻¹ IM or IV</td>
</tr>
<tr>
<td>Unable to take oral medication</td>
<td>Ampicillin or Cefazolin/ceftriaxone</td>
<td>2 g IM or IV</td>
<td>50 mg · kg⁻¹ IM or IV</td>
</tr>
<tr>
<td>Allergic to penicillin or ampicillin</td>
<td>Cephalexin or Clindamycin or Azithromycin/clarithromycin</td>
<td>2 g IM or IV</td>
<td>50 mg · kg⁻¹ IM or IV</td>
</tr>
<tr>
<td>Allergic to penicillin, unable to take oral medication</td>
<td>Cefazolin/ceftriaxone or Clindamycin</td>
<td>1 g IM or IV</td>
<td>50 mg · kg⁻¹ IM or IV</td>
</tr>
</tbody>
</table>

Adapted from Delahaye and colleagues.⁶¹

The regimens indicated here can be used for invasive respiratory procedures and gastrointestinal and genitourinary procedures in which prophylaxis is indicated.

Key: IM, Intramuscular; IV, intravenous.

Box 15-7  Procedures to Possibly Consider for Antibiotic Prophylaxis Because of Associated Bacteremias

- Transesophageal echocardiography
- Percutaneous transluminal coronary angioplasty with or without stenting
- Occlusive device implantation
- Balloon valvuloplasty
- Upper gastrointestinal endoscopy with or without biopsy
- Circumcision
- Cervical smears
- Acupuncture, body piercing, and tattooing

Adapted from Delahaye and colleagues.⁶²

Recommendations regarding specific procedures differ somewhat between U.S. and European guidelines. Procedures common to all guidelines are listed in Box 15-6, and additional procedures to consider from the 2004 British guidelines are listed in Box 15-7. Specific antibiotic recommendations are summarized in Table 15-5.

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B

C


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Bradycardia

DEFINITION

Abnormal bradycardia is a slow cardiac rate that results chronically or episodically in inadequate cardiac output or life-threatening ventricular arrhythmias.

HISTORICAL NOTE

During the early 1700s, peripheral pulsations of the circulation began to be timed, and in 1717 Gerbezius recognized bradycardia as a deviation from the usual pulse rate. Morgagni is believed to have surmised the relationship between bradycardia and syncope in 1761, but he attributed both to melancholy. In 1827, Adams accurately described Adams-Stokes syndrome and proposed that it had a cardiac origin. This idea was not well accepted until Stokes, in 1846, collected reports of seven patients with the condition and agreed with Adams’ concepts. The phrase maladie de Adams-Stokes was originated in 1899 by Huchard.

Understanding the morphologic basis of Adams-Stokes syndrome began after Harvey’s description of the cardiac cycle. Cardiac conduction tissues were first described by Purkinje in 1845, which he mistook as cartilage tissue. The atrioventricular (AV) conduction bundle was described by His in 1893, and in 1896, Aschoff and Tawara described the AV node and its connection to the His bundle.

It has long been known that the heart responds to external electrical stimulation. As long ago as 1804, Aldini successfully stimulated systole in the hearts of decapitated criminals. Apparently it was known during the late 1800s that direct heart puncture with or without injecting drugs would occasionally produce effective cardiac contractions. Mond reported in 1929, Lidwill in Australia successfully paced the heart of a stillborn infant for a time by direct ventricular puncture. In 1932, Hyman atrially paced several patients with what he termed an artificial pacemaker, and Bigelow and colleagues in Toronto paced canine hearts by esophageal and precordial electrodes in 1950.

In 1952 in Boston, Zoll reported successfully pacing hearts of patients with complete heart block with external cutaneous electrodes and a large and relatively nonmobile pulse generator. This method was the only one available when intracardiac surgery came into existence during the mid-1950s, and although stimulation of each heartbeat was accompanied by skeletal muscle contractions, and skin under the electrodes quickly became excoriated, this method kept some cardiac surgical patients alive until sinus rhythm returned. However, for patients in whom sinus rhythm did not return, the agony of skeletal muscle contractions and skin excoriations increased as the days passed. Sheer terror developed with approach of the surgeon who would each day provoke an Adams-Stokes episode by turning off the pacer to see whether an adequate idioventricular rhythm, let alone sinus rhythm, would replace the electrocardiographic image of P waves without any QRS complex.

Change began when Lillehei, in Minneapolis, enlisted the help of Earl Bakken, a television engineer and later founder of Medtronic Corporation, in developing a small portable pacemaker. More importantly, he devised the technique of...
leaving a wire attached to the ventricular epicardium at operation and bringing it out externally. The external electrode was used to pace the heart with minimal patient discomfort.\textsuperscript{96} Later, Thevenet, Hodges, and Lillehei devised a method of inserting the wire into the ventricle through a needle passed through the skin over the precordium without an operation.\textsuperscript{72} These systems used a portable pacemaker system devised by Bakken.

In 1959, Elmquist and Senning in Stockholm reported placing the first totally implantable pacemaker system using epicardial electrodes.\textsuperscript{87} This advance was made possible by invention of transistors during the 1950s. In 1960, Chardack, Gage, and Greatbatch described a self-contained, implantable pulse generator driven by a mercury cell battery for use with implanted epicardial leads.\textsuperscript{65}

During the previous year, Furman and Robinson had reported the use of endocardial electrodes introduced transvenously rather than epicardially.\textsuperscript{14} Their data supported the idea that endocardial and epicardial electrodes perform similarly. This led to widespread availability by 1961 of both endocardial electrodes inserted transvenously and epicardial electrodes inserted by thoracotomy. These early pacemakers paced at a set rate and did not sense spontaneous cardiac activity. They were crude by present standards but allowed 85% of patients having Adams-Stokes episodes to survive for at least 1 year, in contrast to less than 50% before their introduction.

Rapid developments followed, and pulse generators that sensed the QRS and fired only when no spontaneous QRS occurred within a specified time became available during the mid-1960s. Much work led by Greatbatch during the late 1960s and early 1970s to improve the cells (batteries) resulted in commercial availability of lithium cell–powered pulse generators during the early 1970s. The lithium cells were much more reliable and, with hydrogen gas no longer being liberated in the pulse generator, hermetic sealing of the entire device became possible. More complicated electronic circuits were developed to permit programming of rate and stimulus duration as well as better QRS sensing as transistorized circuits with a few components evolved into hybrid circuits with more components, into integrated circuits, and finally into implantable pulse generators containing microprocessors.

Further improvements permitted atrial sensing and pacing as well as ventricular sensing and pacing (universal pacing) and ventricular pacing synchronized with the patient’s atrial contractions, and sequential AV pacing.\textsuperscript{1,11} Currently available pacemakers provide sensing of either body motion or increase in respirations and use the information to alter pacing rate appropriate for patient activity. Finally, the combination of multiprogrammability with diagnostic radio and telephonic transmission has permitted accurate evaluation of pacemaker function and noninvasive adjustment of pacemaker variables for optimal treatment of the patient.

Improvements in pacing electrodes have been made through the years in the form of better wire alloys, antifracture characteristics, electrode pacing threshold properties, and lead insulation. These improvements have diminished the occurrence of high pacing thresholds and lead fracture.

**MORPHOLOGY**

Abnormal bradycardia may be the result of complete heart block, a condition in which P waves (atrial depolarization) occur at a constant interval but are unrelated to the less frequently occurring or absent and often broad QRS complexes (ventricular depolarization).

**Heart Block**

Complete heart block may be present at birth or develop later in life.

**Congenital Complete Heart Block**

Musculature of the atrial septum may be congenitally deficient near the AV valves, such that there is a diminished or absent connection between the atria and the AV node. Lev described morphologic discontinuity between AV node and bundle of His as another basis for congenital complete heart block in otherwise normal hearts.\textsuperscript{1,3} In hearts with AV discordant connections, complete heart block may be present at birth, presumably related to these same mechanisms.

**Spontaneously Developing Complete Heart Block**

Some congenital anomalies of the bundle of His may predispose patients to developing complete heart block. Thus, in hearts with AV discordant connection, unusually long length of the bundle of His is believed to predispose it to fibrosis and loss of function.

Certain disease processes may damage the conduction system. Calcification of the aortic valve may extend into the underlying ventricular septum and damage the bundle of His by a shearing effect during certain phases of the cardiac cycle. Mitral calcification does the same less commonly. Acute coronary occlusions resulting in posteroinferior myocardial infarctions may be associated with temporary AV node ischemia and heart block.

An increase in fibrous tissue of the bundle of His and its branches, accompanied by a decrease in number of conduction fibers, seems to be part of the aging process. Progressive fibrosis and fiber loss in left and right bundle branches and resultant heart block (Lev disease, Lenegre disease) may represent acceleration of this process. Anteroseptal myocardial infarctions produce ischemic necrosis in and around right and left bundle branches and may result in permanent heart block. Chronic ischemic heart disease can gradually result in septal fibrosis, with loss of function in both bundle branches. Dilated cardiomyopathy (see “Dilated Cardiomyopathy” in Section II of Chapter 20) may be associated with long-standing left ventricular fibrosis that may involve the bundle branches and produce complete heart block.

**Surgically Induced Complete Heart Block**

During surgical procedures for repair of ventricular septal defects (isolated or as part of tetralogy of Fallot and other complexes; see Chapters 35, 38, and 52 through 56) or AV septal defects (see Chapter 34), resection of discrete subvalvar aortic stenosis (see Chapter 47), and replacement of the mitral, aortic, or tricuspid valves (see Chapters 11 through 14), the bundle of His or contiguous AV node may be severed or sutured. In the absence of such direct injuries, the conduction bundle or AV node may be functionally damaged by hemorrhage, with resultant complete heart block. Although fibrosis must develop in these surgical areas late postoperatively, it is interesting that complete heart block is rare late after operation.
Other Bradyarrhythmias

Sinus Node Dysfunction

Important sinus node dysfunction may develop without identifiable morphologic changes in the node. Loss of sinus node cells normally associated with aging may accelerate and cause dysfunction, especially in patients with a subnormal nodal cell population at birth. Amyloid deposition may occur within the sinus node and produce dysfunction. Direct damage to the sinus node by surgical procedures occurs but is uncommon. Damage to the sinus node can result in a junctional rhythm that becomes slower as time passes. In the absence of direct injury, surgical procedures in the region of the sinus node, such as the atrial switch operation (see “Atrial Switch Operation” under Technique of Operation in Chapter 52) and Fontan operation (see “Technique of Operation” in Section IV of Chapter 41), may result in late perinodal fibrosis, with consequent loss of sinus node function. This process may be due to damage to the sinus node artery. This transeptal approach to the left atrium, which often involves an incision in the roof of the right atrium and division of the sinus node artery, can also result in temporary or permanent sinus node dysfunction.

Dysfunction of Pathways between Sinus and Atrioventricular Nodes

Preferential conduction pathways between the sinus and AV nodes may be interrupted by congenital absence of electrical continuity in these areas. Surgical procedures, especially atrial switch and Fontan operations, may rarely damage preferential conduction pathways immediately. More commonly, late postoperative fibrosis develops and interferes with conduction along these pathways, and a slow junctional rhythm results.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Pathophysiology

Hemodynamic Effects

Although blood flow into the aorta and large arteries is intermittent (pulsatile), the combined effects of the aortic valve, elasticity of the aorta and great arteries, and characteristics of the arterial distributing system make flow rate relatively constant in capillaries. Thus, cells of the brain and other organs receive continuous nutrient flow. The magnitude of this flow is related to, among other things, net forward flow across the aortic valve with each ventricular systole and heart rate. When the stroke volume is large and heart rate slow, as in trained athletes at rest, elasticity of the aorta and its filling during systole are sufficient to maintain an adequate volume of runoff during a long diastolic period, and thus an adequate nutrient flow to cells of the brain and other organs. When stroke volume is not large, runoff during the late part of chronically long diastolic periods may be inadequate to maintain the proper internal milieu of cells of the brain and other organs. Because the brain is particularly sensitive to hypoxia, cerebral symptoms usually develop before those from dysfunction of other organs.

Cardiac Electrophysiologic Effects

The longer the intervals between periodic depolarizations of ventricular myocardium, the greater the degree of QT prolongation and the higher the likelihood of developing ventricular extrasystoles or tachycardia or both, especially of the torsades de pointes variety (long QT syndrome). Thus, bradycardia predisposes the patient to life-threatening ventricular arrhythmias. Furthermore, with complete heart block, there is the possibility of prolonged ventricular asystole.

Symptoms

Clinical manifestations of first-degree heart block (PR interval > 0.2 second in adults) are rare. Second-degree heart block (intermittent lack of AV conduction) may be manifested by bradycardia and symptoms. In third-degree (complete) heart block (all atrial impulses fail to be conducted to the ventricle), bradycardia is present, and symptoms are frequent.

Approximately a quarter of patients with sinus node dysfunction have ischemic heart disease.

Diagnostic Criteria

Bradycardias are diagnosed largely by electrocardiographic (ECG) criteria.

Atrioventricular Block

Complete AV block and symptomatic incomplete AV block (such as 2:1 second-degree AV block) are diagnosed by standard ECG. When paroxysmal AV block is suspected as the cause of symptoms, prolonged ambulatory ECG monitoring may provide confirmation of the diagnosis (see “Indications for Intervention” later in this section).

Sick Sinus Syndrome

Symptomatic arrhythmias in sick sinus syndrome include profound sinus bradycardia, junctional bradycardia, sinus arrest, sinus node exit block, and the so-called tachycardia-bradycardia syndrome in which paroxysmal atrial tachycardia, flutter, or fibrillation is followed by symptomatic pauses caused by overdrive suppression of the sinus node and subsidiary pacemakers. In most of these patients, the resting ECG may not be diagnostic, and prolonged ambulatory ECG monitoring is required to document the abnormal rhythm. Electrophysiologic study is of limited help because abnormal sinus node recovery times or sinoatrial conduction times are demonstrable in only a small minority of symptomatic patients.

Carotid Sinus Syndrome

A hyperactive carotid sinus reflex is said to be present when digital stimulation of the carotid sinus results in cardiac asystole lasting 3 or more seconds. Carotid sinus syndrome is diagnosed when, in addition to the presence of a hyperactive reflex, the patient’s spontaneous symptom complex can be reproduced by stimulation of one or both

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1The two types of second-degree heart block are Mobitz I, in which AV conduction time is progressively prolonged (Wenckebach period) until one atrial impulse is not conducted to the ventricle, and Mobitz II, in which AV conduction times are constant, but episodically an atrial impulse is not conducted to the ventricles.
(not simultaneously) carotid sinuses. Pacemaker therapy may completely relieve symptoms in patients with only a cardio-inhibitory response. However, the presence of a simultaneous vasodepressor response should also be sought by repetition of massage after intravenous atropine and measurements of the blood pressure. Preservation of the heart rate may not prevent symptoms caused by hypotension in such patients.

**NATURAL HISTORY**

Bradyarrhythmia from both spontaneous heart block and spontaneous sinus node dysfunction tends to occur in elderly patients. The mean age of patients at the time of diagnosis of spontaneously occurring heart block is 70 years. The proportion of patients who have complete heart block developing spontaneously who remain asymptomatic is not known. The most common clinical manifestation is an Adams-Stokes episode. This syndrome is part of the history in 60% to 70% of patients. Symptoms probably eventually develop in most patients. The exact proportion of symptomatic patients is in part determined by functional status of the heart as a whole. Likewise, the tendency toward premature death is related to functional status of the myocardium along with other risk factors.

Patients with Adams-Stokes episodes as a manifestation of complete heart block and who are not paced have a 1-year survival of 50% to 75%, much less than that of an age-sex-race–matched general population. One-year survival is said to be 70% to 80% in patients with complete heart block but without a history of syncope. These differences persist with follow-up to 15 years and appear to be related to the considerably higher prevalence of sudden death in the patients who have syncopal attacks. Syncopal attacks, as well as sudden death, in patients with idioventricular or bundle of His rhythm usually result from sudden ventricular asystole. Syncopal attacks also may be precipitated by a sudden reduction in stroke volume or increased metabolic demands.

**Congenital Complete Heart Block**

Infants born with congenital complete heart block and hearts that are otherwise normal have a prognosis that may be somewhat better than that for patients with spontaneously developing complete heart block. Ten-year survival for congenital complete heart block is about 85%, with most deaths occurring in the first month of life. Deaths occurring after this time are related to Adams-Stokes episodes.

**Surgically Induced Complete Heart Block**

In the early years of cardiac surgery when epicardial and transvenous pacing was not possible, hospital mortality was greatly increased in patients in whom complete heart block developed perioperatively. Unpaced hospital survivors had a 1-year survival of about 40%.

**Sinus Node Dysfunction**

The natural history of patients with this type of bradycardia has not been clearly described.

**TECHNIQUE OF INTERVENTION**

Development of techniques and devices for cardiac pacing has involved surgeons, physicians, interventional cardiologists, and industry, and advances continue to be made. Methods of insertion and the devices implanted are constantly being improved. Whereas in the 1960s pacemakers were usually inserted by cardiothoracic surgeons, currently in many parts of the world they are inserted, managed, and followed by cardiologists, and often by cardiologists with specialized knowledge of cardiac electrophysiology. Because of these developments, it is no longer practical to include detailed descriptions in a textbook of cardiac surgery. Instead, only general information regarding cardiac pacemaking and basic device insertion procedures are discussed.

**Pacing Modes**

There are a number of pacing modes. In addition to the basic characteristics described here, many pacemakers have special tachyarrhythmia functions and other programmable functions. Also, some pacemakers sense some surrogates of increased metabolic activity (e.g., body motion, increased rate or volume of respiration) and increase pacing rate accordingly.

**VVI**

In VVI mode, the ventricle is paced (V), sensing is from the ventricle (V), and response to a sensed spontaneous ventricular depolarization is inhibition (I) of delivering the next electrical stimulus by the pulse generator. The disadvantage of this pacing mode is lack of atrial contributions to ventricular filling. The advantage is simplicity of electrode placement and a relatively long life of the pulse generator.

**AAI**

In AAI mode, the atrium (A, usually the right) is paced, sensing is from the atrium (A), and sensed atrial depolarization inhibits (I) the next programmed electrical impulse. The AAI mode requires normal AV conduction and functioning atrial pathways to the AV node. This type of pacing mode was anticipated and pioneered by Lillehei and colleagues as early as 1963.

The AAI mode is seldom used (<5%), primarily because many patients with sinus node dysfunction ultimately require ventricular pacing. Its advantage is preservation of atrial contribution to ventricular filling.

**VDD**

VDD mode, as well as DVI and DDD modes described subsequently, requires both atrial and ventricular electrodes. It also requires relatively normal sinus node function. In VDD mode, the ventricle is paced (V), both the atrium and ventricle are sensed (D denotes dual chamber or dual function), and the response of the pulse generator may be either the triggering or inhibiting (D) of the next electrical pulse. Generally, sensed atrial depolarization triggers a stimulating pulse to the ventricular electrode at a preset or variable PR interval. Ventricular stimulus is inhibited when spontaneous ventricular depolarization follows atrial depolarization within the set PR interval of the pulse generator. The pulse generator is programmed so that when the PP interval becomes excessively long, the pulse generator functions in VVI mode.
Advantages of the VDD mode are preserved atrial contribution to ventricular filling and ventricular rate that follows the patient’s own atrial rate, thereby responding appropriately to stress and exercise. Disadvantages are need for both atrial and ventricular electrodes and the possibility of producing a reciprocating (loop) tachycardia by retrograde conduction.

**DVI**
Both atrium and ventricle (D) are paced in DVI mode, with an appropriate interval between the stimuli to each. Ventricular (V) but not atrial depolarization is sensed. A sensed ventricular depolarization inhibits (I) the next dual pacing stimulus in noncommitted DVI mode; it does not do so in committed DVI mode.

The advantage is maintaining atrial contribution to ventricular filling even when sinus node function fails. Raza and colleagues, Raichlen and colleagues, and others have documented the hemodynamic advantages of this arrangement. The disadvantage is that AV synchronization is lost when the atrial rate increases during exercise or stress.

**DDD**
DDD mode, or universal pacing mode, can pace both atrium and ventricle (D), sense both atrial and ventricular depolarization (D), and either trigger or inhibit (D) an electrical pacing pulse. Its advantage is universality of application. Disadvantages are that dual stimulation reduces battery lifetime, and loop tachycardia can occur with variations in retrograde conduction from ventricles to atria. These disadvantages can be eliminated or reduced by programming the pacemaker pulse generator characteristics according to changes in the patient’s AV and ventriculoatrial conduction characteristics.

**Electrode Testing**
Each electrode placed is tested at the time of insertion. The **pacing threshold**, or the lowest delivered voltage at which myocardial depolarization occurs, is tested first. For ventricular electrodes, a threshold of 0.3 V or less (usually at 0.5-ms pulse duration) is optimal. A threshold of 0.3 to 0.5 V is frequently observed, and a threshold as high as 1.0 V is acceptable. Higher thresholds are undesirable because they reduce pulse generator life. For atrial electrodes, a stimulating threshold of 1.0 V or less is acceptable. In open chest insertion, use of the electrocautery tends to increase the stimulating threshold.

The electrode is then tested for its **sensing capabilities**. For both endocardial and epicardial ventricular electrodes, a QRS complex in the electrogram of 5 mV or more is desirable. For atrial electrodes, a P wave with peak-to-peak amplitude of 2 mV or more is acceptable.

Other important testing for a transvenously placed electrode includes determining that (1) it does not provoke ventricular tachycardia by its position, (2) its position is mechanically stable, and (3) it does not pace the diaphragm or skeletal muscle. Bipolar electrodes are generally used; they are less subject to interference by skeletal muscle contraction than unipolar electrodes. The latter are sometimes used when the pulse generator surface serves as the indifferent electrode.

**Transvenous Electrode Insertion and Pulse Generator Placement**
After the patient is positioned on the operating table, temporary pacing wires, if present, are secured with their tips outside the operative field and attached to an external pulse generator. The operative field is prepared and draped, including the lower neck and anterior chest wall. Wires are passed from the surgical field for emergency pacing, obtaining endocardial electrograms, pulse generator testing, and lead threshold measurement. An adjustable constant-current, dual-channel, external pulse generator is used to determine atrial capture when simultaneous atrial and ventricular pacing are necessary.

Local anesthesia is administered to achieve a field block. An oblique or transverse incision is made below the clavicle, generally on the left side (on the right for left-handed individuals). A subcutaneous pocket is created over the pectoralis major fascia. The pocket should be appropriate for size of the pulse generator. If no permanent pacing electrodes are in place, electrocautery may be used for the dissection and to achieve hemostasis.

Edges of the incision are retracted to expose the space between first rib and clavicle for access to the subclavian vein. A needle with a syringe attached is used to locate and penetrate the vein. A flexible J-tip guidewire is passed through the needle into the subclavian vein and advanced into the superior vena cava. Position of the guidewire is confirmed by fluoroscopy, and the needle is withdrawn and replaced with a peel-away sheath catheter. The distal 5 cm of the stylet for the ventricular electrode is bent into a small curve and inserted into the electrode. The electrode and stylet are placed into the sheath catheter and advanced into the right atrium, after which the sheath catheter is peeled away and removed. Under fluoroscopic control, the electrode is advanced through the tricuspid valve into the right ventricle and further advanced into the pulmonary trunk to ensure that the coronary sinus has not been entered. The curved stylet is replaced with a straight one that is not fully inserted, leaving the electrode flexible in its distal 5 to 10 cm. The electrode is withdrawn along the ventricular septum until an appropriate anatomic position has been found among the trabeculations near the ventricular apex. The stylet is advanced to the tip of the electrode to stiffen the electrode. It is advanced gently among the trabeculations and “seated.” It is secured passively by the tines on the electrode or by extruding its attachment coil. The stylet is removed.

The electrode is then tested (see “Electrode Testing” earlier in this section). Testing with deep breathing is done to judge and set the final length of catheter within the ventricle when the diaphragm is in its most inferior position. Once a suitable anatomic and functional position has been located, the lead is secured with a small plastic sleeve to the pectoral fascia to prevent inadvertent displacement.

Placing the atrial electrode, if one is to be used, is done after inserting the ventricular electrode. Penetrating the subclavian vein for inserting the atrial electrode is preferentially performed at the beginning of the procedure. After the guidewire for the ventricular electrode is inserted, a second guidewire is inserted into the subclavian vein. Separate penetration of the subclavian vein is desirable to prevent dislodging the ventricular electrode while manipulating the atrial electrode. Alternatively, the guidewire used for ventricular
electrode insertion may be withdrawn and used subsequently for atrial electrode insertion. Bleeding from the subclavian vein puncture site, however, may be a problem.

A second peel-away sheath catheter is inserted into the subclavian vein over the guidewire and the atrial electrode inserted through it over the guidewire. The electrode is advanced into the right atrium with stylet in place. The stylet is withdrawn, permitting the pre-formed J-curve to appear in the electrode. Manipulation of the stylet and gentle rotation of the electrode permit positioning of its tip into the atrial appendage. This position is verified by the lateral to-and-fro motion of the tip and may be confirmed by lateral fluoroscopy. The electrode tip is secured to atrial endocardium by extruding the screw-in coil. The electrode is then tested (see “Electrode Testing” earlier in this section). After a satisfactory position is achieved, the electrode is secured to the pectoralis fascia by a suture.

The appropriate pulse generator is selected, inspected, and checked by the pacemaker system analyzer. The ends of the pacing leads are cleaned to remove blood or tissue and are inserted into the pulse generator. Satisfactory function of the pacing system is verified by ECG before wound closure. The wound is inspected for hemostasis and irrigated with antibiotic solution. The pacing system is cleaned with an antibiotic solution, placed in the pocket, and secured with nonabsorbable sutures. The pacing leads are kept away from the anterior surface of the pulse generator to prevent injury during subsequent pulse generator replacement. The wound is closed in layers, with the first layer isolating the pulse generator pocket from the remainder of the incision.

Electrode Insertion by Thoracotomy and Pulse Generator Placement

When an open technique is necessary, the patient is positioned on the operating table for a sternotomy, left anterior thoracotomy, or epigastric incision. For single-chamber (ventricular pacing) insertion, anterior thoracotomy or epigastric incisions are adequate. When dual-chamber pacing is contemplated or when pacing is required early after a cardiac operation, a median sternotomy is used. Procedures regarding temporary pacing wires, skin preparation, and draping are the same as for the transvenous approach.

In adults, a separate transverse left upper quadrant abdominal or infraclavicular incision is made and a pocket developed in the prefascial space. In infants and usually in children, the pocket is created behind the rectus abdominis muscle. A site for electrode attachment to the right or left ventricle is identified in a region of myocardium uncovered by fat, away from any coronary arteries and from the phrenic nerve, and if possible, not directly under the sternum. If there is uncertainty about the site, an electrode probe can be used to locate an appropriate site for placing the electrode. Screw-in electrodes are commonly used for ventricular pacing because of ease of insertion. They are secured by clockwise rotation of the cork-screw electrode with gentle pressure on the myocardium. Electrodes that lie on the epicardial surface, held in place with fine sutures, are preferable for atrial pacing even though they are more difficult to insert. If space permits, two electrodes are placed in each location. The electrodes are tested as previously described.

A tunnel is created from the pericardial cavity to the previously formed subcutaneous pocket. An appropriate pulse generator is selected, tested, and connected to the electrodes.

Wounds are closed in layers, and one chest tube is left for closed drainage.

Permanent Pacing after Intracardiac Surgery

Complete heart block occurring during cardiac operation is managed by placing temporary pacing electrodes on the right ventricle and right atrium so that AV sequential pacing can be performed using an external pulse generator. The pacing threshold of the temporary electrodes should be tested daily. When it appears that complete heart block or profound bradycardia is likely to be permanent, an implantable pacing system is inserted by the transvenous or open route.

The notable exception to this strategy is when there is a high probability of complete heart block developing at operation or when heart block may develop later and access to the right ventricle by the transvenous route is not possible. This includes patients who have replacement of the tricuspid valve with a mechanical prosthesis. These patients should have permanent epicardial electrodes placed at the time of the cardiac operation. Bioprosthetic valves in the tricuspid position may be crossed by a transvenous electrode without important impairment of prosthetic valve function.

Before discontinuing cardiopulmonary bypass (CPB), cardiac action is established by AV sequential pacing through two temporary right atrial and two temporary ventricular wires attached to an external pulse generator. Single bipolar temporary wires may also be used. Preferably, permanent ventricular electrodes are placed after discontinuing CPB and completing hemostasis, because electrocautery tends to increase the pacing threshold of already implanted leads. Permanent atrial electrodes should also be placed if dual chamber pacing is desired. The ends of the permanent leads are capped and placed subcutaneously in the left upper quadrant of the abdomen or brought through the anterior chest wall to a subcutaneous position below the left clavicle. A loop of lead is left within the pericardial cavity.

If heart block persists, the patient is returned to the operating room. With the patient under local anesthesia and conscious sedation, the surgical field is prepared. A transverse incision is made over the left upper quadrant of the abdomen (or below the clavicle), and the electrode ends are retrieved. The electrodes are tested and attached to the pulse generator, a pocket is created for it, and the incision is closed. The temporary wires are withdrawn.

Alternatively, the pulse generator can be attached to the electrodes and implanted at the time of cardiac repair. The disadvantage is that sinus rhythm may return in a few days, and the pulse generator may no longer be essential. There is also risk of bleeding into the pulse generator pocket, with formation of a hematoma.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Usual care for cardiac surgical patients is given early postoperatively (see Chapter 5). In addition, a chest radiograph is obtained to ascertain position of the leads. Pacing threshold is usually not determined by noninvasive testing prior to hospital discharge, because thresholds obtained at this time are always higher than those obtained 6 weeks to 3 months
later. Reprogramming of the pulse generator at an appropriate voltage is best done later, leaving the relatively higher and safer pacing voltage until that time.

The electrodes are considered to have become stable by about 6 months after implantation.\(^{113}\) Around that time they are rechecked, and the pulse generator is set at the lowest output considered to be safe.

### RESULTS

#### Survival

It is generally agreed that survival of patients with bradycardia is improved by permanent pacing.\(^{35}\) Death early after pacemaker insertion is unusual, and when it occurs it is usually due to coexisting cardiac problems.\(^{85,324}\) This is true for children as well as adults.\(^{318}\) Ten-day mortality is 1.6%, and 30-day mortality is 2.7% (Fig. 16-1).

Survival late after pacemaker insertion is satisfactory, with 5- and 10-year survival of 59% and 39%, respectively\(^{212,111}\) (see Fig. 16-1). Survival is similar in those whose bradycardia is from heart block and those in whom it is related to sinus node dysfunction.\(^{111,324}\) Advanced age decreases late survival (Table 16-1), as does chronic heart failure and presence of ischemic heart disease.\(^{49,10,11,10,2,324}\)

#### Table 16-1 Survival by Patient Age after Pacemaker Implantation

<table>
<thead>
<tr>
<th>Age ≥Years</th>
<th>&lt;</th>
<th>5-Year Survival</th>
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<tbody>
<tr>
<td>40</td>
<td>50</td>
<td>83</td>
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<td>80</td>
<td>90</td>
<td>51</td>
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### Infection and Pulse Generator Erosion

Infection and pulse generator erosion are not always identified separately as complications of pacemaking, and they must therefore be considered together.

Even with meticulous surgical technique and prophylactic antibiotic therapy, infection in the wound and around the pulse generator and leads occurs in 0.5% to 2% of cases.\(^{311,321}\) Treatment consists of inserting an entirely new pacemaker system at a different site and complete removal of the old system.\(^{83}\)

Excessive pressure of the pulse generator or wire against the overlying skin or subcutaneous tissue can cause necrosis and permit their exposure.\(^{321}\) The true prevalence of this condition is unknown because it is often considered infection. Insertion of pulse generators in small pockets with skin closure under tension increases the chance of skin necrosis. When the pulse generator and leads become exposed as a result of pressure necrosis, treatment is the same as for an infected pacemaker. Preventing this problem is best achieved by forming the pulse generator pocket in the immediate prefascial space to permit as much tissue as possible to come between pulse generator and skin.

### Lead and Electrode Malfunction

#### Time-Related Variability of Pacing Thresholds

The lowest possible initial pacing and sensing thresholds are sought at the time of placing the electrodes, because thresholds frequently rise later.\(^{110}\) One or more months after insertion, more than half the leads have a threshold pacing level greater than any level measured initially or during the first month of use.\(^{520}\) Forty-five percent of epicardial electrode leads have either a grossly unstable threshold pacing level or a gradually increasing level (Fig. 16-2) for as long as 10 years after insertion (Fig. 16-3).\(^{520}\) These “spikes” in the threshold pacing level may be associated with episodes of intercurrent infection. Such changes probably account for at least some of the sudden deaths that occur late after initiating pacing for complete heart block after repair of congenital heart disease.

![Figure 16-1](image-url) Survival of 1068 patients with permanently implanted pulse generators. Time zero is time of pacemaker implantation. Vertical lines encompass ±1 standard error. Numbers in parentheses indicate patients remaining at risk. (UAB group, 1961 to 1984; Shepard RB: personal communication; 1985.)

![Figure 16-2](image-url) Variation in pacing threshold after development of complete heart block following repair of “single” ventricle. Note episodic and unpredictable sudden increases in threshold, which could have led to sudden death if output from the pulse generator had been insufficient to overcome them. (From Shepard and colleagues.\(^{529}\))
these symptoms may not be the result of pacing per-
ding either ventricular or atrial endocardial leads. Dislodgment
occurs in less than 2% of cases.\textsuperscript{F10,V4}

Undersensing
Undersensing, or lack of recognition of the heart’s depo-
larization, is related most commonly to inadequate placement
of the electrode. At times it can result from fibrosis at the
electrode-myocardial junction. This complication leads to
competitive pacing. Undersensing can generally be treated by
noninvasive programming to increase sensitivity of the pulse
generator.

Electrode Dislodgment
Electrode dislodgment, with or without right ventricular or
atrial perforation, is the most common complication of insert-
ing either ventricular or atrial endocardial leads. Dislodgment
occurs in less than 2% of cases.\textsuperscript{F10,V4}

Lead Fracture
Lead fracture, with consequent loss of pacing, is an infre-
tant early complication of pacemaking but is not uncom-
mon years after implantation.

New Symptoms from Pacing in VVI Mode
Syncope or near-syncope is one of the most important symp-
toms resulting from pacing. Syncope as a manifestation of
pacemaker syndrome occurs in less than 10% of patients being
paced in VVI mode. Arterial hypotension may also develop.
These symptoms usually occur when ventriculoatrial conduc-
tion is intact and the indication for pacing has been sinus
node dysfunction.\textsuperscript{N6} The exact etiology of symptoms is uncer-
tain, but they may be due to lack of atrial contribution to
ventricular filling secondary to AV asynchrony, with or
without atrial contraction against a closed AV valve. Also, AV
valve regurgitation may be caused by asynchronous contrac-
tion of atria and ventricles.\textsuperscript{M10} Diagnosis is suspected when
those symptoms and signs are present and can sometimes be
verified by an increase in blood pressure when pacing is
stopped and a decrease when it is restarted. Treatment is
VDD or DDD pacing.

Dizziness occurs in about one third of patients. Because
both dizziness and syncope are common in elderly patients,
these symptoms may not be the result of pacing per-

\textbf{INDICATIONS FOR INTERVENTION}

The most common indication for permanent cardiac pacing
is symptomatic bradycardia.\textsuperscript{F12} It may be intermittent or per-
manent and due to complete heart block, second-degree AV
block, or sinus node dysfunction. Symptoms must be directly
attributable to the bradycardia and may include syncope, diz-
ziness, exercise intolerance, and heart failure. When ambula-
tory ECG monitoring is negative for abnormal bradycardia,
electrophysiologic study is indicated in patients with unex-
plained transient neurologic symptoms. The finding of pro-
longation of the HV interval (time from onset of activation of
the bundle of His to the earliest onset of ventricular depo-
larization) of at least 70 milliseconds supports a diagnosis
of paroxysmal AV block as the cause of the symptoms and
justifies elective pacemaker implantation.\textsuperscript{N8} In the absence of
neurologic symptoms, however, the finding of such HV pro-
longation rarely if ever warrants prophylactic pacemaker
implantation.\textsuperscript{D8}

Another indication is surgically induced complete heart
block, because of the risk of an Adams-Stokes episode. Patients
in sinus rhythm after repair of congenital malforma-
tions, but in whom complete heart block follows repair and
persists for a number of days before reversion to sinus rhythm,
are at increased risk for developing late symptomatic heart
block. These patients should be considered for prophylactic
pacemaker implantation before hospital discharge, particu-
larly when subsidiary escape pacemakers have been absent or
unreliable.

In some situations, permanent pacing may be indicated in
asymptomatic patients because of risk of an Adams-Stokes
episode.\textsuperscript{F11} These situations include profound bradycardia
(ventricular rate < 40 beats \textperiodcentered min\textsuperscript{-1}), second-degree AV block
at the infra-His level, advanced second-degree AV or com-
plete heart block after myocardial infarction, and congenital
heart block with a wide QRS escape rhythm. Other rhythms
may be an indication for pacing in asymptomatic patients.
These include new bundle-branch block with transient
second-degree AV block postmyocardial infarction, bifascicu-
lar bundle-branch block with intermittent type II second-
degree AV block, sinus node dysfunction, and transient
post-surgical AV block that reverts to bifascicular block in
children.\textsuperscript{F11,H16} In sinus node dysfunction, for example, when
symptoms are relatively infrequent, the decision to advise
permanent pacing may rest on the demonstration of asym-
ptomatic sinus pauses, sinoatrial exit block, or both.

A special situation is extensive intraatrial operations such
as the Senning or Mustard operation (see “Senning Tech-
nique” and “Mustard Technique” under Technique of Oper-
ation in Chapter 52) or the Fontan operation (see Chapter
41). Junctional rhythm often develops late postoperatively
with the potential of tachybradycardia and sudden death. This
situation is an indication for atrial pacing (AAI).\textsuperscript{M10}

In response to publication of studies advancing the knowl-
edge of the natural history of cardiac arrhythmia optimally
-treated by cardiac pacing and important advances in pacing
Box 16-1  Indications for Permanent Pacemaker Insertion Based on ACC/AHA/HRS Guidelines: Acquired Atrioventricular Block in Adults

**Class I**
1. Third-degree and advanced second-degree atrioventricular (AV) block at any anatomic level associated with:
   a. Bradyarrhythmias with symptoms or ventricular arrhythmias presumed to be due to AV block
   b. Arrhythmias and other medical conditions requiring drug therapy that result in symptomatic bradycardia
   c. No symptoms, but with documented periods of asystole ≥ 3 seconds or any escape rhythm < 40 beats \( \cdot \) min\(^{-1} \) or with an escape rhythm below the AV node
   d. No symptoms but with atrial fibrillation and bradycardia with 1 or more pauses of at least 5 seconds
   e. Catheter ablation of the AV junction
   f. Postoperative AV block that is not expected to resolve after cardiac surgery
   g. Neuromuscular diseases with AV block (myotonic muscular dystrophy, Kearns-Sayre syndrome, Erb dystrophy, peroneal muscular dystrophy)
   h. Exercise in the absence of myocardial ischemia
2. Second-degree AV block with associated symptomatic bradycardia
3. Asymptomatic persistent third-degree AV block with average awake ventricular rates of 40 beats \( \cdot \) min\(^{-1} \) or faster if cardiomegaly or left ventricular dysfunction is present, or if site of block is below the AV node

**Class IIa**
1. Third-degree AV block with escape rate ≥ 40 beats \( \cdot \) min\(^{-1} \) in asymptomatic patients without cardiomegaly
2. Asymptomatic second-degree AV block at intra- or infra-His levels at electrophysiologic study
3. First- or second-degree AV block with symptoms similar to those of pacemaker syndrome or hemodynamic compromise
4. Asymptomatic type II second-degree AV block with narrow QRS

**Class IIb**
1. May be considered for neuromuscular diseases (see above) with any degree of AV block with or without symptoms

**Class III (Pacemaker Not Indicated)**
1. Asymptomatic first-degree AV block
2. Asymptomatic type I second-degree AV block at the supra-His (AV node) level or that level not known to be intra- or infra-Hisian
3. AV block that is expected to resolve and unlikely to recur

Modified from Epstein and colleagues.\(^{19} \)

Box 16-2  Indications for Permanent Pacemaker Insertion Based on ACC/AHA/HRS Guidelines: Chronic Bifascicular Block\(^{a} \)

**Class I**
1. Advanced second-degree atrioventricular (AV) block or intermittent third-degree AV block
2. Type II second-degree AV block
3. Alternating bundle-branch block (Level of evidence: C)

**Class IIa**
1. Reasonable for syncope not demonstrated to be due to AV block when other likely causes have been excluded, specifically ventricular tachycardia
2. Reasonable for an incidental finding at electrophysiologic study of a markedly prolonged HV interval (≥100 ms) in asymptomatic patients
3. Reasonable for an incidental finding at electrophysiologic study of pacing-induced infra-His block that is not physiologic

**Class IIb**
1. May be considered in the setting of neuromuscular diseases such as myotonic muscular dystrophy, Erb dystrophy (limb-girdle muscular dystrophy), and peroneal muscular atrophy with bifascicular block or any fascicular block, with or without symptoms
2. Permanent pacemaker implantation is not indicated for fascicular block with first-degree AV block without symptoms.

Modified from Epstein and colleagues.\(^{19} \)

\(^{a}\)Bifascicular block refers to electrocardiographic evidence of impaired conduction below the AV node in two or three fascicles of the right and left bundles; it is commonly associated with syncope and precedes third-degree AV block associated with increased incidence of sudden death.

\(^{b}\)Class I = Conditions for which there is evidence and/or general agreement that treatment is beneficial, useful, and effective. Class II = Conditions for which there is conflicting evidence and/or divergence of opinion about benefit, usefulness, and/or efficacy of treatment. Class III = Conditions for which the procedure is not useful and/or effective or is harmful.

Key: ACC, American College of Cardiology; AHA, American Heart Association; HRS, Heart Rhythm Society.

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Section II  Tachycardia

**DEFINITION**

Abnormal tachycardia is a rapid heartbeat out of proportion to metabolic demands on the circulation.
HISTORICAL NOTE

Surgical procedures that successfully controlled many abnormal tachycardias resistant to drug treatment were developed during the 1970s and 1980s. Electrophysiologic studies accomplished by cardiac catheterization were necessary for precise diagnosis of many abnormal tachycardias, and cardiac electrophysiology rapidly became a field of special interest and competence among a small group of cardiologists. With the advent of interventional cardiology, methods for highly selective catheter ablation of areas identified by electrophysiologic studies have become successful and are replacing more invasive and somewhat cumbersome techniques of intraoperative mapping and cryoablation.

TACHYCARDIA FROM ATRIOVENTRICULAR NODAL REENTRY

Atrioventricular (AV) nodal reentrant tachycardia is the most common cause of paroxysmal tachycardia. One of its characteristics is the electrophysiologic phenomenon of dual AV nodal pathways. The fast pathway (with a normal AV conduction rate) is believed to be located within or near the AV node, and the slow one adjacent to and usually inferior to the node, lying closer to the coronary sinus.

A successful surgical approach to this problem, using cryosurgical ablation, was developed and used by Sealy, Cox, Holman, and colleagues. Results of this type of surgical therapy have been good, with no deaths among 23 patients (CL 0%-8%) who underwent surgical correction without the production of heart block. Currently, however, catheter ablation techniques are used for this purpose, and they are directed at selective ablation of the slow or fast pathway, usually the slow one, to eliminate the reentry circuit (and thus the tachycardia) while avoiding the need for implanting a permanent pacemaker. This can be successful in up to 90% of patients. Occasionally, open cryosurgical ablation is performed in symptomatic patients who require open cardiac surgery for other indications.

ECTOPIC ATRIAL TACHYCARDIA

Ectopic foci of activation in either right or left atrium can provoke paroxysms of atrial tachycardia. When localized by electrophysiologic studies, they can be treated successfully by catheter ablation. However, most ectopic atrial tachycardias, particularly those originating in the right atrium, have multiple sites of origin and are best treated pharmacologically.

INDICATIONS FOR INTERVENTION

Development of modern devices for cardiac pacemaking and for implantable cardioverter-defibrillators (ICD) has made sophisticated understanding of cardiac electrophysiology and electrical engineering necessary for proper care of patients with these conditions. Currently these requirements are met by few cardiac surgeons. Furthermore, most interventional therapies for these abnormal atrial tachycardias can now be performed using percutaneous techniques.

Section III Wolff-Parkinson-White Syndrome

DEFINITION

Wolff-Parkinson-White (WPW) syndrome as originally described is a condition in which episodes of rapid heart rate (paroxysmal tachycardia) occur in otherwise healthy young people in combination with an ECG demonstrating delta waves and a broad QRS complex (bundle branch block with
short PR interval).\textsuperscript{710} WPW is one of the preexcitation syndromes, a term that implies activation of a cardiac chamber partially or wholly by an impulse arising in another chamber and arriving earlier than would be expected if the impulse had proceeded over the normal conduction system pathway.

WPW syndrome characteristically allows paroxysmal atrial tachycardia (PAT) by atrioventricular (AV) conduction occurs over an accessory AV conduction pathway, or bypass tract, a concept first proposed in 1932 by Holtzmann and Scherf.\textsuperscript{162} This was confirmed in the same year by Burchell and colleagues, who also showed that ventricular preexcitation could be temporarily abolished by injecting procaine into the AV groove at the site of earliest ventricular activation.\textsuperscript{16}

In 1893, Kent described muscular bridges connecting right atrium to right ventricle in several mammalian species, and Wood and colleagues supported those observations in 1943.\textsuperscript{56,919} Truex and colleagues in 1958 and 1960 demonstrated the presence of muscular accessory pathways in human hearts, and Lev and colleagues added further information on accessory pathway morphology in the early 1960s.\textsuperscript{14,15,57,77} Further proof of the morphologic basis of WPW syndrome came in 1968, when Cobb, Sealy, and colleagues reported dividing the accessory pathway; PR interval and QRS complex became normal, the delta wave disappeared, and ventricular preexcitation and recurrent supraventricular tachycardia were eliminated.\textsuperscript{78} In that operation, an epicardial approach was used and a transmural ventricular incision made below the AV groove. Iwa and colleagues published a confirmatory report in 1970 and introduced the endocardial approach.\textsuperscript{19} Sealy and colleagues then also adopted an endocardial approach from within the atria, which consisted of separating atrium from anulus after dissecting away the AV fat pad.\textsuperscript{317} Sealy, Gallagher, and their colleagues also pioneered a successful surgical approach for patients whose accessory pathways were in the septal area and introduced cryosurgical ablation.\textsuperscript{54,511} This method was combined with the epicardial approach using CPB by Guiraudon and colleagues.\textsuperscript{523,525,512}

These surgical developments provided much of the information that made catheter ablation of the accessory pathways possible beginning in the early 1980s.\textsuperscript{317,199,88} Early experiences in patients used direct current (DC) as the energy source, but limitations were imposed by this method. Catheter ablation became reproducible and safe when radiofrequency (RF) energy was introduced.\textsuperscript{31,88,87} Different effects can be achieved by varying the RF output mode, frequency, waveform, and power output. Currently, catheter ablation techniques have replaced surgical techniques for interventional therapy of supraventricular tachycardia of all types and at all ages, except for occasional patients being operated on for other cardiac conditions.

MORPHOLOGY

Accessory AV conduction pathways (Kent bundles) mediating WPW syndrome may occur at any point around the anulus of either AV valve, except along the junction of the mitral anulus and aortic valve.\textsuperscript{32} However, they are most commonly located:

- Along the strong, well-formed mitral anulus, adjacent to the free wall of the left ventricle laterally or posteriorly (WPW type A)
- At the less well-developed tricuspid valve anulus anterosuperiorly, adjacent to the right ventricular free wall (WPW type B)
- Along the tricuspid anulus, adjacent to the anterior aspect of the ventricular septum
- Along the tricuspid or mitral anulus, adjacent to the posterior aspect of the ventricular septum, near the crux cordis

Accessory pathways adjacent to the posterior aspect of the ventricular septum lie in the potential space overlying the inlet portion of the septum and may be on either its right or left ventricular aspects.\textsuperscript{311} Kent bundles are said to have an average width of 1.8 mm.\textsuperscript{314} Multiple functioning bundles are present in 10% to 20% of cases.\textsuperscript{15,512,512}

From the standpoint of cardiac surgeons and interventional cardiologists, location of accessory AV pathways is important, as are the normal location of the AV node and bundle of His (see “Conduction System” in Chapter 1) and details of the structures and spaces around the AV valve anuli and fibrous skeleton of the heart. The central fibrous body, where mitral, tricuspid, and aortic valves meet, is the most prominent part of the fibrous skeleton. The area of fibrous continuity between aortic and mitral valves, the aortic-mitral anulus, contributes to the fibrous skeleton. The leftward extension of this anulus is the left fibrous trigone. The right fibrous trigone is at the right-sided extremity of the mitral-aortic anulus and is part of the central fibrous body. It lies adjacent to the AV portion of the membranous septum at the point where tricuspid, mitral, and aortic anuli come together. Atrial muscle is not in juxtaposition with ventricular muscle in the area between left and right fibrous trigones (along the aortic-mitral anulus), and thus accessory AV connections are not found in this area. As the surgeon views the mitral valve through the opened left atrium, the right fibrous trigone is just anterior to the medial commissure, and the left fibrous trigone is just lateral to the lateral commissure. As the surgeon views the tricuspid valve, the central fibrous body is in the region of the muscular portion of the AV septum (see “Cardiac Valves” in Chapter 1).

Normal anatomy in the region of the crux cordis and contiguous posterior septal area is of critical importance in therapy to ablate accessory AV conduction pathways in the region of the posterior aspect of the ventricular septum. This anatomy was described by Sealy and Gallagher as a “toppled pyramid enclosing a fat-filled space.”\textsuperscript{511} The apex of the pyramid is the right fibrous trigone, and its base is the
His bundle electrogram is recorded at the time of the P wave in the standard ECG, a His bundle electrogram 60 to 100 milliseconds later, and ventricular electrical activity at the onset of the QRS complex (Fig. 16-5, A).

In WPW syndrome, with the Kent bundle offering an AV bypass tract, the electrical impulse travels antegrade down the normal pathway but also antegrade down the Kent bundle, where delay normally imposed by the AV node is absent. This results in ventricular preexcitation at the insertion of the Kent bundle and short PR interval, delta wave, and wide QRS complex characteristic of WPW syndrome (Fig. 16-5, B).

The normal AV conduction pathway and the accessory pathway constitute the basis for the reciprocating tachycardia (circus movement) sometimes seen in patients with WPW syndrome. Most commonly, the circus movement uses the normal AV conduction system as the antegrade limb and bypass tract as the retrograde limb of the reentrant circuit (orthodromic circus movement tachycardia). Less commonly, the accessory pathway is used in an antegrade manner, and the normal AV conduction system in a retrograde manner (antidromic circus movement tachycardia).220

When atrial fibrillation develops, rapid conduction via the accessory pathway may result in life-threatening ventricular responses, sometimes degenerating into ventricular fibrillation.

**Symptoms**

Patients usually present because of palpitations, with or without symptoms of acute cardiac failure. Palpitations and documented episodic tachycardias have often been present for 10 to 15 years and repeated hospitalizations may have been required.212 More than half of patients with paroxysmal tachycardia and WPW syndrome give a history of syncope or near-syncpe.212 Rarely, they present after resuscitation from an episode of sudden death.

**Signs**

Diagnosis is made from the characteristic ECG (see Fig. 16-5). Atrial fibrillation or flutter may coexist. Preexcitation and presence of accessory AV conduction pathways are

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**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Pathophysiology**

Electrical impulses originate in the sinoatrial (SA) node and travel to the AV node through preferential pathways (see “Conduction System” in Chapter 1). Normally, fibrous anuli of mitral and tricuspid valves prevent direct transmission of electrical impulses from atrium to ventricle (fibrous tissue, in contrast to muscle and specialized cells, does not conduct), and conduction occurs only via the AV node and bundle of His. At the AV node, a delay in AV conduction normally occurs before the impulse passes to the bundle of His and ultimately to the Purkinje cells. This delay is reflected in the normal His bundle electrogram, in which an atrial
confirmed by electrophysiologic testing in a specially equipped cardiac electrophysiology laboratory.

**NATURAL HISTORY**

Electrocardiographic diagnosis of preexcitation WPW syndrome is made in about 0.25% of healthy young people, with documented tachyarrhythmias occurring in about 2% of those with preexcitation. However, in other patient subsets of WPW, prevalence of tachyarrhythmias is as high as 80%. Half the infants and children with supraventricular tachycardia difficult to control medically have WPW or concealed accessory muscle bundles (see Section IV later in this chapter).

Patients with WPW may present at any age, including the early months of life. The syndrome is more common in males. Most adults with WPW have otherwise normal hearts, although it may complicate a variety of acquired and congenital cardiac defects, including Ebstein anomaly. Patients with Ebstein anomaly often have multiple right-sided accessory pathways, and preexcitation is said to be limited to the atrialized portion of the ventricle. Rossi and Thiene have shown in patients having arrhythmogenic death that a few of them have accessory conduction pathways combined with very mild downward displacement of the tricuspid septal leaflet.

Among patients with WPW and tachyarrhythmias, 80% have paroxysmal supraventricular tachycardias of a reciprocating type, 15% have atrial fibrillation, and 5% have atrial flutter. Sinus node dysfunction is said to be more common in patients with WPW than in those without it.

Patients with WPW, otherwise normal hearts, and no tachycardia have normal cardiac function and life expectancy. Morbidity is considerable in those with recurrent tachycardia, and sudden death occurs in a small proportion. These sudden deaths are most likely the result of combined paroxysmal atrial fibrillation and fast antegrade conduction across the accessory AV pathways.

Some children and young adults with WPW and recurrent tachycardia lose the tendency toward developing tachyarrhythmias as they grow older. Also, preexcitation may be intermittent with loss of the delta wave, a situation suggesting a benign prognosis.

**TECHNIQUE OF INTERVENTION**

The object of catheter ablation (or operation) is electrical isolation of the ventricles from the atria except for the normal AV nodal pathway. Patients are brought to a cardiac electrophysiology laboratory. The study is performed under sedation with fentanyl and midazolam and accessory pathways are localized. An electrode catheter is appropriately positioned and RF current delivered. Repeat ablations at subsequent procedures are required in a few patients.

**RESULTS**

Surgical procedures for termination of WPW syndrome were successful in 80% to 90% of patients. Interruption of the accessory pathways prevents both reentrant AV arrhythmias and those due to atrial tachycardia, flutter, or fibrillation associated with rapid antegrade conduction across the accessory pathways.

RF catheter ablation is highly successful. Accessory pathway conduction was eliminated in 164 (99%) of 166 patients in one study, without mortality. Preexcitation or AV reentrant tachycardia occurred in only 15 (9%; CL 7%-12%), all of whom underwent a second successful catheter ablation.

**INDICATIONS FOR INTERVENTION**

Symptomatic tachyarrhythmias associated with one or more accessory AV pathways are an indication for catheter ablation.

When cardiac operation is indicated in an asymptomatic patient with WPW, accessory pathways should probably be interrupted by catheter ablation techniques before operation, because serious postoperative tachycardias and life-threatening atrial fibrillation can result from their presence. When catheter ablation is not available, a surgical procedure is indicated for interruption of the accessory pathways by either the endocardial or epicardial approach. The well-tested endocardial approach was described in the first edition of this text and has been clearly illustrated by others.

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Section IV  Atrial Fibrillation and Flutter

**DEFINITION**

Atrial fibrillation is a disorder of cardiac rhythm characterized by rapid (350-500/min), irregular disorganized atrial impulses and ineffective atrial contractions. P waves are absent from the ECG, and the bipolar electrogram reveals beat-to-beat polarity, morphology, amplitude, and cycle length that vary. The QRS complex is irregularly irregular. Atrial flutter is a disorder of cardiac rhythm characterized by rapid (250-350/min) regular atrial impulses. QRS complexes are uniform in morphology, and P waves may have sawtoothed configuration.

**HISTORICAL NOTE**

The first clear description of atrial fibrillation is attributed to Herring in 1903 (pulsus irregularis perpetuus), although this was before the era of electrocardiography. Withering, in his studies on digitalis, was probably also aware of atrial fibrillation, because he noted that digitalis was a “moderator and regulator of rhythm.” The beneficial effect of digitalis in atrial fibrillation was clearly noted in 1836 by Bouillaud in his classic textbook, quoted by Meijler. By 1914, MacKenzie and Sir Thomas Lewis had framed the controversy on the mechanism of action of digitalis, presaging continuing discussions as to the etiology of atrial fibrillation and electrophysiologic state of the atria during atrial fibrillation.

Pharmacologic interventions, notably digitalis (to slow the rate) and quinidine (to convert the rhythm), were the mainstays of treatment. There are obvious advantages of sinus rhythm, and in 1962, Lown and colleagues and in 1963, Oram and colleagues published their landmark studies of electrical cardioversion as treatment for atrial fibrillation. Perhaps only 15% of patients with persistent or permanent atrial fibrillation respond to these interventions. Therefore,
there has been a continuing interest in finding an interventional solution to the problem of atrial fibrillation.

Catheter-induced His bundle ablation introduced by Scheinman and colleagues, and Gallager and colleagues in 1982 controlled the tachycardia of established atrial fibrillation but required implanting a pacemaker. In 1990, Guiraudon and colleagues reported seven of nine patients free of atrial fibrillation after an operation designed to isolate a corridor of atrial tissue connecting the sinus and AV nodes. Creating a maze by multiple atrial incisions was developed by Cox and colleagues in 1991. The left atrial isolation procedure was described in 1980. This operation confined atrial fibrillation to the left atrium and obviated the need for a permanent pacemaker while restoring cardiac hemodynamics. Vulnerability to systemic thromboembolism remained unchanged. In 1982, Scheinman and colleagues, as noted previously, described catheter ablation of the His bundle with insertion of a permanent pacemaker to restore regular rhythm as a means of controlling ventricular rate. Risk of thromboembolism was unaffected. Guiraudon and colleagues described the corridor procedure in 1985. This procedure isolated a strip of atrial septum (the “corridor”) containing both the sinoatrial node and the AV node so that the sinoatrial node could once again pace the ventricles, even though the atria continued to fibrillate. AV synchrony was not restored, and risk of thromboembolism persisted. Understanding the electrophysiology of atrial fibrillation based on work of Boineau and colleagues and Alessie and colleagues led to development of the atrial transaction procedure. Initial success in a patient was followed by recurrence of atrial fibrillation. Further advances in the understanding of atrial fibrillation using more sophisticated means of atrial mapping led to the concept that interruption of the multiple macro-reentrant circuits responsible for the arrhythmia would be possible. The surgical procedure was based on the concept of a maze and was named the maze procedure.

As cited by Cox and colleagues, following dialogues between Mackenzie and Lewis, there evolved three theories regarding the electrophysiologic mechanism of atrial fibrillation. Rotherberger believed there was a single automatic atrial focus, the inference being that its resection or isolation might cure atrial fibrillation. Engleman suggested the presence of multiple small automatic foci. Garrey experimentally disproved both hypotheses by isolating smaller and smaller segments of fibrillating atrial tissue. His observations suggested that (1) some critical atrial mass was necessary to sustain atrial fibrillation and (2) the underlying mechanism was reentry, not automaticity. Based on experiments using programmed electrical stimulation, Moe hypothesized the existence of multiple wavelets with different refractory periods within the atrial mass. Inhomogeneous tissue refractoriness lends itself to reentry, not automatic mechanisms. Moe’s theories were later confirmed by Alessie’s group using multiplexed computerized recordings in rabbit atria. Boineau and colleagues mapped circus motion around the superior vena cava orifice in a dog with naturally occurring atrial flutter. They concluded that in addition to functional factors (nonuniform repolarization), anatomic factors also contribute to atrial dysrhythmias. Cox and colleagues then created atrial fibrillation in experimental animals and mapped the electrophysiologic events. In their 1991 publication they concluded, “The presence of macro-reentrant circuits and the absence of either micro-reentrant circuits or evidence of atrial automaticity suggests that atrial fibrillation should be amenable to surgical ablation.” They subsequently demonstrated the ability to terminate atrial fibrillation in humans by performing the classic maze procedure. In 1994, Haissaguerre and colleagues reported successful ablation procedures for atrial fibrillation using a catheter-based technique. Since the publication of these two landmark studies, many modifications of the initial ablation techniques to terminate atrial fibrillation have been introduced.

PATHOPHYSIOLOGY

Theories of the mechanism of atrial fibrillation involve two processes: focal triggers of enhanced automaticity and multiple wavelets of macro-reentry activation migrating across the atria. Rapidly firing foci, located mostly in pulmonary veins and also but less frequently in the right atrium, superior vena cava, or coronary sinus, can initiate atrial fibrillation in susceptible patients. Fractionation of multiple wave fronts as they spread across the atria results in self-perpetuating “daughter wavelets” that cause complete absence of coordinated atrial systole. The reentry circuits follow different pathways each time after initiation and have been thought in the past to be random.

Recent evidence suggests that there may be more organization than previously thought. Three patterns of atrial fibrillation have been identified by Allessie and colleagues:

- Single wave fronts
- One or two wave fronts
- Multiple activation wave fronts propagating in different directions across the atria

Focal triggers as the only mechanism of atrial fibrillation probably apply to patients with normal atria; triggers plus macroreentry (substrate) mechanisms apply to enlarged or diseased atria.

Risk factors for developing atrial fibrillation include inflammation, oxidative stress, and atrial morphology. In addition, genetic susceptibility factors related to several ion channels have been implicated in its pathogenesis. Missense mutations of the gap junction protein connexin-40 (encoded by the GJA5 gene), which plays a critical role in electrical intercellular coupling, has been implicated in a small number of cases of atrial fibrillation. Lu and colleagues have found that microRNA-328 contributes to adverse atrial electrical remodeling in atrial fibrillation by targeting L-type calcium channel genes.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Classification

Classification of atrial fibrillation begins with the first detected episode. If two or more episodes occur, atrial fibrillation is considered recurrent. Recurrent atrial fibrillation is designated as paroxysmal, persistent, or permanent as described in Box 16-5. These categories are not mutually exclusive. An individual patient may have several episodes of paroxysmal atrial fibrillation and occasional persistent atrial fibrillation or
the reverse. It is practical to categorize a given patient by the most frequent presentation. The definition of permanent atrial fibrillation is often arbitrary. This terminology applies to episodes lasting more than 30 seconds without a reversible cause.

Secondary atrial fibrillation in the setting of acute myocardial infarction, cardiac surgery, pericarditis, myocarditis, hyperthyroidism, or acute pulmonary disease is considered separately, and treatment of the underlying disorder usually terminates the arrhythmia. The term lone atrial fibrillation refers to individuals younger than 60 years of age without clinical or echocardiographic evidence of cardiopulmonary disease, including hypertension. The term nonvalvar atrial fibrillation refers to patients without rheumatic mitral valve disease, prosthetic heart valve replacement, or valve repair.

Diagnosis, Symptoms, and Signs

Shortness of breath is a common presenting symptom. Cardiac conditions associated with atrial fibrillation include hypertension, ischemic or valvar heart disease, cardiomyopathy, cardiac tumors, and pericarditis, and presenting symptoms and signs are often those associated with these conditions. Noncardiac conditions associated with atrial fibrillation are chronic obstructive pulmonary disease, thyroid disease, electrolyte imbalance, and alcohol abuse. Vagally mediated atrial fibrillation resulting from high vagal tone occurring after meals or exercise and during sleep or rest can be exacerbated with digitalis. The ECG shows very short atrial intervals at a rate faster than the ventricular rate. An irregular ventricular rate is usually present. Spontaneous conversion of atrial fibrillation is common, with up to 70% of patients with first-time atrial fibrillation reverting to normal sinus rhythm. Frequency of spontaneous conversion decreases with each subsequent episode.

NATURAL HISTORY

Atrial fibrillation is not a benign arrhythmia and presents a difficult clinical challenge. It is the most common cardiac arrhythmia, accounting for about one third of arrhythmia diagnoses. It is estimated that 2.2 million people in the United States and more than 5 million people worldwide have atrial fibrillation. It is present in approximately 1% of the general population and 6% of those older than age 65 years. There are about 360,000 new patients diagnosed annually in the United States. According to the Centers for Medicare and Medicaid Services, atrial fibrillation resulted annually (up until 1990) in 227,000 hospitalizations (50% as emergencies) at a cost of $6.6 billion.

Atrial fibrillation is associated with thromboembolism, including stroke or pulmonary embolism, and results from slow and stagnant blood flow in the atria. Risk of stroke associated with atrial fibrillation is 5% to 12% per year. Prospective studies on the treatment of atrial fibrillation place the risk of stroke at 5% to 8% in patients receiving placebo treatment. Risk of stroke may be reduced by 37% to 86% by anticoagulation with warfarin, but at a cost of bleeding risk in 0.5% to 2.8% of patients per year.

Factors that increase the risk of stroke in patients with atrial fibrillation include older age, diabetes, heart failure, previous myocardial infarction, and previous embolism. Chronic atrial fibrillation is associated with cellular changes that progress to atrial myocardial fibrosis. The progressive nature of the condition leads to enlargement of the atria and eventual loss of function of the atrial myocardium. Tachycardia-induced cardiomyopathy is an end-stage complication of atrial fibrillation.

TECHNIQUE OF INTERVENTION

Two treatment approaches are used to manage patients with atrial fibrillation: (1) control of ventricular rate and anticoagulation and (2) restoration and maintenance of sinus rhythm.

Ventricular Rate Control

Ventricular rate control can be accomplished with a variety of drugs, including digoxin, β-blockers, and calcium channel blockers. Adequacy of ventricular rate control is usually assessed with the patient at rest. However, assessment of ventricular rate should also be done during exercise, because activity may result in an excessively high ventricular rate. Persistently elevated ventricular rate may induce tachycardia-mediated cardiomyopathy. Risk of thromboembolism increases 48 hours after the onset of atrial fibrillation. If sinus rhythm is not restored during this time, anticoagulant therapy should be initiated. Random trials evaluating oral anticoagulation in patients with atrial fibrillation and subjected to meta-analysis demonstrated a 61% reduction in stroke compared with placebo. Risk stratification models have been introduced to identify patients with atrial fibrillation who benefit from oral anticoagulation. The ACC/AHA/European Society of Cardiology (ESC) guidelines for managing patients with atrial fibrillation have developed such a model using risk factors that predict an increased risk of thromboembolism (Table 16-2). Aspirin is the agent of choice for patients with no risk factor, and warfarin for those with one or more risk factors.

### Table 16-2

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;75 years</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>1</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>1</td>
</tr>
<tr>
<td>Renal failure</td>
<td>1</td>
</tr>
<tr>
<td>Previous embolism</td>
<td>1</td>
</tr>
</tbody>
</table>

### Clinical Classification of Atrial Fibrillation

The joint American College of Cardiology/American Heart Association/European Society of Cardiology task force has recommended the following nomenclature for classifying atrial fibrillation. Classification begins with the first detected episode of atrial fibrillation. If a patient has two or more episodes, atrial fibrillation is considered recurrent. Recurrent atrial fibrillation is designated as paroxysmal, persistent, or permanent.

**Paroxysmal**
Atrial fibrillation lasting 7 or fewer (most <24 hours) days and terminating spontaneously

**Persistent**
Atrial fibrillation lasting more than 7 days that does not terminate spontaneously, but requires electrical or pharmacologic cardioversion to restore normal sinus rhythm; if the first detected episode of atrial fibrillation does not terminate spontaneously, it is also designated persistent

**Permanent**
Atrial fibrillation in which sinus rhythm cannot be sustained after cardioversion or the patient and physician have decided against further efforts to restore sinus rhythm

*Both paroxysmal and persistent atrial fibrillation may be recurrent.*
with one severe or more than one moderate risk factor. Either can be used with one moderate risk factor.

Warfarin and other vitamin K antagonists are cumbersome to use and require frequent laboratory monitoring. This has led to the search for other drugs that do not require laboratory monitoring. Several have been evaluated in clinical trials, including clopidogrel, idraparinux, and dabigatran. In a large randomized clinical trial of 18,113 patients, dabigatran (a potent direct inhibitor of thrombin) at a dose of 110 mg twice daily was associated with rates of stroke and systemic embolism that were similar to those associated with warfarin, as well as lower rates of hemorrhage. In separate trials, clopidogrel plus aspirin or idraparinux were found to be less effective than warfarin.

### Restoring and Maintaining Sinus Rhythm

Restoring and maintaining normal sinus rhythm is desirable because symptoms of discomfort and anxiety related to the arrhythmia are eliminated, hemodynamics are improved, cardiac rate is controlled physiologically, and the risk of thromboembolism may be reduced.

### Cardioverison

Pharmacologic cardioversion involves use of a variety of agents from various classes (Vaughan-Williams) of antiarrhythmic drugs (Tables 16-3 and 16-4). Ibutilide is a class III agent used intravenously for converting atrial flutter and atrial fibrillation to sinus rhythm. It also lowers atrial defibrillation energy requirements and facilitates transthoracic electrical cardioversion. Ventricular tachyarrhythmia has been associated with the use of this drug in patients with low left ventricular ejection fraction, so it should only be used if QT interval is less than 480 milliseconds. Other drugs employed are class IA (quinidine, procainamide, disopyramide), class IC (flecainide, propafenone), or class III (amiodarone, sotalol) agents. Each has potentially serious proarrhythmic and other side effects and is effective in only 40% to 60% of cases.

Electrical cardioversion is often combined with drug therapy.

### Ablation to Block Atrioventricular Conduction

When medical therapy is ineffective in controlling episodes of rapid ventricular rate, catheter ablation of the AV junction to induce complete heart block and implantation of a permanent pacemaker will control it, although atrial flutter or fibrillation persist. Intracoronary ethanol ablation of the AV conduction system is an alternative to radiofrequency (RF) ablation.

### Interruption of Macro-Reentrant Circuits

A series of operative techniques based on contemporary electrophysiologic understanding has led to useful methods of operative or catheter-based intervention for treating atrial fibrillation.
**Cox-Maze III Procedure**

Multiple incisions are made in the atria that not only interrupt conduction routes of the most common reentrant circuits but also direct the sinus node impulse to the AV node along a specified route. The entire atrial myocardium (except for the atrial appendages and the pulmonary veins) is electrically activated by providing multiple blind alleys about 2 to 3 cm wide off the main conduction route between the sinoatrial node and the AV node, thus preserving atrial transport function. A modification of the technique as described by Cox and colleagues, called the maze III procedure with minor changes, is described here.

Bicaval cannulation is required (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). A cannula is inserted directly into the superior vena cava, and the inferior vena cava is cannulated through the right atrium as close as possible to the diaphragm. Small venous cannulae (24F) may be used if active venous uptake is provided by vacuum suction applied to the reservoir of the oxygenator (see “Vacuum-Assisted Venous Return” in Section II of Chapter 2). Perfusion is normothermic to maintain the heartbeat during initial phases of the operation on the right atrium.

The right atrial appendage is excised, removing all trabeculations attached to the appendage. Alternatively and preferably, an incision (see Fig. 16-6, A) is made through the tip of the right atrial appendage, extending to the base of the appendage medially and laterally to preserve natriuretic receptors. This incision is extended toward the midpoint of the right atrium. A longitudinal incision is made in the lateral wall of the right atrium along the crista terminalis. This incision extends onto the superior and inferior vena cava. The lower end of the incision is immediately closed to a point about 2 cm cephalad to the inferior vena cava cannula by a continuous suture of 4-0 polypropylene to prevent tearing during retraction. At this point, a vertical incision is made extending anteriorly. The inside of the right atrium is exposed (Fig. 16-6, B) so that the intraatrial incision may be extended to the tricuspid valve anulus at about the midpoint of the posterior leaflet. A 3-mm cryolesion is placed at approximately the 2-o’clock position on the tricuspid anulus for 2 minutes at −70°C. All muscle fibers of the right atrial wall are divided, exposing the fat of the AV groove and occasionally the right coronary artery. The atrial incision is closed from the anulus of the tricuspid valve to the free wall of the right atrium by a continuous 4-0 polypropylene suture. An incision is made on the medial aspect of the remnant of the appendage (Fig. 16-6, C). This incision extends to the tricuspid valve anulus at the midpoint of the anterior leaflet or approximately at the 10-o’clock position. Another 3-mm cryolesion is placed at the tricuspid anulus for 2 minutes at −70°C.

Systemic cooling is then initiated. The aorta is occluded preparatory to the left atrial portions of the operation. Cold blood cardioplegic solution is administered to the heart via the coronary sinus through an appropriate cannula (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). The left atrium is opened by incision just posterior to the interatrial groove near the orifices of the right pulmonary veins. The incision is extended superiorly and inferiorly onto the left atrium around the right pulmonary veins. The atrial septum is incised above the fossa ovalis. The incision is curved across the limbus of the fossa ovalis and across the membrane of the fossa to the inferior margin of the fossa near, but not into, the tendon of Todaro (Fig. 16-6, E). The left atrial incision is continued across the left atrium toward the left pulmonary veins to isolate and encircle them. The heart is retracted to the right to expose the left atrial appendage (Fig. 16-6, F), which is excised at its base. It is incised in a cephalad direction near the AV groove across its base and back into the left atrium. The incision in the left atrial appendage is joined to the pulmonary vein incising incision at a point near the left superior pulmonary vein. The incision in the base of the left atrial appendage is closed back to the encircling incision, and the portion of the encircling incision below the left atrial appendage is closed with continuous sutures of 3-0 polypropylene (Fig. 16-6, G). These sutures are passed from the outside into the left atrium and retrieved from within the atrium (Fig. 16-6, H). The encircling incision closure is continued cephalad and around the superior aspect to the midpoint of the encircling incision. The encircling incision is closed inferiorly to the midpoint. An incision is made across the floor of the left atrium to the midpoint of the anulus of the posterior leaflet of the mitral valve. This incision is carefully opened by sharp dissection.

The coronary sinus is exposed by incision into the fat of the AV groove. The circumflex coronary artery may also be visualized in the incision. A 15-mm cryoprobe is placed posteriorly on the coronary sinus, and a cryolesion is created at −60°C for 3 minutes. After 1 minute, a 3-mm cryoprobe is placed at the mitral valve anulus at −70°C for 2 minutes. Timing of freezing with the two probes is coordinated so thawing can occur simultaneously. Mitral valve repair or replacement is performed at this point if required. The incision in the floor of the left atrium is closed by a continuous suture of 4-0 polypropylene, beginning at the mitral anulus and continuing to the encircling incision (Fig. 16-6, I). The sutures are joined and continued to close the encircling incision over to the right pulmonary veins.

The atrial septum is a thin membrane within the fossa ovalis. The limbus is muscular and thicker. There are discrete layers of the right and left atria that represent the infolding of the atria at the interatrial groove rather than true septum. These layers should be closed separately (Fig. 16-6, J). The septal closure begins at the inferior border of the fossa ovalis using continuous sutures of 4-0 polypropylene. Suturing continues across the limbus and along the left atrial fold to the free margin. A second layer of closure is started at the limbus and continued along the right atrial fold to the junction, with the longitudinal incision in the right atrium. The remainder of the pulmonary vein encircling incision is closed and joined to the left atrial septal closure (see Fig. 16-6, J).

A venting catheter is inserted via the left superior pulmonary vein through a separate purse-string suture. Air is evacuated from the left cardiac chambers and aorta, and the aortic occlusion clamp is removed (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). The heart is reperfused and defibrillated if necessary. The longitudinal incision in the right atrium is closed beginning at the superior vena cava and working inferiorly (Fig. 16-6, K). The suture is joined to the right atrial septal closure, then continued to the vertical right atrial incision. The vertical incision is closed.
Figure 16-6 Maze III procedure. A, Operation is performed via median sternotomy. Cannulae for venous uptake are placed in superior vena cava and through the low right atrium into inferior vena cava. Small venous cannulae (24F) and vacuum-assisted venous return are employed. Cardiopulmonary bypass is established, and tourniquets are tightened around venae cavae. First incision divides right atrial appendage and extends obliquely to midpoint of right atrial free wall. Medially, incision extends to atrioventricular groove. Longitudinal incision is made from superior to inferior vena cava along crista terminalis. Lower 2 cm of incision is closed with a continuous suture of 4-0 polypropylene to prevent tearing during retraction. Vertical incision is made from point of closure to atrioventricular groove. B, Vertical incision is extended to tricuspid valve anulus in area of posterior leaflet (2-o’clock position, surgeon’s view), working on endocardial surface of atrium cutting through the entire atrial wall. Residual myocardial fibers are ablated by applying a 3-mm cryolesion (~70°C for 2 minutes) at tricuspid anulus. This portion of incision is closed with 4-0 polypropylene suture. C, Incision of medial aspect of right atrial appendage is continued into atrial groove to tricuspid valve anulus (10-o’clock position, surgeon’s view) by dissecting on endocardial surface. A cryolesion is placed at anulus of tricuspid valve to ablate residual myocardial fibers. This portion of incision is closed with 4-0 polypropylene suture.

Continued
Operation is completed by closing the right atrial appendage opening, beginning at the midpoint of the right atrium and continuing through the appendage incision.

The maze procedure has been performed experimentally and clinically as a closed heart procedure. Radial incisions in the atria have been proposed as a modification of the maze III procedure by Nitta and colleagues. Atrial incisions radiate from the sinoatrial node toward the AV anular margins to allow a more physiologic atrial activation sequence that may improve atrial transport function. These operations have not substantially reduced the time or complexity required to complete the standard maze III operation.

Modified Maze Procedure
The maze III procedure is an effective means of relieving atrial fibrillation, but it is a complex and sometimes prolonged procedure. Consequently, it is performed infrequently. A number of modifications of the operation and use of various
energy sources to ablate atrial myocardium have been introduced to simplify the operation and reduce operative time.

Modified operations include those applied to only one atrium, the unilateral maze procedure. The right-side maze operation creates the usual incisions for the maze procedure on the right atrium only. The left-side Maze procedure is usually a pulmonary vein-encircling incision, with or without extension to the mitral anulus and excision of the left atrial appendage.

Ablation modalities that have been used to obviate the need for incision and closure of atrial tissues include cryoablation or controlled freezing, microwave, RF, and laser energies. Of prime consideration with the use of any energy source is consistent creation of transmural lesions that ensure conduction block. Cryoablation has been a widely used modality and is an integral part of the standard maze III procedure to produce tissue ablation at the AV valve anuli and on the coronary sinus. Cryoablation is somewhat cumbersome to apply to atrial tissues and requires specially modified instrumentation. Microwave has been the least employed energy source, and a device to deliver microwave energy has been removed from the market. Laser energy applications are in clinical trial.

RF energy has been the most frequently used energy source; it heats and shrinks myocardial cells to destroy them. The energy may be applied to produce a focal or linear lesion as alternatives to incisions in conventional maze operations. It can be applied through a unipolar electrode to the endocardial surface of the atria, but may also be applied on the outside of the heart. The objective is to create full-thickness destruction of the wall of the atrium, resulting in scar tissue that blocks reentry pathways that sustain atrial fibrillation. When the energy is applied through an electrode placed directly on the endocardium, surface heating limits depth of...
penetration because once the tissue is destroyed or charred, impedance to energy flow by the injured tissue inhibits further tissue destruction. Cooling the electrode tip and contact surface with saline solution (irrigated RF-Cardioblate, Medtronic Inc., Minneapolis, Minn.) allows heating to be directed several millimeters below the surface, resulting in a lesion about 4 mm deep. RF energy applied through bipolar electrodes has the potential of assuring a full-thickness lesion. Electrodes placed along the jaws of clamps are placed on the endocardial and epicardial surfaces, with the atrial wall trapped in between. Energy flows until all myocardial tissue capable of conducting the energy is destroyed. Impedance then rises, and a steady state of energy flow is established. Bipolar devices should solve the problem of irregular
thickness due to trabeculation of the atrial wall, provided uniform electrode contact is assured with atrial tissues. Although thin areas will be destroyed early in the energy flow cycle, thick areas will continue to conduct energy until heating and destruction of tissue is complete. Gillinov and McCarthy showed conduction block in 7 of 10 patients with one application of bipolar RF energy using the Atricure clamp device (Atricure Inc., West Chester, Ohio). Repeat application of the energy achieved block in the remaining three patients. Bipolar probes have been developed that provide access to areas inaccessible to bipolar clamps, such as the valve anuli, vena cavae, and tissue overlying the coronary sinus. However, these probes, as well as cryoprobes, may not create completely transmural lesions.

RF ablation maze procedures performed on both right and left atria appear to achieve about 80% success in restoring sinus rhythm. The number and length of surgically created incisions are reduced compared with the standard maze III procedure by using RF ablation lines as alternatives to or extensions of incisions. The set of surgical incisions for the modified RF maze procedure is shown in Fig. 16-7, A. After establishing cardiopulmonary bypass, an incision is
Figure 16-7  Modified radiofrequency (RF) maze III procedure.  

A, Incisions are depicted. Incision is made through right atrial appendage. Curved incision is made in right atrium extending from atrioventricular groove toward right superior vena cava, crossing crista terminalis. Note relation of this incision posterior and caudal to site of sinoatrial node. Left atrial appendage is amputated at the base. Left atrium is incised on right side posterior to interatrial groove. Left-sided incisions are made later in procedure. B, Primary incision is extended laterally and posteriorly into superior vena cava by RF ablation lesion. It is extended similarly into inferior vena cava. Ablation of inferior isthmus is performed by extending a linear lesion from posterior aspect of inferior vena cava across inferior isthmus to anulus of tricuspid valve at its posterior leaflet. Right atrial appendage incision is extended to tricuspid valve anulus by radiofrequency ablation. Aorta is occluded and cold cardioplegia infused through coronary sinus.
C, Left atrial appendage is amputated at the base. Working through base of appendage, RF ablation lesion is created anterior to left pulmonary veins. This lesion is connected to base of appendage by RF ablation lesion. Appendage is closed by suture. Working through the primary incision, left pulmonary vein RF ablation lesion is extended posterior to veins to completely encircle them. Encircling lesion is extended to anulus of mitral valve across coronary sinus. Right pulmonary vein encircling lesion is completed by extending RF ablation lesion from primary incision posterior to veins. The two pulmonary vein isolation lesions are joined across posterior and superior aspect of left atrium. D, Atrial septum is ablated on left side from fossa ovalis to primary left atrial incision (inset), and on right side from fossa ovalis across limbus to primary incision in right atrium.
Completed repair. Figure 16-7, cont’d E, Completed repair showing closure of all incisions.

made through the right atrial appendage. An incision is made in the right atrial lateral wall that curves from the fat over the AV groove toward the right superior pulmonary vein, crossing the crista terminalis. The left-sided surgical incisions to amputate the left atrial appendage and to enter the left atrium posterior to the interatrial groove are also shown, but these incisions are actually made later. Working through the primary incision in the lateral wall of the right atrium (Fig. 16-7, B), linear RF ablation lesions are created with a bipolar clamp or probe to extend the primary incision laterally and then posteriorly into the superior vena cava to the level of the caval tourniquet. An inferior isthmus ablation is performed to control atrial flutter by extending the inferior vena cava ablation line across the inferior isthmus to the tricuspid valve. The appendage incision is extended to the tricuspid valve anulus by ablation.

A clamp is placed on the ascending aorta, and cold cardiopugic solution is infused by cannula into the coronary sinus (see “Technique of Retrograde Infusion” in Chapter 3). The left atrial appendage is amputated at its base. Working through the base of the appendage, an ablation line is created anterior to the left pulmonary veins and joined to the base of the appendage. The appendage is closed by suture. Working through the primary incision posterior to the interatrial groove into the left atrium (Fig. 16-7, C), the left pulmonary vein encircling ablation lesion is completed. This encircling ablation lesion is extended to the anulus of the mitral valve. The right pulmonary vein isolation is completed by extending the primary incision (which is anterior to the veins) posterior to the veins with a RF ablation lesion. The pulmonary vein encircling ablation lesions are connected by RF tissue ablation in one or two locations. A coronary sinus ablation lesion may be added, extending from the mitral anulus along the course of the coronary sinus. Thickness of the septal tissues makes full-thickness ablation by RF energy somewhat unreliable. In other areas where RF is employed, such as around the AV valves, in the vena cavae, around the pulmonary veins, and over the coronary sinus, the atrial tissues are thin and smooth, making full-thickness tissue penetration by ablation energy easier and more reliable. The atrial septum, therefore, is ablated on both the left atrial endocardial surface from the fossa ovalis to the primary left atrial incision, and on the right atrial endocardium from the fossa ovalis over the limbus to the primary incision in the right atrium (Fig. 16-7, D). Surgical incisions are closed in the usual fashion (Fig. 16-7, E).

Modified radiofrequency maze III procedures that combine unipolar and bipolar ablation lesions offer the promise of even smaller surgical incisions, as well as assurance of complete-thickness wall lesions. Bipolar ablation is performed for long linear lines crossing thick or irregular atrial wall. Unipolar ablation is performed to extend the bipolar lesions to areas where the tissues are more delicate, such as around the AV valves, in the cavae, or across the coronary sinus. These lesions can also be created with a cryoprobe, but as noted earlier, the lesions created with unipolar RF probes or cryoprobes may not be consistently transmural. Fig. 16-8 shows a lesion set that combines unipolar and bipolar modalities and allows the operation to be performed through four surgical incisions 1 or 2 cm in length, in addition to the incision to amputate the left atrial appendage.

Anatomic studies in human hearts by Castellá and colleagues have shown that bipolar clamps cannot be used safely to create lesions in the left atrium at the mitral anulus because of possible injury to the coronary sinus and circumflex coronary artery. In the right atrium, clamp placement toward the tricuspid anulus that excluded the right coronary artery left 8 to 18 mm of atrial muscle free from the bipolar electrodes. These authors suggested that lines to the AV anuli should be completed with the cut-and-sew technique.
Figure 16-8  Modified radiofrequency (RF) maze III procedure using bipolar and unipolar ablation. A, Small incision is made at tip of right atrial appendage. Bipolar full-thickness RF ablation (lines) of lateral wall toward midportion of atrium are depicted. Small incision is made in lateral wall of right atrium anterior to crista terminalis, corresponding to middle of atrial septum. Bipolar RF lesions are made on lateral wall of right atrium directed to atrioventricular groove and toward superior vena cava posterior to site of sinoatrial node. Latter lesion is extended by unipolar RF ablation (stippled) posteriorly onto thin part of superior vena cava. Small incision is made at inferior vena cava–right atrial junction. The two surgical incisions are joined by bipolar ablation. Left atrial appendage is excised and oversewn. Left atrium is opened by incision behind interatrial groove on right side. B, Bipolar full-thickness RF ablation is made through right atrial appendage medially to atrioventricular groove and extended to the tricuspid anulus, using unipolar energy. Working through cavoatrial incision, a bipolar ablation lesion is made across inferior isthmus toward midportion of posterior leaflet of tricuspid valve. This lesion is extended to anulus by unipolar ablation. Unipolar ablation is used to extend from surgical incision into inferior vena cava. Bipolar ablation of atrial septum is performed.

Continued
Less Invasive Surgical Procedures
During the last decade, a primary objective of most new surgical procedures has been to make them less invasive. Off-pump and minimally invasive techniques incorporating video-assisted thorascopy have been developed. These techniques have used differing energy sources and lesion sets and have principally involved pulmonary vein isolation and amputation of the left atrial appendage.

Catheter-Based Interventions
A number of catheter-based endocardial techniques have been devised to treat atrial fibrillation, based on the assumption that trigger sites for initiation of atrial fibrillation are found principally within the orifices of the pulmonary veins. These techniques are often not as successful in controlling atrial fibrillation as the maze III procedure. Nevertheless, it is likely more patients will be treated with these techniques in the future because of their less invasive nature.

RESULTS
Ventricular Rate Control
The AFFIRM clinical trial of 4040 patients with atrial fibrillation persisting for more than 6 months has shown at 5-year follow-up that cardiac rate control and anticoagulation results in 40% of patients in normal sinus rhythm and comparable outcomes compared with more aggressive treatment to control the cardiac rhythm. There was no difference in survival, stroke, functional status, or quality of life. Combined rates of death, stroke, major bleeding, and cardiac arrest were 29% in the rate control group vs. 28% in the rhythm control group. Other randomized trials have failed to demonstrate a benefit of rhythm control over rate control, including trials in patients with heart failure and an ejection fraction of 35% or less.

Cardioversion
Drug and electrical cardioversions are nearly always successful for the first episode of atrial fibrillation or flutter. Failure to achieve sinus rhythm increases with subsequent episodes. Recurrence during the first year after cardioversion is at least 50%. The rhythm control arm of the AFFIRM study employed amiodarone, sotalol, propafenone, or procainamide for aggressive medical treatment of atrial fibrillation. At 5-year follow-up, 60% of patients were in normal sinus rhythm, although they required more hospitalizations than the rate control group.

Ablation of Atrioventricular Conduction
Quality of life has been considerably improved by catheter ablation of the AV junction. Other than abolishing rapid ventricular rate, it does not protect against thromboembolism or other consequences of atrial flutter or fibrillation.

Rhythm Control by Surgical Intervention
Maze III Procedure
Cox and colleagues reviewed outcomes in 346 patients who underwent the maze procedure, 299 of whom underwent the maze III modification. Operative mortality was 2%
(CL 1.3%-3.1%). Overall success in curing atrial fibrillation was 99%. There was no permanent damage to the sinoatrial node. Left atrial contractile function after operation occurred in 93% of patients, and right atrial function in 99%.

Schaff and colleagues performed 221 maze procedures in which 75% of patients underwent concomitant operations for associated cardiac disease. Early mortality was 1.4% (CL 0.6%-2.7%), and 85% to 90% of patients were free of atrial fibrillation. In addition to restoring sinus rhythm, mean ejection fraction increased in these patients from 31% to 53%, but 26% had reduced left ventricular ejection fraction.

Arcidi and colleagues reported overall cure of atrial fibrillation in 97% of 99 patients having the maze III procedure, 78 of whom underwent another cardiac operation, usually on cardiac valves.

The effect of the maze procedure on stroke was studied in 306 patients followed for up to 12 years. Fifty-eight of these patients had stroke before operation, and there were two perioperative strokes. After operation, only one patient experienced stroke. Warfarin anticoagulation was used in only 45 of the patients who received mechanical or mitral valve prostheses.

**Modified Maze Procedures**

The left side unilateral maze procedure is commonly performed by creating either a pulmonary vein–encircling incision or lesion, with or without extension to the mitral valve anulus, or with a cryolesion on the mitral valve anulus, and excision of the left atrial appendage. When energy sources rather than surgical incisions are used to interrupt the macroreentrant circuits, and when fewer lesions are created in the atria, results have been less optimal. Left atrium–only modified maze procedures using RF ablation for creating lesions encircling the pulmonary veins and a lesion extending from this to the mitral anulus were described by Melo and colleagues. Sinus rhythm was restored in 44% of patients. Others have reported greater success (77%-82%) using left atrial RF lesions applied either endocardially or epicardially. Pasic and colleagues created encircling RF ablation lines around right and left pulmonary veins separately, joining the left pulmonary vein ablation line to the mitral valve anulus across the coronary sinus, and joining the separate pulmonary vein lines with another lesion on the roof of the atrium. The left atrial appendage was not excised. Freedom from atrial fibrillation was 92% at 6 months. Mohr and colleagues reported that 81% of 234 patients were in normal sinus rhythm 6 months after having left-side-only atrial ablation using RF energy.

The longest clinical experience with radiofrequency ablation of both atria is that of Sie and colleagues. Two hundred patients were treated with the biaxial modified maze procedure using irrigated RF ablation. Follow-up extended to 80 months, with mean follow-up of 41 months. Normal sinus rhythm or atrial rhythm was present in 73% of patients; 20% remained in atrial fibrillation or flutter, and 6.3% required a permanent pacemaker.

Clinical series have compared left-side-only RF ablation vs. ablation of both atria. In a meta-analysis of 5885 patients undergoing surgical ablation, Barnett and Ad reported that bilateral procedures demonstrated better freedom from atrial fibrillation at all time points (up to 3 years) than left atrial procedures. In a study of 575 patients with permanent atrial fibrillation (duration > 6 months) by Gillinov and colleagues, the Cox-maze procedure and lesion sets resembling it resulted in a similarly low prevalence of late postoperative atrial fibrillation. Pulmonary vein isolation and lesion sets that did not include a lesion to the mitral anulus were less effective. Older age, larger left atrium, and longer duration of atrial fibrillation preoperatively were risk factors for increased prevalence of postoperative atrial fibrillation.

**INDICATIONS FOR OPERATION**

Patients should be considered for operation when maximal medical therapy has failed to relieve symptoms associated with atrial fibrillation. Symptoms that interfere with lifestyle or ability to work include dyspnea on exertion, easy fatigue, lethargy, malaise, and anxiety or sense of doom during periods of atrial fibrillation. Separation of symptoms due to atrial fibrillation from associated cardiac conditions, primarily valvar heart disease, may be difficult. Operation is not recommended when there is severe left ventricular dysfunction not directly attributable to atrial fibrillation, or when there is associated cardiac or noncardiac disease that would increase the risk of operation. Performing a maze procedure is advisable for patients who are undergoing mitral valve surgery and have documented evidence of atrial fibrillation. Epicardial pulmonary vein isolation can be performed in selected symptomatic patients with aortic valve or coronary artery disease.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Maze Procedures for Paroxysmal Atrial Fibrillation**

Patients with paroxysmal atrial fibrillation are often symptomatic with palpitations, irregular heart rhythm, and breathlessness due to intermittent episodes of rapid ventricular rate. They may be refractory to medical treatment. Isolated paroxysmal atrial fibrillation is not a common indication for maze procedures, because satisfactory results can be obtained with catheter ablation, but symptomatic patients may benefit from this therapy. Forty-two patients with paroxysmal atrial fibrillation were treated with a maze III procedure by Lonnerholm and colleagues. A subgroup of 17 patients who had normal sinus rhythm prior to operation and no associated cardiac operation was carefully studied to determine outcomes and atrial function. Sixteen of 17 were in normal sinus rhythm after operation; one was atrially paced. Two years after operation, 10 of 12 patients had normal sinus rhythm (83%; CL 65%-94%), one was paced, and one had nodal rhythm. Left and right atrial size decreased at 2 months, but there was a gradual decrease of left atrial transport function during 2-year follow-up. Fifteen patients (88%; CL 74%-96%) had signs of left atrial contraction.

In patients with paroxysmal atrial fibrillation who are undergoing mitral valve surgery, pulmonary vein isolation may be adequate therapy, particularly when atrial fibrillation is of short duration. If it is of longer duration, a bilateral maze III procedure would be performed. For patients with coronary artery disease or aortic valve disease where a left atriotomy is not otherwise indicated, epicardial pulmonary vein isolation is reasonable.

Pulmonary vein isolation as the sole lesion set can be arrhythmogenic, especially in patients with enlarged or
diseased left atria. In this setting, atrial flutter is a frequent postoperative event.\textsuperscript{c16} Atrial flutter and other arrhythmias also occur after more extensive ablation procedures.\textsuperscript{c38} Ablation of ganglionated plexi that enter the heart along the pulmonary veins has been proposed as a mechanism to reduce the frequency of atrial fibrillation following pulmonary vein isolation procedures. Several clinical trials of catheter ablation of paroxysmal atrial fibrillation by pulmonary vein isolation in which obliteration of these ganglionic plexi was also performed have demonstrated clinical benefit in terms of lower frequency of recurrence of atrial fibrillation.\textsuperscript{c11,p14,s5} Experimental studies, however, have demonstrated early reinnervation and vagal activity.\textsuperscript{o2,s1} Thus, the role of ablation of ganglionic plexi during surgical pulmonary vein isolation procedures for paroxysmal atrial fibrillation has not been clearly established.

Standards for Assessing Success or Failure

Uniform standards for assessing success or failure of the various surgical procedures for treatment of atrial fibrillation have not been consistently employed. According to Cox, all occurrences of postoperative atrial fibrillation, atypical left atrial flutter, and classic right atrial flutter should be classified as failures.\textsuperscript{c16} The methods by which these arrhythmias can be detected postoperatively are variable and controversial. Ad and colleagues evaluated three modalities to determine success of the Cox-maze III procedure: electrocardiography, 24-hour Holter monitoring, and long-term monitoring (5 days).\textsuperscript{s1} Mean time to monitoring was 9.8 months postoperatively. Electrocardiographic monitoring underestimated success by 12% compared with long-term monitoring. Nearly 50% of the events detected were shorter than 5 minutes for the entire 5-day period. They have suggested that use of a specific algorithm-driven clinical protocol postoperatively, including longitudinal follow-up and long-term monitoring, will increase the success of the various surgical procedures.\textsuperscript{o2}

The central challenge in defining success of ablation procedures for atrial fibrillation is its episodic nature (Fig. 16-9). Frequency of detecting return of atrial fibrillation will therefore depend on frequency and duration of “snapshots” of rhythm (Fig. 16-10).\textsuperscript{a12} The U.S. Food and Drug Administration has approved use of an implantable loop recorder for continuous monitoring of heart rhythm (Fig. 16-11) using a detection algorithm based on regularity of R-R intervals.\textsuperscript{c16,m6} Data from this device, as well as from pacemakers and implantable cardioverter-defibrillators, will be required to ascertain the true success of these procedures.

Atrial Fibrillation and Flutter Occurring after Cardiac Surgery

Atrial flutter or fibrillation occurs in 20% to 40% of patients after coronary artery bypass grafting.\textsuperscript{e1,g18} Daubert and Mabo, in a review of five controlled trials, reported a prevalence of 27% to 39%.\textsuperscript{d3} Occurrence after cardiac valve operations is even greater.\textsuperscript{b7} Improved operative techniques, anesthesia, and myocardial management have not decreased prevalence. The arrhythmia usually occurs within the first 3 days after operation, although it may occur later. It occurs spontaneously, usually follows a self-limiting course, and becomes chronic in only a small percentage (<5%) of patients.\textsuperscript{b7,o4} More than 90% of patients have no prior history of atrial arrhythmia and are in normal sinus rhythm within 6 to 8 weeks after operation. Tachycardia can produce symptoms of anxiety and light-headedness. When heart rate is very high for a prolonged period, it may result in hemodynamic compromise, particularly in patients with left ventricular dysfunction. There is an increased risk of thromboembolism associated with atrial fibrillation, with the incidence of stroke approximately three times higher than in patients without postoperative atrial fibrillation.\textsuperscript{c30,e1,m7} Hospital and late mortality are also increased.\textsuperscript{a8,e1,s5}

The cause of atrial fibrillation after cardiac surgery is not known and is likely related to a number of factors, most of which are uncontrollable. These include increased catecholamine release, pericardial inflammation, alterations in balance of other neurohormonal agents or electrolytes (hypokalemia), and cellular electrical properties. Age, with its accompanying degenerative changes in atrial myocardium, and systemic arterial hypertension are important risk factors.\textsuperscript{b7,d3} Other risk factors include decreased left ventricular function, chronic obstructive pulmonary disease, chronic renal failure, and diabetes. Withdrawal of β-blockers has also been implicated.\textsuperscript{d3}

Preventing atrial arrhythmias in the postoperative period would be optimal. A number of medications have been administered before and after cardiac operations as prophylaxis against atrial fibrillation. Bharucha and Kowey\textsuperscript{b7} reviewed management and prevention of atrial fibrillation after cardiac operations and suggested that the only
medications with proven benefit are β-blockers. Medications with possible benefit include digitalis, propranolol, sotalol, amiodarone, corticosteroids, and statins. Meta-analysis indicates that β-blockers, sotalol, and amiodarone reduce the frequency of postoperative atrial fibrillation compared with placebo groups, although the magnitude of reduction is variable. These studies include non-blinded trials. Atrial pacing may be beneficial when combined with medical prophylaxis. Calcium channel blockers have not proven to be effective.

Because postoperative atrial fibrillation has a self-limited course in most patients with no history of prior atrial arrhythmia, treatment strategy is directed toward control of ventricular response. First-line drugs of choice are β-blockers. Digoxin is sometimes administered via rapid intravenous administration, partly because of tradition and because it may be helpful in slowing the ventricular response and restoring sinus rhythm, but scientific data are not supportive. Calcium channel blockers (verapamil, diltiazem), which affect the AV node, also control ventricular rate, but the effect is transient unless given as a continuous intravenous infusion. They are no more effective than β-blockers in controlling ventricular rate. Intravenous amiodarone may be beneficial in controlling ventricular rate or restoring sinus rhythm. Pharmacologic cardioversion is desirable, but there is no drug that is uniformly successful. Ibutilide given intravenously has been most effective in patients with atrial flutter, but it is proarrhythmic and may cause sustained ventricular tachycardia (torsades de pointes) in about 2% to 4% of patients.

Anticoagulation is initiated if sinus rhythm is not restored within 48 hours after the onset of atrial fibrillation, because the risk of thromboembolism increases at that point. This is especially important if electrical cardioversion is anticipated. Conventional recommendations for anticoagulation are followed. Intravenous heparin or one of its analogs is administered with warfarin and continued until a therapeutic level of anticoagulation is established.

Electrical cardioversion may be performed. Ordinary transthoracic cardioversion is usually successful. Cardioversion may be applied urgently for patients with rapid ventricular response and hemodynamic instability. Antiarrhythmic drugs are continued for at least 3 weeks following successful electrical cardioversion.

Guidelines for prevention and management of postoperative atrial fibrillation have been published jointly by the ACC, AHA, and ESC and are summarized in Box 16-6.

Pacing and Other Methods of Atrial Electrical Cardioversion

Temporary epicardial wire pacing electrodes placed during cardiac operations and used for diagnostic or therapeutic purposes have been part of standard postoperative cardiac care for many years. Ideally, two electrodes are placed...
on the right atrium and the right ventricle. An atrial electrode may be used to diagnose atrial arrhythmia simply by attaching the wire to the chest lead of the ECG. This magnifies the atrial electrical activity and permits identification of large P waves of sinus rhythm, rapid spikes of atrial flutter, or the disorganized atrial electrical activity of atrial fibrillation. Attaching atrial electrodes to a rapid-rate external pacemaker with rate set at 400 to 800 beats · min⁻¹ overdrives the atrial arrhythmia rate. Gradual reduction of the pacing rate may capture the atrium at a lower rate and convert atrial rhythm to normal sinus. Experience has shown that success in conversion to sinus rhythm occurs in about one of four patients. Success is higher when atrial overdrive pacing is done for atrial flutter (65% of patients converted) and when the patient is pretreated with an intravenous β-blocker (metoprolol 2.5 to 5 mg intravenously).²⁹

Temporary defibrillation electrodes may also be placed on the atria at the time of cardiac operation and used to deliver low-energy direct current cardioversion of atrial fibrillation. Liebold and colleagues reported use of epicardial defibrillation wire electrodes placed on the left and right atria during cardiac operations in 100 consecutive patients.¹¹⁶ Atrial fibrillation occurred in 23 patients (23%). The atrial electrodes were used to deliver synchronous monophasic shocks with low energies ranging from 2 to 10 J. Defibrillation was successful in 16 of 20 patients (80%). Sedation was required during defibrillation in 30% of patients. Electrode wires and a device to reduce the output of a standard defibrillator to 9 J has been developed (Syncerus, Guidant, Santa Clara, Calif.). Patel and colleagues²⁶ used this device in 45 patients; 16 (35%) developed atrial fibrillation. Fifteen patients were successfully cardioverted at initial treatment, one 6 hours later, and 4 after atrial fibrillation recurred. This technique was based on experimental defibrillation in experimental models.²⁷,²⁸ Waldo suggested that this technique of low-energy atrial defibrillation with temporary epicardial wire electrodes should become standard in treatment of atrial fibrillation after open heart surgery.²⁹ More important, he proposed that use and success of temporary electrodes opened the way for implantable atrial defibrillators to provide automatic atrial defibrillation. Wells and colleagues reported implanting a defibrillator (Attrioverter) connected to electrodes placed in the right atrium and coronary sinus in 81 patients with recurrent atrial fibrillation who did not respond to antiarrhythmic drugs.³⁰ Successful defibrillation of the atrium was accomplished in 96% of 227 episodes of atrial fibrillation in 41 patients without inducing ventricular arrhythmia. Devices are available that can detect and treat atrial tachyarrhythmias with pacing and high-energy defibrillation.³⁵

Section V Ventricular Tachycardia and Ventricular Fibrillation in Ischemic Heart Disease

HISTORICAL NOTE

In 1938, Parkinson and colleagues apparently first noticed the association between ventricular aneurysm and intractable ventricular tachycardia.³² However, the problem seemed to be known to Sir Thomas Lewis, who stated in 1909 the need for studying and understanding the condition by a controlled method of inducing tachycardia.³³ This need was met in 1967 when Durrer and colleagues in Holland, and Coumel and colleagues in France, introduced the technique of programmed electrical stimulation of the human heart.³⁴³⁵

The first surgical approach to treating life-threatening ventricular tachycardia in patients with ischemic heart disease was reported in 1959 by Couch using simple aneurysmectomy.³⁶ Fontaine, Frank, and Guiraudon reported surgical epicardial mapping as an adjunct to this kind of surgery in 1974, and Gallagher and colleagues reported successful use of ventricular aneurysm resection guided by electrophysiologic mapping in 1975.³⁷,³⁸ In 1978, Guiraudon and colleagues introduced encircling endocardial ventriculotomy as a method of directly treating life-threatening ventricular tachycardia in patients with ischemic heart disease.³⁹ Harken and colleagues reported electrophysiologically directed endocardial resection as a method of treatment in 1980.⁴⁰

An entirely new concept of interventional management was introduced in 1980 when Mirowski and colleagues reported implanting a cardioverter-defibrillator in humans.⁴¹ This important event was preceded by more than 10 years of work directed at this endpoint and nearly 100 years of experimental and clinical studies of increasing sophistication.⁴²,⁴³,⁴⁴,⁴⁵

MORPHOLOGY

Sustained ventricular tachycardia is an uncommon complication of ischemic heart disease in the absence of a previous
myocardial infarction. It occurs most commonly in patients in whom a large area of infarction has developed, and particularly in those with a left ventricular aneurysm. These patients have, as a group, more left ventricular impairment than patients without this life-threatening complication. Thus, Kirklin and colleagues reported that patients undergoing operations for ventricular tachycardia had a mean ejection fraction of 30%, similar to that of patients undergoing surgical treatment for left ventricular aneurysm, whereas those undergoing isolated coronary artery bypass grafting had a mean ejection fraction of 51% (P = .0001). However, life-threatening ventricular tachycardia develops in only a minority of patients with ischemic heart disease and left ventricular aneurysm with impaired left ventricular function. Although all the determinants of which patients are affected by ventricular tachycardia are not clear, septal involvement in the scarring seems to be one of them. The morphologic substrate for ventricular tachycardia in ischemic heart disease resides for the most part in the subendocardium of the left ventricle and left ventricular aspect of the ventricular septum. This substrate is most commonly near the border of an aneurysm or infarct. Virtually all hearts with a myocardial infarction have a mixture of myocardial cells and fibrous tissue in at least some areas of the left ventricle; such areas provide a basis for slow conduction and conduction block, two conditions necessary for ventricular reentry to occur. Thus, in areas of the subendocardium where ventricular tachycardia may begin, bundles of viable myocardial cells are embedded in dense connective tissue. These bundles may consist of Purkinje fibers or ventricular muscle fibers or both. These generally parallel muscle bundles do not appear to connect to fibers within the ventricular wall, and in regions where ventricular tachycardia seems to originate, there may be no surviving myocardial cells above the subendocardium. Thus, the surviving subendocardial muscle bundles are generally connected to the rest of the ventricle across the borders of subendocardial portions of the scar.

This arrangement of parallel bundles of myocardial fibers separated by fibrous or connective tissue forms a nonuniform anisotropic (conducting in one direction) structure that is considered an ideal substrate for reentrant circuits. Conduction between muscle bundles is probably slow, whereas conduction along the length of the muscle bundles is probably rapid. The fractionated character of electrograms recorded from such regions is also probably related to the nonuniform anisotropic anatomy. It is hypothesized that the larger the proportion of left ventricle involved with these morphologic characteristics, the greater the possibility that reentrant circuits develop, activate contiguous subendocardium, and provoke ventricular tachycardia or ventricular fibrillation. Actual time and place of development of the electrical phenomenon responsible for ventricular tachyarrhythmia (VT) appears to be determined by chance.

Even among individuals with life-threatening ventricular arrhythmias but without any other evidence of cardiac disease, a morphologic substrate likely to be responsible for the arrhythmia is usually found. Sugrue and colleagues report several different types of histopathologic abnormalities in such patients coming to autopsy, including myocardial cellular hypertrophy, interstitial fibrosis, myocardial degenerative changes, and acute myocarditis.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Pathophysiology**

Most life-threatening ventricular arrhythmias in patients with ischemic heart disease arise as a result of macro- or micro-reentry circuits, but some result from normal or abnormal automaticity or triggered activity. In many patients, the abnormal impulse breaks through onto the endocardial surface near its origin, resulting in the earliest ventricular electrical activation at this point. Its breakthrough onto the epicardial surface may be some distance away.

**Symptoms**

In some patients, sudden death is the first manifestation of important ventricular tachyarrhythmia. In others, premature ventricular contractions, ventricular tachycardia, or ventricular fibrillation causes the first symptoms during recovery from a myocardial infarction. In still others, frequent palpitations, sometimes accompanied by faintness or syncope, are the presenting complaint.

**Signs**

The diagnostic finding is a verified history of life-threatening ventricular tachycardia or fibrillation, or sustained ventricular tachycardia induced during electrophysiologic study.

**NATURAL HISTORY**

Sustained ventricular tachycardias and fibrillation may occur within the first 48 hours after an acute myocardial infarction but do not worsen prognosis; they are presumably ischemic in origin. Such arrhythmias occurring later in the course of recovery are less common but worsen prognosis. Episodes are often multiple, and when they occur, in-hospital mortality is as high as 60%. Such patients generally have inducible ventricular tachycardia when studied by programmed electrical stimulation, and a poor long-term prognosis even with intense medical therapy. Marchlinski and colleagues reported only 20 (50%; CI 41%-59%) of 40 such patients alive after a mean follow-up period of 20 months, with more than half the deaths occurring suddenly. As is the case in other patients with ischemic heart disease, prognosis of medically treated patients with life-threatening ventricular tachyarrhythmias is adversely affected by presence of severe proximal anterior descending coronary artery stenosis.

Some patients present after resuscitation from sudden death. The most important risk factors for sudden death in patients are advanced functional disability, as indicated by New York Heart Association functional class; lack of response to therapy, as judged by programmed electrical stimulation; and depressed left ventricular function. The natural history of individuals resuscitated from sudden death is highly variable, but in general is not favorable. Seward and colleagues found that 34% of resuscitated patients died suddenly within 3 years of their first episode.

Ability of medical treatment to improve natural history is limited because an effective antiarrhythmic drug can be identified by electrophysiologic testing in less than 35% of cases. Empirical therapy with high-dose amiodarone has been favorable in several large series. However, in an...
appreciable number of patients, severe adverse drug reactions or aggravation of arrhythmic symptoms develop.\textsuperscript{2,3,5}

**TECHNIQUE OF INTERVENTION**

Because even type of intervention remains arguable, techniques for intervention continue to be modified.

A direct surgical approach, usually at the time of ventricular aneurysmectomy and coronary artery bypass grafting, consists of electrophysiologic mapping at surgery and procedures designed to isolate the presumed arrhythmogenic focus from the rest of the ventricular mass. Mapping has been done sequentially or with special arrays of electrodes and computer-based electrophysiologic analyses that allow all the information to be obtained during a few heartbeats.\textsuperscript{19,21,34,48}

Cryoablation techniques have been used to electrically isolate the arrhythmogenic focus. When the ventricular tachycardia is monomorphic, catheter ablation techniques in the cardiac electrophysiologic laboratory can also be effective. This, however, has been the case in a minority of patients.

The implantable cardioverter-defibrillator (ICD) has come to be the most appropriate method of treating most patients with life-threatening ventricular tachyarrhythmias resulting from ischemic heart disease. Implantation methods have improved over time such that it has become possible to insert an ICD using techniques similar to pacemaker insertion. Two electrodes are required and, although larger in diameter than those employed for pacemaking, may be inserted by needle and guidewire technique using direct puncture of the subclavian vein. ICD pulse generators are larger than those of a pacemaker. A larger subcutaneous pocket is required, but the device can be placed in a prepectoral position below the clavicle. Operation for inserting and testing the device is performed under local anesthesia with intravenous conscious sedation, although general anesthesia is sometimes required.

**RESULTS**

**Direct Surgical Approach**

Most patients with ischemic heart disease undergoing interventional therapy for life-threatening ventricular tachyarrhythmias die in cardiac failure, not suddenly or with an intractable arrhythmia.\textsuperscript{39,48} This fact, plus its considerable early and late risks approach, accounts for lack of enthusiastic acceptance by cardiologists of direct surgical treatment of life-threatening ventricular tachycardia in patients with ischemic heart disease. Improved early mortalities have been reported by others, but a highly favorable effect on long-term survival has not been demonstrated.\textsuperscript{19,21,34,48,50} Again, this is largely related to the fact that left ventricular structure and function tend to be poor in this subset of patients.

**Implantable Cardioverter-Defibrillator**

Increasing evidence as to the efficacy of ICD devices, coupled with low hospital mortality after their insertion, has made them virtually the therapy of choice in patients with ischemic heart disease in whom life-threatening intractable ventricular tachyarrhythmias develop.\textsuperscript{2,5,44,47,54} Operative mortality associated with transvenous ICD implantation is 0.5% to 0.8%.\textsuperscript{52,71} Even with this device in place, poor left ventricular function adversely affects prognosis.\textsuperscript{58} Recurrence of life-threatening ventricular arrhythmias is observed in 30% to 50% of patients after ICD implantation, yet only 1% to 2% of patients die of sudden cardiac death.\textsuperscript{51}

ICDs successfully terminate ventricular fibrillation in 98% of cases. Ventricular tachycardia is successfully converted by overdrive pacing in 89% to 91% of cases, and when not successful, defibrillation shock terminates the arrhythmia in 98% of cases. Antiarrhythmia pacing features add 5% to 10% to the cost of ICDs, but it has been shown that antiarrhythmia pacing is activated frequently (68% of patients) and will terminate the arrhythmia in as high as 96% of arrhythmia episodes.\textsuperscript{20} Inappropriate pacing or shocks are delivered typically for atrial fibrillation, with rapid ventricular response in 5% to 11% of patients. Dual-chamber sensing and pacing ICDs should largely eliminate inappropriate pacing or shocks in patients with associated atrial arrhythmias.

Prospective randomized trials have shown improved patient survival for patients treated with an ICD compared with those receiving drug therapy, including those receiving class III antiarrhythmic drugs, with estimated risk reduction of 39% at 1 year and 31% at 3 years.\textsuperscript{51}

**INDICATIONS FOR INTERVENTIONAL THERAPY**

Results of drug therapy for managing patients with ischemic heart disease and recurring ventricular tachyarrhythmias have been disappointing.\textsuperscript{93} Some patients requiring surgical therapy for a left ventricular aneurysm with otherwise excellent ventricular function and important coronary stenoses only in the anterior descending coronary artery may be treated by bypass grafting to the anterior descending coronary artery, resection of the left ventricular aneurysm, and electrophysiologically directed cryoablation for the control of the tachyarrhythmia. Patients whose tachycardia is monomorphic should be considered for catheter ablation, which is successful in about half of patients.\textsuperscript{23}

Most patients with life-threatening ventricular arrhythmias, however, are best treated by insertion of an ICD. In response to publication of numerous studies showing that ICD insertion can alter the natural history of cardiac arrhythmia and major advances in the technology of automatic cardioversion by pacing therapy or defibrillation by shock therapy, the ACC, AHA, NASPE, and HRS appointed a committee of physicians to develop guidelines for implantation of ICDs.\textsuperscript{51} An updated summary of these indications is listed in Box 16-7.\textsuperscript{19} This comprehensive document is a definitive statement on indications for cardiac pacing. Because device development continues to advance rapidly, these indications may be subject to frequent revision.

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**Section VI**

**Intractable Ventricular Tachycardias**

**ARRHYTHMOGENIC RIGHT VENTRICULAR DYSPLASIA**

Right ventricular dysplasia is an uncommon and somewhat poorly defined entity. Uhl anomaly, a condition in which the free wall of the right ventricle is “like parchment,” with only
a few myocardial fibers between epicardium and endocardium, is often included within this group of patients. In other patients, the right ventricular free wall has both thick and thin areas of pathologic development. The basic pathologic process is believed to be progressive replacement of myocardial fibers in the subepicardium and mid-myocardium by fatty tissue. Characteristically, the right ventricle is enlarged and deformed by bulging areas over the infundibulum, apex, and basal portion of the inferior wall. Involvement of the right ventricle is initially regional and may progress to global involvement of the right ventricle. The left ventricle may eventually be involved, but the septum is spared. The disease is often familial, with autosomal dominant inheritance but incomplete penetrance.

Intractable ventricular tachycardia may develop in childhood or in adult life in patients with arrhythmogenic right ventricular dysplasia. Strands of partially degenerated myofibrillar fascicles, which connect with normal myocardium, are believed to provide a basis for slow conduction and reentry. Electrophysiologic studies are indicated. Rarely, a site of monomorphic inducible sustained ventricular tachycardia can be identified, and catheter ablation is then the treatment of choice (Epstein A: personal communication; 1991). More often it is polymorphic and multifocal and resistant to drug therapy. Right ventricular isolation is then an effective therapy. This extensive procedure does not change regional right ventricular systolic or diastolic performance. In some patients, a properly oriented simple ventriculotomy, cutting across the arrhythmogenic focus, is recommended, although at times a localized resection has been done.

### ARRHYTHMOGENIC LEFT VENTRICULAR DYSPLASIA

In arrhythmogenic left ventricular dysplasia, a rare cause of intractable ventricular tachycardia, the histopathologic substrate is the same as in arrhythmogenic right ventricular dysplasia but with more fibrosis. Preoperative and intraoperative electrophysiologic studies are said to identify the condition, and encircling endocardial ventriculotomy is performed to stop the arrhythmia.

### IDIOPATHIC INTRACTABLE VENTRICULAR TACHYCARDIA

Idiopathic intractable ventricular tachycardia has also occasionally been treated surgically. In one report, the tachycardia...
seemed to originate in the left ventricular free wall in one of three cases and in the ventricular septum in the other two cases. Most commonly, idiopathic intractable ventricular tachycardias are treated with calcium channel blocking agents and other drugs. In a small subset of patients, this tachycardia arises in the right ventricular outflow tract and is amenable to catheter ablation.\textsuperscript{15} 

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**Definition**

*Cardiac trauma* is damage done to the heart by penetrating or nonpenetrating injuries.

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**Section I  Penetrating Cardiac Trauma**

**Historical Note**

The first suggestion that wounds of the heart and great vessels could be sutured may have been by Roberts in 1881. In 1882 and 1895, studies of experimental closure of cardiac wounds in animals were reported. On September 9, 1896, Rehn in Germany successfully repaired a penetrating cardiac wound. Mead reported that Williams first successfully performed a heart operation in the United States when, in 1889 at Provident Hospital in Chicago, he repaired a stab wound. The first published report of a successful heart operation in the United States was by Hill, who repaired a stab wound in Montgomery, Alabama, in 1902. In his report, Hill not only described successfully suturing the wound, but also summarized 37 other cases reported by that time.

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**Morphology**

When a sharp, long-bladed instrument is violently driven into the midportion of the thorax and penetrates the pericardium, a laceration of the heart or great vessels commonly results. The right ventricle alone is involved in 35% of patients reaching a hospital after their traumatic episode. Occasionally, however, a missile may produce a tangential laceration of a ventricle or penetrate a cardiac chamber and come to rest within it.

**Clinical Features, Diagnostic Criteria, and Natural History**

**Pathophysiology**

Most stab wounds of the heart result in acute pericardial tamponade, although occasionally, rapidly exsanguinating hemorrhage may result. The patient thus usually presents
with symptoms and signs of acute cardiac tamponade complicated by acute blood loss. (For a discussion of cardiac tamponade, see “Acute Cardiac Tamponade” under Clinical Features and Diagnostic Criteria in Section I of Chapter 23.)

Missile wounds usually result in acute hemorrhagic shock, which may be rapidly fatal. If not, the patient enters the hospital profoundly hypotensive, with tachycardia and collapsed veins.

Penetrating cardiac wounds are frequently accompanied by wounds involving the pleural space, the intrapericardial thoracic vessels, the lung, and occasionally by wounds of the liver and other abdominal viscera.

Symptoms and Signs

External evidence of a penetrating wound is usually apparent, although in the case of injury with a stiletto, the external wound may initially escape discovery. The external wound and evidence for either hemorrhagic shock or acute pericardial tamponade dominate the clinical presentation.

Special Studies

If the patient’s condition permits, a chest radiograph is made. In the rare situation of an initially stable patient, or in a patient recovering from repair of a penetrating wound in another organ and now suspected of having also suffered a cardiac laceration, usual techniques of cardiac investigation are used. Two-dimensional echocardiography, particularly transesophageal echocardiography (TEE), is the technique best adapted to these situations. Its use minimizes, in nonemergency situations, subxiphoid exploratory pericardiotomy.\textsuperscript{8,52,54}

**TECHNIQUE OF OPERATION**

When a patient presents with a penetrating wound of the chest in a location and direction that could involve the heart, the assumption is made that a penetrating wound of the heart exists. Resuscitative measures, including endotracheal intubation, volume replacement, and insertion of chest tubes, are performed promptly on admission to the emergency department, except in stable patients without shock or respiratory distress.

All centers properly prepared for treating patients with cardiac wounds have well-developed protocols.\textsuperscript{36} Only general methods of management are described here.

**Stab Wounds**

Patients with stab wounds of the heart and great vessels usually survive when treatment is adequate, except for those in extremis on admission (most of whom have suffered immediate and massive hemorrhage from laceration of a great vessel).

If the stabbing device is still in place when the patient is admitted to the emergency department, it is not removed until the incision is made and ideally not until the pericardium is opened.

When the patient arrives in the emergency department unconscious and without vital signs or semiconscious with gasping respirations, a thready pulse, and no blood pressure, and all evidence points to a cardiac or great vessel wound as the cause, prognosis is poor; immediate thoracotomy (see discussion under “Missile Wounds” later in this chapter) is indicated if the emergency department is prepared for this type of major surgery.\textsuperscript{45,11,56} If not, a large-bore needle (13F) is inserted into the pericardial space through the subxiphoid route, and the patient is transported rapidly to an operating room. Because of the pathophysiology of acute cardiac tamponade (see Chapter 23), removal of even 40 to 50 mL of blood usually improves the hemodynamic state, at least temporarily. When the patient is in shock but has vital signs, a pericardiocentesis is performed as described, followed by rapid transfer to the operating room. When the patient’s condition is stable and a cardiac stab wound is only suspected, investigation can be accomplished in the emergency department or in the operating room if a noncardiac procedure is indicated. This evaluation is best performed by TEE.

Once in the operating room, the patient is rapidly anesthetized, prepared, and draped for operation. A large-bore needle is placed in an easily accessible large vein as these preparations are being made. Surgical draping should be wide, with the chest and abdomen fully exposed. Median sternotomy is made and the pericardium opened. (In institutions in which cardiac surgery is not frequently performed, an anterolateral incision, usually left-sided, is made, because this incision can be made rapidly and is the most generally useful.)

Blood is rapidly aspirated from the pericardial space with high-vacuum suckers. Ventricular wounds are best controlled initially by digital compression. Atrial and caval wounds are generally not well controlled in this manner, and wide Allis (Allis-Adair) clamps serve ideally to establish hemostasis by apposing the wound edges. If this is not possible or if the wound edges tear after application of clamps, a Foley catheter with a large balloon volume can be inserted into the cardiac chamber or vein and inflated. Only after digital or instrumental control of active bleeding has been accomplished should attention be turned to suturing the wounds. At this time, physiologic resuscitation should be completed. Blood volume is reconstituted with donor-specific matched or unmatched type O-negative blood to augment previously infused crystalloid or colloid, and blood pH is restored toward normal with bicarbonate. Supplementation calcium is usually given.

Ventricular wounds are best sutured with interrupted pledgeted mattress sutures of No. 2-0 or 3-0 polyester or polypropylene. A great danger in myocardial lacerations is their enlargement by the act of passing sutures in a fully filled and beating ventricle. It is often appropriate to induce inflow occlusion to empty the heart and provide a quieter field. After an interval of hyperventilation, the vena cavae are occluded using vascular clamps, followed by clamp occlusion of the ascending aorta after the heart has emptied a few beats later. The cardiac wound is sutured over the next 2 to 3 minutes; thereafter, the caval and aortic clamps are released. The heart will have continued to beat slowly during the occlusion period. Occasionally, a ventricular laceration is so extensive that it requires cardiopulmonary bypass (CPB) and patch-grafting of the ventricular free wall. Wounds near a major coronary artery are similarly sutured, with pledges on both sides of the artery and the sutures passing beneath it. If the left anterior descending coronary artery has been damaged, a coronary artery bypass graft should be placed (see Chapter 7). Atrial or caval wounds are closed by continuous No. 4-0 or 5-0 polypropylene sutures. Suturing is done beneath the clamp or carefully over the top of the inflated balloon of a
Foley catheter, and the clamp is removed (or balloon deflated) only after the suture line is largely in place.

Unless there is near certainty that the pleural spaces have not been violated, both are opened widely through the median sternotomy. The internal thoracic arteries, a potential source of hemorrhage, are examined and, if damaged, are suture-ligated. Damaged areas of lung are oversewn or stapled. The hilum of each lung is examined for injury to the pulmonary vessels.

Drainage catheters are placed in each pleural space (see “Positioning Chest Tubes” under Completing Cardiopulmonary Bypass in Section III of Chapter 2), and one may be placed in the pericardial space as well. If hemostasis within the pericardium has been satisfactory, the pericardium is loosely closed with widely spaced interrupted sutures. The sternotomy is closed in the usual manner (see Section III of Chapter 2).

Missile Wounds

Patients with missile wounds of the heart are far less likely to survive than those with stab wounds. Patients who are unconscious or without vital signs, or who are semiconscious but without a measurable blood pressure, should receive immediate thoracotomy if the emergency room is properly prepared. A left anterolateral incision is made, curving beneath the breast, and the thorax is entered through the fifth or sixth interspace. An assistant spreads the wound with two handheld retractors, or a self-retaining thoracotomy retractor is inserted, and digital control of the hemorrhage is obtained. If trained surgeons are in attendance and the repair appears to be a simple one, repair is then performed. Otherwise, the patient is transferred to a prepared operating room while digital control of the hemorrhage is maintained. If digital control of the hemorrhage is not possible, survival is unlikely and any further intervention inadvisable.

Patients not meeting these criteria for operation in the emergency department are transported immediately to the operating room. Principles of management are the same as described for penetrating wounds, but the result is less often successful.

SPECIAL FEATURES OF POSTOPERATIVE CARE

If a central venous catheter was not inserted in the operating room, it is placed postoperatively. Principles of care are the same as those used for patients after other forms of cardiac surgery (see Chapter 5).

A special consideration is the possibility that a major coronary artery has been damaged by the trauma or at operation. Thus, during the first few postoperative hours, if the hemodynamic state is unexpectedly unsatisfactory despite appropriate ventilator filling pressures—and particularly if the electrocardiogram suggests coronary injury—emergency coronary arteriography is performed. If a major vessel is interrupted or importantly narrowed, emergency coronary artery bypass grafting is performed.

During the early postoperative period, it must be kept in mind that penetrating wounds may have perforated a cardiac septum or damaged an atroventricular or, rarely, a semilunar valve. Should any evidence suggest such an injury, appropriate studies are indicated. TEE is particularly informative. If the findings are positive, in unstable patients, immediate repair should be considered. If the hemodynamic state remains satisfactory, however, delay for 8 to 12 weeks permits a more secure repair.

RESULTS

Prompt and effective therapy allows good results in most patients with stab wounds of the heart. Overall, about 80% of patients survive. Results for missile wounds are less satisfactory and depend upon extentiveness of the wound, condition of the patient on admission, and associated injuries. Overall survival is about 40%. The functional result in surviving patients is usually excellent, even when patch-grafting of the left ventricular free wall has been necessary.

INDICATIONS FOR OPERATION

Presence of a penetrating wound to the heart is an indication for immediate operation. A stab wound over the heart without bleeding or hypotension may indicate that no penetration has occurred, and is therefore not an indication for operation. TEE is helpful in this situation.

Occasionally, patients convalesce apparently satisfactorily and without special treatment (usually a stab wound rather than injury by a missile), only to come to medical attention weeks to years later because of a murmur or heart failure. Special studies usually demonstrate a ventricular septal defect (VSD), laceration of a cardiac valve, or aorta-to–pulmonary artery or aorta-to–brachiocephalic vein fistula. Operation is indicated, and a good result can usually be obtained.

Section II  Nonpenetrating Cardiac Trauma

HISTORICAL NOTE

In earlier times, cardiac rupture was the only sequela of nonpenetrating (closed or blunt) cardiac trauma to receive attention. Apparently, this catastrophic event was originally observed by Senac in 1778. Although rupture of the ventricular septum was described in 1847 by Hewett, not until 1959 did Campbell and colleagues at the University of Minnesota first successfully repair a VSD produced by nonpenetrating trauma. More recently, surgical attention has focused on rupture of cardiac valves as a consequence of nonpenetrating cardiac injuries, although in 1927 Adam described such injuries as well as the natural history of patients with valvar rupture secondary to trauma. Cardiac contusion has more recently been recognized as one of the complications of nonpenetrating cardiac trauma.

MORPHOLOGY

When the heart is compressed between two objects, such as the sternum and the vertebral column, intracardiac—and particularly intraventricular—pressure suddenly becomes elevated, and the free atrial or ventricular walls, ventricular septum, tensor apparatus of the atroventricular valves, or
aortic valve cusps may rupture. The same holds true when there is sudden deceleration of the chest with the heart thrust forward against the sternum. Rarely, a coronary artery fistula to a cardiac chamber develops after nonpenetrating chest trauma.

Less violent nonpenetrating injury may result simply in contusion of the myocardium. Such contusions may vary from small areas of subepicardial or subendocardial petechiae to full-thickness injury of the cardiac wall. Radionuclide angiography has shown that the anteriorly situated right ventricle is particularly susceptible to contusion.\textsuperscript{51,13}

Commotio cordis is a syndrome of sudden death seen infrequently after low-energy trauma to the anterior chest wall. Experimentally, Link and colleagues found this to occur within a narrow window during the repolarization phase of the cardiac cycle, 30 to 15 ms before the peak of the T wave.\textsuperscript{1,2} Clinically, this has been reported in children struck in the chest with a baseball.\textsuperscript{51}

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Cardiac Contusion**

Patients with cardiac contusion may exhibit no symptoms, precordial pain, or symptoms indistinguishable from those of angina. Dysrhythmias of different types may develop. Electrocardiographic abnormalities may be present shortly after injury or can be delayed 12 to 24 hours. Abnormalities may be transient or longer lasting, depending on extent of myocardial damage.\textsuperscript{52,12} Q waves may develop similar to those seen in acute myocardial infarction. Myocardial enzymes may become elevated after injury and, if so, provide a near-positive diagnosis of cardiac contusion.\textsuperscript{52} However, the electrocardiographic and enzymatic criteria are relatively insensitive and nonspecific indicators of cardiac contusion.\textsuperscript{51}

A more sensitive indicator is radionuclide angiography. Demonstration of decreased right or left ventricular ejection fraction in a previously healthy person and abnormalities of left ventricular segmental wall motion suggest myocardial contusion.\textsuperscript{12} This diagnostic study also permits sequential examination and indicates that considerable myocardial dysfunction can fail to impair the hemodynamic state; in other cases, if myocardial dysfunction does impair the hemodynamic state, it can revert to normal within a few weeks.\textsuperscript{51}

**Cardiac Rupture**

When rupture of the heart occurs, the most common site is the right atrium. In most cases, immediate and severe acute cardiac tamponade develops. An exception is when there has been concomitant rupture of the pericardium, and then there is exsanguinating hemorrhage. Cardiac rupture may occur immediately upon injury or several days later; in the interim, there may be no suggestion of impending catastrophe. Rupture occasionally may be localized, involving primarily a branch of a coronary artery.\textsuperscript{51}

**Ventricular Septal Rupture**

When the ventricular septum ruptures, it usually occurs at the time of injury. The characteristic murmur of a VSD appears. When the rupture is small, the hemodynamic state remains good. When it is large, the patient exhibits signs and symptoms of pulmonary venous hypertension, and cardiac output is likely to be low.

**Atrioventricular Valve Rupture**

When rupture of the tensor apparatus or leaflet of an atrioventricular valve is a complication of closed trauma, its occurrence is usually immediate. Most commonly, the tricuspid valve is ruptured, and this may be accompanied by rupture of a branch of the right coronary artery into the right ventricle.\textsuperscript{51} Thus, initial clinical manifestations are minimal, and the diagnosis is not suggested until a number of weeks have passed, by which time the characteristic signs and symptoms are present\textsuperscript{59} (see “Tricuspid Regurgitation” under Clinical Features and Diagnostic Criteria in Chapter 14).

Less frequently, the tensor apparatus of the mitral valve is ruptured.\textsuperscript{51} Patients usually exhibit sudden pulmonary venous hypertension and rapidly developing symptoms including frank pulmonary edema.\textsuperscript{51} Occasionally, mitral regurgitation may slowly worsen, and operation is required several weeks to several months after injury.\textsuperscript{1,3,11}

**Aortic Cusp Rupture**

Rarely, an aortic valve cusp is ruptured by nonpenetrating cardiac trauma. Acute pulmonary edema can be precipitated by rupture of two cusps, but symptoms may become evident only after an apparently symptom-free interval.\textsuperscript{51}

**NATURAL HISTORY**

**Cardiac Contusion**

Only fragmentary information is available concerning the natural history of patients with myocardial contusion, because this condition often goes undiagnosed. The natural history is probably similar to that of acute myocardial infarction. When the area involved is small, premature death is uncommon. When it is of moderate size, and particularly when there is associated damage to the left anterior descending coronary artery, a typical large left ventricular aneurysm may develop.\textsuperscript{51,10} The natural history then is that of other large left ventricular aneurysms (see Chapter 8). When the area involved is extensive, death may occur relatively early after injury in the same modes as after acute myocardial infarction. Pericarditis and hemopericardium may develop as complications of cardiac contusion.\textsuperscript{51,32,35} The natural history then becomes that of these conditions (see Chapter 23), with possible late development of cardiac tamponade and chronic constrictive pericarditis.

**Cardiac Rupture**

Cardiac rupture is generally rapidly fatal without operation. However, if the rupture is small, and particularly if it involves the right atrium or right ventricle and the pericardium is intact, the hemopericardium that develops may tamponade the bleeding, and the hemodynamic state may remain reasonably good. Some patients survive such an episode, as evidenced by the very old finding of Cabriolanus (in 1604) of healed cardiac wounds in persons who had been thought to be well.\textsuperscript{51}
Ventricular Septal Rupture

As in congenital VSDs, the natural history of ventricular septal rupture depends on the size of the defect (see Chapter 35). When it is small, the early posttraumatic hemodynamic state is good, as is the long-term outlook. When it is large, the hemodynamic state may not be good early after the injury, and chronic heart failure may ensue.

Atrioventricular Valve Rupture

In the same way that excision of the tricuspid valve is well tolerated (see Chapter 14), so is acute traumatic rupture of the tricuspid valve. Often the diagnosis is not made at the time of injury. Usually, within 2 to 3 months the patient exhibits decreased exercise tolerance, and signs of tricuspid valve regurgitation become evident.

In mitral valve rupture, as in spontaneous rupture of chordae tendineae or postinfarction mitral regurgitation, the patient often becomes acutely ill within a few hours of injury. Perhaps because traumatic mitral valve rupture is associated with a variable amount of cardiac contusion and myocardial dysfunction, this condition often results in deterioration and death within 24 hours.

Aortic Cusp Rupture

Natural history of acute aortic cusp rupture may be similar to that of acute aortic regurgitation occurring with infective endocarditis and cusp perforation (see Chapters 12 and 15), although there may be a symptom-free interval.

TECHNIQUE OF OPERATION

When diagnosis is rupture of a cardiac free wall, immediate operation is undertaken, but preparations must be made for CPB. If the patient’s condition permits, the femoral artery is exposed and cannulated (after heparinization) before median sternotomy. After median sternotomy, it may be seen that the rupture involves only a small area. In that case, digital control and placement of pledgeted mattress sutures suffice. If digital control cannot be obtained, CPB is established; blood is aspirated from the pericardium for venous return, and a reduced systemic blood flow rate is used. As soon as a single venous cannula can be inserted into the right atrium, CPB is converted to usual techniques and flow rates. Repair of the free wall rupture is improvised but, in the case of the ventricle, is generally similar to repair of a myocardial rupture complicating acute myocardial infarction (see Chapter 8).

Posttraumatic VSDs and traumatic injuries of the tricuspid valve are managed in a manner similar to that for congenital and postinfarction VSDs and other types of tricuspid valve regurgitation (see Chapters 9, 14, and 35). In tricuspid valve rupture the tensor apparatus is usually involved. An attempt should be made to reconstruct the leaflets using pericardium, and the tensor apparatus using artificial chordae of polytetrafluoroethylene (PTFE) suture. For trauma to the mitral valve, repair, if possible, is advised (see “Repair of Mitral Regurgitation” under Technique of Operation in Chapter 11). Occasionally, mitral valve replacement is necessary. In the rare case of rupture of a single aortic valve cusp, repair is possible; when two cusps are involved, valve replacement is usually necessary.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Care usually given to patients after cardiac surgery is used (see Chapter 5).

RESULTS

Except in massive traumatic cardiac ruptures, results of repair in young and otherwise healthy persons are good. Aggressive therapy can salvage a number of patients if carried out in an institution in which cardiac surgery is frequently performed.

INDICATIONS FOR OPERATION

Cardiac Contusion

There is no indication for surgical treatment of patients with cardiac contusions. Close follow-up is indicated, however, in case delayed ventricular arrhythmia, cardiac rupture, or constrictive pericarditis develops.

Cardiac Rupture

When a patient survives the acute rupture long enough to reach a hospital, immediate operation is indicated.

Ventricular Septal Rupture

Unless the patient is asymptomatic and the ventricular septal rupture small, surgical closure is indicated. However, the possibility of preoperative improvement by use of percutaneous techniques should be considered (see “Percutaneous Closure of Defect” under Special Situations and Controversies in Chapter 9). If the hemodynamic state remains good during the early posttraumatic period, repair is deferred to 8 to 12 weeks after injury so that a more secure closure can be made.

Atrioventricular and Aortic Valve Rupture

Because important valvar regurgitation usually develops after atrioventricular or aortic valve rupture, operation is advisable. When the tricuspid valve has ruptured, operation is rarely urgently necessary and is often best delayed 8 to 12 weeks after the injury. In mitral or aortic valve rupture, operative repair is often urgently indicated.

REFERENCES

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# Cardiac Tumor

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**DEFINITION**

Cardiac tumors include benign and malignant neoplasms arising within the cardiac chambers or in the myocardium. Metastatic neoplasms to the heart are not included.

**HISTORICAL NOTE**

First recognition of a heart tumor is attributed to Columbus in 1559, followed by Malpighi, who in 1666 wrote a dissertation entitled “De polypo cordis.” Morgagni wrote of heart tumors in 1762. By 1931, Yater was able to publish an extensive dissertation and tabulation of primary cardiac tumors using a classification similar to that used today. Clinical diagnosis of a primary tumor—a sarcoma—was first recorded in 1934. The first antemortem diagnosis of a myxoma was made in 1951 using angiography. A major diagnostic landmark was echocardiographic diagnosis of a left atrial myxoma in 1968, which was confirmed at operation and successfully treated. In 1934, Beck partly removed an intrapericardial teratoma, and in 1951 Maurer successfully excised an intrapericardial lipoma. Among the earliest surgical approaches to myxomas was that of Bahnson and Newman, who in 1952 removed a myxoma from the right atrium via a right anterior thoracotomy using a short period of caval occlusion at normothermia. The patient died 24 days later of complications related to transfusion and electrolyte imbalance. Using cardiopulmonary bypass (CPB), Crafoord in 1954 successfully excised a myxoma from the left atrium, as did Bigelow in 1955, using hypothermia and inflow occlusion. Successful excision of a right atrial myxoma was reported in 1957 and in 1958. A left ventricular myxoma was excised in 1959 by Kay. The first successful excision of a right ventricular myxoma was reported in 1960. By 1964, 60 intracardiac myxomas had been successfully removed. Biatrial myxomas were first removed in 1967. In 1967, Gerbode and colleagues described recurrence of a left atrial myxoma 4 years after initial excision.

**TYPES OF CARDIAC TUMORS**

In a study from the Armed Forces Institute of Pathology, approximately 70% of cardiac tumors were benign and 30% malignant and potentially capable of invasion or metastasis (Table 18-1). In a more recent study of 533 primary tumors removed surgically, 10% were malignant.

**Table 18-1 Prevalence of Neoplasms of the Heart and Pericardium**

<table>
<thead>
<tr>
<th>Type</th>
<th>No.</th>
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<tr>
<td><strong>Benign Tumors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Myxoma</td>
<td>130</td>
<td>29</td>
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<td>Lipoma</td>
<td>45</td>
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<td>Papillary fibroelastoma</td>
<td>42</td>
<td>9.5</td>
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<td>Rhabdomyoma</td>
<td>36</td>
<td>8.1</td>
</tr>
<tr>
<td>Fibroma</td>
<td>17</td>
<td>3.8</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>15</td>
<td>3.4</td>
</tr>
<tr>
<td>Teratoma</td>
<td>14</td>
<td>3.2</td>
</tr>
<tr>
<td>Mesothelioma of AV node</td>
<td>12</td>
<td>2.7</td>
</tr>
<tr>
<td>Granular cell tumor</td>
<td>3</td>
<td>0.7</td>
</tr>
<tr>
<td>Neurofibroma</td>
<td>3</td>
<td>0.7</td>
</tr>
<tr>
<td>Lymhangioma</td>
<td>2</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>SUBTOTAL</strong></td>
<td>319</td>
<td>72</td>
</tr>
<tr>
<td><strong>Malignant Tumors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Angiosarcoma</td>
<td>39</td>
<td>8.8</td>
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<tr>
<td>Rhabdomyosarcoma</td>
<td>26</td>
<td>5.8</td>
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<tr>
<td>Mesothelioma</td>
<td>19</td>
<td>4.2</td>
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<tr>
<td>Fibrosarcoma</td>
<td>14</td>
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<tr>
<td>Malignant lymphoma</td>
<td>7</td>
<td>1.6</td>
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<td>Extraskeletal osteosarcoma</td>
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<td>Neurogenic sarcoma</td>
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<tr>
<td>Malignant teratoma</td>
<td>4</td>
<td>0.9</td>
</tr>
<tr>
<td>Thymoma</td>
<td>4</td>
<td>0.9</td>
</tr>
<tr>
<td>Leiomyosarcoma</td>
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<td>0.2</td>
</tr>
<tr>
<td>Liposarcoma</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Synovial sarcoma</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td><strong>SUBTOTAL</strong></td>
<td>125</td>
<td>28</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>444</td>
<td>100</td>
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Data from McAllister and Fenoglio. Key: AV, Atrioventricular.
Section I  Myxoma

DEFINITION
Cardiac myxomas are primary cardiac tumors that are generally pedunculated but may have a broad base. Cells are uniform, small, and polygonal, with round or oval nuclei and a moderate amount of cytoplasm. They lie in a myxomatous stroma in which other elements may be seen. One feature that distinguishes them from thrombi is that they are covered by endothelium and have endothelium-lined crevices and clefts. The notion that myxomas are derived from thrombi has been thoroughly dispelled.

MORPHOLOGY
Myxomas are intracavitary tumors occurring within any of the cardiac chambers, but they have a predilection for the atria, particularly the left. They are usually 5 to 6 cm in diameter, with a range of 1 to 15 cm. Characteristically, they are polypoid and pedunculated, projecting into a cardiac chamber. They can be gelatinous or mucoid, often with areas of hemorrhage. Generally, they are not sessile but have a short, broad-based attachment. The external surface of papillary forms of the neoplasm consists of a frondlike mass that is friable and likely to produce emboli.

Histology
Myxomas are composed of cells, primitive capillaries, and foci of extramedullary hematopoiesis within a myxoid matrix of acid mucopolysaccharide. The stroma contains variable numbers of reticulocytes and elastin fibers, smooth muscle cells, and collagen deposits. The matrix also contains polygonal cells with scant eosinophilic cytoplasm, either single and stellate or multinuclear and in small nests. At the periphery of the tumor, the cells form a monolayer with clustering in the crevices, thereby simulating primitive capillaries. The stalk has abundant large arteries and veins that communicate with the subendocardium, and at this interface, lymphocytes and plasma cells are prominent. Microscopic foci of calcium and areas of metaplastic bone are found in 10% of myxomas. The nucleus of the polygonal cells is typically irregular and slightly hyperchromatic, but mitoses are not seen. The cells contain fine parallel filaments similar to those seen in glomangioma and fibromyxosarcoma. These filaments are believed to be the contractile components of smooth muscle cells. Immunologically identifiable smooth muscle–type filaments are recognized in endocardial cells, which are more abundant in the left atrium, especially in the region of the fossa ovalis, than in other chambers.

Tumor Biology
The notion that myxomas are derived from thrombi has been thoroughly dispelled. Ferrans and Roberts believe the organelle content of myxoma cells does not provide sufficient information to determine the cell of origin. Although myxoma cells have a “vasoformative” tendency, in their view the cytoarchitectural features of the variously differentiated blood vessel–like structures differ from those of normal blood vessels. Thus, myxomas are considered to arise from pluripotential mesenchymal cells capable of differentiating into various types of cells, a view supported by the finding of bone and bone marrow tissue in myxomas. Histologic examination of the atrial septum in 11 autopsied patients younger than age 4 months revealed myxomatous or myxofibrous tissue in the endocardium near the fossa ovalis, further supporting the concept that myxomas are derived from embryonal undifferentiated mesenchymal cells, perhaps during endothelial-mesenchymal transformation, leading to cardiac septation and valve formation.

Based on immunohistochemical identification of three neuroendocrine markers in 24 excised atrial myxomas, Krikler and colleagues have suggested that these tumors originate from endocardial sensory nerve tissue. Occasional association of cardiac myxomas with cutaneous leiomyomatosis and systemic findings such as fever, hypergammaglobulinemia, and weight loss resemble manifestations of other tumors of neural origin. Increasing numbers of reports document the malignant potential of myxomas. Extensive local invasion has been noted. Death attributable to metastatic spread of an atrial myxoma was once reported as a result of fatal brainstem compression from an expanding cerebellar mass with histologic features identical to those of a large, pedunculated left atrial myxoma also found at autopsy. There have been many reports of local recurrence and of distant metastases with invasion of vessel walls, aneurysmal change, and independent growth.

Atrial Myxoma
Most atrial myxomas, whether left or right, arise from the atrial septum, usually from the region of the limbus of the fossa ovalis. About 10% have other sites of origin, particularly the posterior and anterior atrial walls and the appendage (in order of frequency). Importantly, atrial masses thought to be myxomas but not originating from the intraatrial septum may have more complex pathology. On the left atrial side, they may be extensions of hilar lung tumors such as mesothelioma, sarcoma, or carcinoma. On the right side, they may be intracaval extensions of renal or uterine tumors. Most myxomas—80% to 90%—are in the left atrium. Right atrial myxomas tend to be more solid and sessile than left atrial myxomas, with a wider attachment to the atrial wall or septum. In one reported case, an atrial myxoma presenting in the right atrium arose from the inferior vena cava.

Atrial myxomas may be multicentric (within a single chamber) or biatral. The most common arrangement (75%) of biatrual tumors involves attachment of two stalks to opposite sides of the same area of the septum. Of 312 cases of right and left atrial myxomas reviewed by Newman and colleagues, only two were complicated by presence of an atrial septal defect; Natarajan and colleagues reported four cases. Such cases may have right-to-left shunts.

Ventricular Myxoma
Found commonly on the right ventricular free wall or ventricular septum, ventricular myxomas are sometimes described as infiltrating the ventricular myocardium. In about 15% of reported cases, right ventricular myxomas are associated with other cardiac myxomas. Left ventricular myxomas are rare. Both right and left ventricular myxomas can
extend into the outflow tract and cause partial outflow tract obstruction.\textsuperscript{82}

Valvar Myxoma

Myxomas arising from the mitral, tricuspid, or pulmonary valves have been reported.\textsuperscript{6,81,82,72}

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Pathophysiology**

Myxomas may produce (1) symptoms of hemodynamic derangement from obstruction of flow within the cardiac chambers or deformation of a cardiac valve, (2) symptoms associated with embolization, and (3) constitutional symptoms, the least common manifestation.\textsuperscript{31,32} In rare circumstances, atrial myxomas may become infected; only 2 of 12 reported cases were diagnosed before death.\textsuperscript{31,33} Central nervous system embolism has been a constant association.

**Hemodynamic Derangement**

Myxomas may obstruct pulmonary or systemic venous drainage or may impair flow across the atroioventricular valves, the likelihood of these events being greater with larger tumors. The obstruction is characteristically progressive.\textsuperscript{83} When obstruction is intermittent, syncope, often related to postural change, or sudden death may occur. This happens in less than one fourth of patients with left atrial myxomas, about one third of those with right atrial or right ventricular myxomas, and about half of those with left ventricular myxomas.\textsuperscript{4,84,85,86,87} Impairment of valve closure, either by obstruction or leaflet damage, may cause regurgitation.\textsuperscript{87} Valves may be structurally damaged by frequent tumor impingement, a sequence that also causes regurgitation. Although regurgitation is the dominant abnormality, obstruction predominates in a few patients.\textsuperscript{88} Symptoms are commonly of short duration, are episodic, and may be associated with syncope.\textsuperscript{89}

**Embolism**

A major feature of cardiac myxomas is embolization. Emboli may arise from tumor fragmentation or detachment of the entire tumor, or from thrombi or infected foci on the surface of the neoplasm.\textsuperscript{82,90} Systemic emboli occur in 30% to 45% of patients with left atrial myxomas.\textsuperscript{91} They have been reported in every organ and may occlude coronary arteries.\textsuperscript{81,82,83,92,93} About 50% of emboli involve intracranial or extracranial arteries to the central nervous system.\textsuperscript{82,83,85,87,88,94} Cerebral emboli characteristically cause major permanent neurologic deficits. On rare occasions, they are amenable to excision.\textsuperscript{88,89,90,91,92,93} Large emboli may obstruct the aortic bifurcation.\textsuperscript{83} Although left ventricular myxomas are rare, prevalence of embolism from them is high (64%), apparently unrelated to tumor size, and greater to the brain than elsewhere.\textsuperscript{91} Left atrial myxomas that come to attention because of embolization tend to be small when examined after that event.\textsuperscript{95} Embolism from right-sided tumors occurs in about 10% of cases and may cause massive fatal pulmonary obstruction.\textsuperscript{88} However, pulmonary arterial obstruction from this mechanism is much less common than true thromboembolism to the pulmonary arteries in patients who have sustained systemic tumor emboli from a left atrial myxoma.\textsuperscript{10,16} Multiple emboli from right-sided tumors may be a cause of pulmonary hypertension.\textsuperscript{97} Paradoxical embolism is rare.\textsuperscript{94,97,101}

**Constitutional Manifestations**

In about 30% of patients, the only manifestation of a cardiac myxoma is a plethora of constitutional symptoms and certain laboratory findings. Large left atrial myxomas are particularly apt to produce constitutional symptoms.\textsuperscript{99} Symptoms include fever, weight loss, clubbing of the fingers and toes, Raynaud phenomenon, and myalgia and arthralgia.\textsuperscript{83,92} By themselves, these findings are not pathognomonic. Because the presence of antibodies to fresh heart muscle has been demonstrated preoperatively in some patients, with appropriate postoperative diminution, it is speculated that an immune reaction to the neoplasm or to heart muscle mediated by presence of the neoplasm may cause the constitutional symptoms.\textsuperscript{C22} Total globulin levels are often elevated, and the electrophoretic patterns may reveal prominent $\alpha_2$, $\beta_1$, or $\gamma$ heterogeneous globulin peaks. Immunoelectrophoresis localizes the elevated globulins in either the immunoglobulin (Ig)M or IgA fractions. Elevated globulin levels are associated with an increased erythrocyte sedimentation rate and C-reactive protein levels.\textsuperscript{100} Further nonspecific symptoms may be related to seeding of multiple small emboli in muscle and joints, and hemorrhage or degeneration within the tumor. Other unusual manifestations of cardiac myxomas include polycythemia with or without associated arterial hypoxia, and clubbing (with both left and right atrial myxomas) associated with a right-to-left shunt at the atrial level through a patent foramen ovale or atrial septal defect.\textsuperscript{10,17,88,94} Hemolytic anemia occurs in about one third of cases, particularly in association with a calcified myxoma; this and the thrombocytopenia that sometimes occurs are probably due to mechanical destruction of formed blood elements. These features are reversible with tumor removal.\textsuperscript{11,92,94}

**Familial versus Nonfamilial Myxoma**

Nearly all solitary myxomas have a normal DNA ploidy, and nearly all are nonfamilial. Nonfamilial (“sporadic”) cardiac myxomas are disorders primarily of middle-aged women. The tumors are usually single (94%) and in the left atrium (about 75%); they uncommonly have associated conditions, they rarely recur, and only about 20% have abnormal DNA ploidy.\textsuperscript{112}

Myxomas have a familial occurrence in about 5% of patients.\textsuperscript{112} They have a pattern of Mendelian dominant inheritance\textsuperscript{113} and are primarily disorders of young men. They are less common in the left atrium (62%), are more often multiple (33%), and in about 20% of patients are associated with unusual conditions. These conditions include Sertoli cell tumors of the testes, Cushing syndrome as a result of primary adrenocortical nodular dysplasia, pituitary tumors, centrofacial and labial lentiginosis (brown macules with regular edges, sometimes termed spotty pigmentation), cutaneous myxomas, and multiple myxoid mammary fibroadenomas.\textsuperscript{111,14,15,16} Familial myxomas have the same histologic appearance as nonfamilial myxomas and produce the same symptoms. However, they have a strong tendency to recur.\textsuperscript{112} Some patients with these complex findings have no identifiable cardiac myxoma; in a few others the myxoma has been found unexpectedly at autopsy.\textsuperscript{3,83,111} Familial cardiac myxomas are aneuploid in
virtually all cases, supporting the concept that they are neoplasms.

Symptoms

*Left atrial myxomas* produce symptoms similar to those of mitral stenosis (see Chapter 11) in most patients, with dyspnea and hemoptysis predominating. Symptoms are commonly of short duration, episodic, and associated with syncope. They may rapidly become severe and intractable and are associated with heart failure. *Right atrial myxomas* may also produce episodic symptoms, and these may progress rapidly. Abdominal proptuberance from hepatomegaly and ascites and peripheral edema are frequent presenting complaints. In the review by Morrisey and colleagues, all 18 patients had right heart failure, with a prominent *a* wave, raised venous pressure, hepatomegaly, ascites, and peripheral edema; absence of orthopnea and paroxysmal nocturnal dyspnea was notable. Symptoms that result from embolization include neurologic deficits, coldness and pain in an extremity, angina or infarction from coronary embolization, and dyspnea from pulmonary embolization. Constitutional symptoms may be subtle or absent when the tumor is small, but occasionally constitute the entire symptomatology.

**Signs**

Diagnosis of atrial myxoma is sometimes made immediately after hospital admission by histologic examination of an embolus removed from a peripheral artery. However, absence of myxoma cells in the embolus does not rule out myxoma, because thrombus forming on the neoplasm may be the cause of the embolism. Before the advent of echocardiography, interpretation of auscultatory findings for *left atrial myxomas* was aided by a combination of phonocardiographic and hemodynamic studies. A loud first heart sound is prolonged by vibrations coinciding with the *c* wave of the left atrial pressure tracing and also with a characteristic notch in the left ventricular pressure curve; these vibrations occur after mitral valve closure when the tumor momentarily comes to rest in the left atrium. For mobile tumors moving from the left ventricle to the left atrium in early systole, a notch in the ascending limb of the left ventricular pressure tracing is attributed to a sudden increase in left atrial volume, which itself is manifested in the left atrial pressure pulse by a prominent *c* wave and subsequent dominant *v* wave. Accordingly, the first heart sound may be preceded by a loud ejection sound resulting from forceful ejection of the tumor from the left ventricle back into the left atrium. When the tumor stays in the left atrium during the entire cardiac cycle, the diastolic murmur and pressure tracings may be indistinguishable from those of mitral stenosis (i.e., there is no notch in the ventricular pressure wave, and the *y* descent is relatively slow). The second heart sound is normally split, of low intensity, and followed by a third heart sound described as either an opening snap or a ventricular gallop. The opening snap occurs after the mitral valve opens and is thought to be due either to the tumor striking the heart wall or to the diastolic sound of mitral regurgitation caused by increased blood flow. Systolic murmurs have also been recorded and have been attributed to associated mitral regurgitation.

With *right atrial myxomas*, a loud early systolic sound is heard, usually regarded as a widely split first heart sound, corresponding to expulsion of the tumor from the right ventricle. This sound is likely to correspond to a notch in the upstroke of the right ventricular pressure curve. A pulmonary ejection murmur with a delayed and accentuated pulmonic second sound and an early, late, or prolonged tricuspid diastolic murmur or rumble is heard. A systolic murmur is due to tricuspid regurgitation.

**Ventricular myxomas** are sufficiently rare that their auscultatory features are not fully known, but murmur may suggest aortic or pulmonary stenosis. Occasionally, friction rubs are heard, presumably a result of physical contact of the tumor with the endocardium of one of the cardiac chambers. Rarely, patients presenting with constitutional manifestations exhibit cyanosis and clubbing of the fingers and toes, or a gallop rhythm and sinus tachycardia.

**Laboratory Studies**

Results of laboratory studies are usually normal. In rare instances of presentation with constitutional manifestations, some findings may be characteristic but not pathognomonic. Among them are anemia, thrombocytopenia, and findings associated with an immune response (see “Constitutional Manifestations” earlier in this section).

**Electrocardiography**

Electrocardiographic findings associated with myxomas are not specific, but include arrhythmias and conduction disturbances, particularly atrial fibrillation and bundle branch block, and abnormal P waves.

**Chest Radiography**

Features on a plain chest radiograph are not specific. Generalized cardiomegaly or specific chamber enlargement may be evident, particularly in the case of large left atrial myxomas causing obstruction. Septal lines, especially at the base and in the mid-zone of the lung, are fairly common findings because of coexisting pulmonary venous hypertension.

**Echocardiography**

Transthoracic echocardiography (TTE) supplemented by transesophageal echocardiography (TEE) has become the most appropriate screening and diagnostic imaging modality for myxomas (and most other cardiac tumors). Mitral valve stenosis can be excluded, and tumor prolapse through the atrioventricular valve may be demonstrated. Tumor prolapse is characteristic evident if echoes are seen behind the anterior leaflet, particularly if they move into the left ventricle during diaстole. Echocardiography is invaluable in identifying the precise origin of the myxoma (Figs. 18-1, 18-2).

**Computed Tomographic and Magnetic Resonance Imaging**

Atrial myxomas and other cardiac tumors can also be identified with computed tomography (CT) or magnetic resonance imaging (MRI), either alone or in combination with echocardiography. Asymptomatic tumors are occasionally identified when CT or MRI scans are performed for other indications.
Cardiac Catheterization and Angiography

Unless other types of cardiac or coronary artery disease require assessment, catheterization and angiography no longer constitute the investigative method of choice. If invasive study is required for suspected left atrial tumors, a selective right heart study is performed by injecting radiopaque media into the pulmonary artery and filming as the dye passes through the left atrium. This method usually gives a clear demonstration of the tumor, whereas selective left ventricular cineangiography often fails to delineate it. For right atrial myxomas, catheter placement into the right atrium is contraindicated, and injection is made into one of the venae cavae.

NATURAL HISTORY

Myxomas occur in older adults and are two to three times more common in women than in men. They are rare in children and have not been described in infants. MacGowan and colleagues estimate the incidence of atrial myxoma to be 0.5 per million population per year. The older literature contains reports of familial myxoma (three restricted to siblings and three with a parent-child relationship). Current knowledge indicates that the natural history of patients with familial myxomas is different from that of patients with nonfamilial, sporadically occurring myxomas (see “Familial versus Nonfamilial Myxoma” under Clinical Features and Diagnostic Criteria earlier in this section).

Myxomas are usually benign, but rarely the tumor metastasizes. Metastases have been reported in brain arteries, sternum, vertebral column, pelvis, scapula, and soft tissues of the back. Metastasis can occur despite benign gross and microscopic appearances, but it is rare. The course of surgically untreated patients with cardiac myxomas is highly variable and cannot be clearly defined. However, once symptoms of dyspnea and hemoptysis develop in the case of left atrial myxomas, or symptoms of abdominal protuberance from ascites or hepatomegaly develop in the case of right atrial myxomas, death usually follows within 1 to 2 years. Little information is available about the frequency of embolization in patients with myxomas, the tendency to repeated embolization if the tumor is not removed, or the course without treatment of patients presenting with constitutional symptoms only.

TECHNIQUE OF OPERATION

Single, nonfamilial left atrial myxomas in patients older than about age 50 can simply be excised. Familial myxomas in younger patients should be treated more aggressively. Preparations for operation, median sternotomy, CPB, and myocardial management are the usual ones for adult cardiac surgery (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2 and “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). Direct caval cannulation is routinely practiced for removal of atrial myxomas. A left atrial vent is not used.
Left Atrial Myxoma

The approach is bilateral. For initial exploration and orientation, the usual incision is made in the left atrium posterior to the interatrial groove (Fig. 18-3, A). Blood is removed from the left atrium, and the point of attachment of the tumor to the atrium is determined by inspection (Fig. 18-3, B). Assuming it is attached to the atrial septum, which is usually the case, the tumor is not removed from the left atrium. Instead, an oblique right atriotomy is made and the interior of the right atrium examined in case a second tumor is present (Fig. 18-3, C). As much as possible of the interior of the right ventricle is also inspected through the tricuspid valve. The atrial septum is then opened with a knife near the center of the fossa ovalis, and a sufficient amount of atrial septum is excised to include the tumor attachment and, if possible, uninvolved tissue 5 mm beyond it. The superior half of the fossa ovalis and adjacent limbus are, if possible, included in the excision, because cells thought to be the precursor of myxoma are more abundant in this area. The tumor is then removed from the heart through the left or right atriotomy, whichever is larger (Fig. 18-3, D). Very large tumors may have to be removed piecemeal, although every attempt is made to keep the tumor intact and to avoid tumor embolization. After the tumor is removed, the interior of the left atrium is copiously irrigated with saline solution to evacuate any residual tumor fragments. The defect in the atrial septum is closed either by direct suture or, if too large for this, with a pericardial or synthetic patch (Fig. 18-3, E).

Figure 18-3  Resection of left atrial myxoma. A, Two atrial incisions are used. Tumor is explored via left atrial incision (dashed line). Later, tumor will be removed from right atrial approach. B, As for exposure of mitral valve, left atrium is opened and explored and attachment of myxoma to atrial septum identified. (Tumor may be isolated from pulmonary vein orifices at this point by small packing sponges.) C, From opened right atrium, tumor attachment to atrial septum is usually apparent. A circular septal incision is made to surround the tumor origin (seen as a dimple). Key: Ao, Aorta; IVC, inferior vena cava; PT, pulmonary trunk; RA, right atrium; RV, right ventricle; SVC, superior vena cava.

Continued
If the tumor is attached to the left atrial wall rather than the septum, the zone of attachment is excised, preferably with the full thickness of the adjacent wall, but if this is impractical, with endocardium and some underlying muscle. The wall defect created can be closed by direct suture or with a patch of autologous or bovine pericardium. The atria are closed and usual precautions against air embolization taken (see “De-airing the Heart” in Section III of Chapter 2). The rest of the procedure is completed in standard fashion.

**Right Atrial Myxoma**

Separate left and right atriotomies are not necessary unless there is preoperative evidence of an associated left atrial myxoma. Instead, the right atrium only is opened by the usual oblique incision (see Chapter 30, Fig. 30-14), and after attachments of the tumor are defined, it is excised with the adjacent portion of atrial septum in the manner described in the preceding text. The left atrium is then carefully inspected via the surgically created atrial septal defect. Only if a tumor is seen in the left atrium is that chamber opened by a separate incision. The atrial septal defect is closed as described in the preceding text, and the remainder of the procedure is completed as described.

**Other Myxomas**

Removal of ventricular myxomas does not require excision of full-thickness ventricular wall, because such a procedure would increase risk and no recurrences have been recorded.
following less radical removal. Tumors in the left ventricular outflow tract can sometimes be removed via an aortic approach. Otherwise, the approach is through the right atrium for right ventricular tumors and left atrium for left ventricular tumors. The ventricle is opened directly only when the atrial approach is inadequate for tumor removal. The procedure should include careful inspection of the interior of both right and left atria to exclude the presence of additional atrial tumors, which have been found in 15% of patients with right ventricular myxomas.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative management is conducted in the usual fashion (see Chapter 5).

RESULTS

Survival

Early (Hospital) Death

Hospital mortality after removal of atrial myxomas is less than 5% (Table 18-2). Virtually all deaths are in patients with advanced disability or old age, the mode of death being generally related not to the atrial myxoma but to coexisting cardiac or degenerative disease. Early risks seem somewhat higher after removal of myxomas from the ventricular cavities. Among 32 patients who underwent removal of right ventricular myxoma, there were three hospital deaths (9%; CL 4%-18%), and among 14 patients in whom a left ventricular myxoma was removed, there were three hospital deaths (21%; CL 10%-38%).

Table 18-2  Results of Operation for Removal of Cardiac Myxomas

<table>
<thead>
<tr>
<th></th>
<th>LA</th>
<th>RA</th>
<th>Biatrial</th>
<th>RV</th>
<th>LV</th>
<th>Total</th>
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<td>10</td>
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<td>0</td>
<td>0</td>
<td>66</td>
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<tr>
<td>Bjesmo and Ivert</td>
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<td>6</td>
<td>1</td>
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<tr>
<td>Bortolotti et al.</td>
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<td>Centofanti et al.</td>
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<td>0</td>
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<td>Murphy et al.</td>
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<tr>
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<td>37</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>407</td>
</tr>
</tbody>
</table>

Time-Related Survival

Death after hospital discharge is uncommon, but recurrence of the myxoma (see “Recurrence” later in this section) can lead to fatal complications. Most other late deaths are from causes other than the cardiac tumor. Excellent long-term results have been reported in a number of studies (Fig. 18-4). Presumably, these contained only patients with nonfamilial myxomas. Too few patients with familial myxomas have been reported for adequate assessment of long-term survival. Presumably, their survival is considerably worse than that of those with nonfamilial myxomas. Premature late death may occur more commonly when prosthetic valve replacement is necessary at time of myxoma removal because of complications from the prosthesis.

Recurrence

What has been classified as recurrence can be due to (1) tumor implantation (seeding at the time of removal), (2) incomplete removal, or (3) growth from a new focus (multicentric origin). Recurrence of a “sporadic” myxoma is unusual, occurring in only about 1% to 3% of patients, and myxomas with a normal ploidy rarely recur. In contrast, 30% to 75% of patients with familial myxomas experience
Papillary fibroelastomas usually develop on a valve leaflet, most commonly an aortic cusp or mitral leaflet. Less commonly, they appear on the tricuspid valve and ventricular septum, or rarely, on the aortic wall.\textsuperscript{F6,F8,O2,Y2}

**Clinical Features and Diagnostic Criteria**

This uncommon tumor rarely appears to cause trouble at its site of origin.\textsuperscript{I2,Y2} More often, it is responsible for embolization, either by detachment and embolization of one or more of its fronds or by inciting thrombus formation on its surface, with subsequent thromboembolism. Reported sites of embolism include primarily the brain and coronary arteries.\textsuperscript{G12,M8,M13,T5} They have also been observed in the lungs and retinal arteries.\textsuperscript{W2,Z1} Diagnosis in all living patients has been made by echocardiography and most accurately by TTE and TEE with Doppler color flow interrogation.\textsuperscript{D2,F8,G12,O2,S7,S12,S25,T5} Characteristically, by echocardiographic interrogation the tumor is small (about 1 cm\textsuperscript{2}), usually pedunculated and mobile, with a homogenous speckled pattern and stippling along its edges\textsuperscript{K6} (Fig. 18-6).

**Natural History**

Little is known about the natural history of papillary fibroelastomas of the heart, except that they tend to produce emboli. Embolization is the presumed mechanism of sudden death in some patients.

**Indications for Operation**

Surgical removal is indicated whenever diagnosis of cardiac myxoma is made. Historically, it was considered an urgent procedure, particularly if the patient had a history of embolism or syncpe, because it had been noted that 8\% to 10\% of patients died of embolic complications while awaiting operation.\textsuperscript{N7,S28,T3} However, more recent experience suggests that elective operation (as opposed to urgent) has resulted in no greater mortality or morbidity.

**Special Situations and Controversies**

Yu and colleagues in China have reported totally thorascopic surgical resection, often left atrial and two right atrial myxomas, using peripheral cannulation for CPB.\textsuperscript{Y4}

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**Section II Papillary Fibroelastoma**

**Definition**

Papillary fibroelastomas are benign tumors representing less than 10\% of all cardiac tumors, and they are important because, like myxomas, they are a curable and identifiable cause of strokes and other embolic events.

**Morphology**

Papillary fibroelastomas are usually small tumors but may extensively involve structures such as the mitral valve.\textsuperscript{G12} They have characteristic papillary fronds, which can be recognized grossly (Fig. 18-5). At times they have been thought to be myxomas, but their histologic appearance is diagnostic. The fronds have a central core of dense connective tissue sometimes lined by hyperplastic endocardial tissue. They have been said to resemble normal chordae tendineae.\textsuperscript{M6}

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**Figure 18-5** Papillary fibroelastoma removed from left ventricular outflow tract. (From Vivacqua and colleagues.\textsuperscript{V9})

Papillary fibroelastomas usually develop on a valve leaflet, most commonly an aortic cusp or mitral leaflet. Less commonly, they appear on the tricuspid valve and ventricular septum, or rarely, on the aortic wall.\textsuperscript{F6,F8,O2,Y2}

**Clinical Features and Diagnostic Criteria**

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**Special Situations and Controversies**

Yu and colleagues in China have reported totally thorascopic surgical resection, often left atrial and two right atrial myxomas, using peripheral cannulation for CPB.\textsuperscript{Y4}
RESULTS

Tumor recurrences have not been reported.

INDICATIONS FOR OPERATION

When a cardiac papillary fibroelastoma is discovered in a patient who has experienced an embolic event, removal is indicated. Whether the incidental finding of such a tumor is an indication for removal is arguable; when the tumor is on the mitral or aortic valve or the left ventricular endocardium, removal is advisable in patients at low risk for operative intervention.

Section III  Rhabdomyoma

DEFINITION

Cardiac rhabdomyomas are histologically specific cardiac tumors that tend to occur in patients with tuberous sclerosis. They are probably the same entity termed by some as cardiac hamartomas, Purkinje cell tumors, and histiocytoid cardiomyopathy.\(^{G1, N8}\)

MORPHOLOGY

Cardiac rhabdomyomas are benign, yellow-gray tumors, the microscopic characteristic of which is the so-called spider cell containing a central cytoplasmic mass suspended by fine, fibrillar processes radiating to the periphery. The cells are considered altered myocytes.\(^{G1}\) They are about twice the size of normal myocytes and are round or polygonal, with large hyperchromatic nuclei and eosinophilic granules in the cytoplasm. At times, there is no discrete myocardial tumor but only a gray-white area in the ventricular endocardium.\(^{G1}\) Rhabdomyomas occur almost invariably in the ventricles, with both sides equally involved and commonly in multiple locations. Whether rhabdomyomas are true neoplasms or myocardial hamartomas is controversial, but the latter is generally considered more likely.\(^{B24, F4}\) Consistent with this view is that at least half the patients have tuberous sclerosis, with multiple hamartomatous lesions in the brain. Cardiac rhabdomyomas may be associated with hamartomas in other organs as well.\(^{G1, \delta}\)

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Cardiac rhabdomyomas are the most common primary tumors in children.\(^{A3, B12, G6, M15}\) They may occur in siblings.\(^{S11}\) Presentation is frequently at birth or in the first few days of life with severe cardiac failure, the result of obstruction of cardiac pathways.\(^{S10}\) Cardiac rhabdomyomas are relatively common findings in infants presenting with incessant ventricular tachycardia.\(^{G1}\) At least one instance has occurred in which a rhabdomyoma of the right atrium caused atrial arrhythmias in an infant.\(^{G7}\) Occasionally the tumor is discovered somewhat later in a child known to have tuberous sclerosis, mental retardation, and in many cases, seizures.

Diagnosis can often be suspected based on clinical features and results of two-dimensional (2D) echocardiography (Fig. 18-7). Cardiac catheterization may be carried out to determine whether inflow to or outflow from the ventricles is obstructed. In some patients, no structural abnormality is found by any imaging technique, and diagnosis is inferred from the findings at electrophysiologic study of an area in the ventricle at which sustained monomorphic ventricular tachycardia can be induced.\(^{G1, \delta}\) Diagnosis has been made in the fetus by 2D echocardiography.\(^{B13}\)

NATURAL HISTORY

Little documentation exists concerning the natural history of patients with cardiac rhabdomyomas. Bass and colleagues determined by 2D echocardiography that 8 of 16 (50%; CL 36%-64%) infants with tuberous sclerosis had a cardiac rhabdomyoma.\(^{B4}\) Nir and colleagues corroborated a high prevalence of rhabdomyomas in patients with tuberous sclerosis.\(^{N9}\) It was previously assumed that mortality was high in patients with rhabdomyoma, due either to their tumor or to associated tuberous sclerosis. However, there is good documentation of spontaneous regression in number and size of these tumors.\(^{N9, T1}\) Nir and colleagues noted tumor regression in children younger than 4 years, less so in older children.\(^{N9}\)
In a 20-year experience, Smythe and colleagues noted regression of tumors in 100% of 24 patients studied by angiography or echocardiography. Twenty had complete resolution.

TECHNIQUE OF OPERATION

Because rhabdomyomas usually protrude into the right or left ventricular cavity, removal is done with the aid of CPB, hypothermic circulatory arrest, or both. Approach may need to be through the ventricular wall, but at times operation can be done through the atrioventricular or semilunar valve. Excision is limited to the area of the tumor. Occasionally, only the intracavitary portion is excised to relieve obstruction. The remaining intramyocardial portion will probably regress. In infants with incessant ventricular tachycardia, the only gross finding may be a grayish-white discoloration of the endocardium at the site identified by electrophysiologic mapping.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Usual postoperative care is given (see Chapter 5). Catecholamine support may be necessary because of the extensive myocardial dissection.

RESULTS

With appropriate indications, results of surgical treatment are generally satisfactory. Black and colleagues operated on seven patients presenting with left ventricular outflow tract obstruction during a 27-year period; all survived. Importantly, during the same interval, 23 other patients with rhabdomyoma did not need surgical intervention, and all were alive at late follow-up. Spontaneous regression is likely to occur before age 2. In these patients and those treated surgically, if tuberous sclerosis has not developed, a lasting good result can be anticipated.

INDICATIONS FOR OPERATION

In the presence of known tuberous sclerosis and severe mental retardation with seizures, operation may be contraindicated, especially if the patient has multiple cardiac tumors and no cardiac symptoms. In the absence of tuberous sclerosis, an aggressive surgical approach is indicated if outflow tract obstruction or major ventricular arrhythmia is present. In patients without arrhythmias, observation may be warranted because of the possibility of spontaneous tumor regression. Should obstruction or arrhythmia occur, operation is indicated.

Section IV  Fibroma

DEFINITION

Cardiac fibromas are benign tumors, grossly resembling uterine leiomyomas, with a whorled appearance on cut section. Microscopically, cardiac fibromas consist of spindle cells mixed with collagen and elastic fibers. Mitotic figures are rare, and foci of dystrophic calcification are common. Controversy exists as to whether fibromas should also be considered hamartomas.

MORPHOLOGY

Fibromas occur almost exclusively within the ventricular myocardium and frequently in the ventricular septum. Patients with fibromas coming to surgical treatment tend to have large, bulky tumors that are not infiltrating. They are characteristically solitary, circumscribed, firm, gray-white, and often centrally calcified. They do not have a distinct capsule and may occasionally be multiple.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Clinical presentation is variable. Symptoms include dyspnea, syncope, heart failure, and chest pain. Ventricular tachycardia and sudden death have been reported. Currently, echocardiography is the most widely used modality for diagnosis. MRI and cardiac angiography may be useful in defining tissue characteristics and extent of tumor involvement.

NATURAL HISTORY

Natural history of untreated patients is unknown. The prevalence of asymptomatic ventricular fibromas is also unknown, and it is impossible to predict the exact risk of sudden death. The presumption is that these tumors eventually cause death from ventricular fibrillation or by obstructing ventricular inflow or outflow.

TECHNIQUE OF OPERATION

During CPB and appropriate myocardial management, incision is made through the epicardium and myocardium overlying the tumor. The tumor is enucleated by blunt and sharp dissection, which, even when the tumor is large, is possible. If the tumor involves the septum, reconstruction can be achieved by closing the septum in layers or with a prosthetic patch. Occasionally, mitral valve repair or replacement may be necessary. The ventricle is reconstructed by direct suture. When the tumor is very large and complete removal
seems impossible, partial removal may result in good palliation.\textsuperscript{57} In infants, children, and young adults who are otherwise in good health, cardiac transplantation should be considered if the tumor is deemed to be unresectable (see Chapter 21).\textsuperscript{V1}

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Usual postoperative care is given (see Chapter 5).

**RESULTS**

In a series of 18 patients reported by Cho and colleagues who were treated surgically and followed for up to 34 years, there was one operative death and no late death.\textsuperscript{C12} Fourteen patients were asymptomatic, one was in New York Heart Association functional class II, and two were in class III. There was no recurrence of tumor and no change in size of residual tumor in the one patient who had subtotal resection.

**INDICATIONS FOR OPERATION**

Diagnosis in a symptomatic patient (often an infant or child) is an indication for operation. Operation should be considered for asymptomatic patients with large tumors to prevent progressive cardiac deformity and atrioventricular valve dysfunction.\textsuperscript{C12}

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**Section VI  Pheochromocytoma**

**DEFINITION**

Pheochromocytomas are potentially lethal, functionally active chromaffin tumors of the sympathetic nervous system that occur rarely within the pericardium and on the surface of the heart.

**HISTORICAL NOTE**

Occurrence of pheochromocytomas in the middle mediastinum and within the pericardium was unknown until 1960.\textsuperscript{N2,P5} Occurrence and treatment of cardiac pheochromocytomas were first discussed comprehensively by Orringer and colleagues in 1985.\textsuperscript{O4}

**MORPHOLOGY**

Cardiac pheochromocytomas are soft, fleshy tumors that are usually flattened by the pressure of the pericardium. They are typically benign and have large cellular trabeculae composed of mature pheochromocytes with marked cellular and nuclear pleomorphism. Nests of tumor cells may infiltrate the cardiac tissue. Chromaffin cells, from which these tumors are derived, normally are concentrated in the adrenal medulla, but they occur in small numbers along the aorta, in blood vessel walls, and in various organs including the heart. Pheochromocytomas produce large amounts of catecholamine, primarily nor-epinephrine, accounting for the hypertension characteristic of patients with these tumors.
CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Severe arterial hypertension is the characteristic finding in patients with pheochromocytomas. Markedly elevated urinary catecholamines are diagnostic. Localization of the pheochromocytoma in the middle mediastinum and heart is accomplished by a combination of CT imaging and scintigraphy with 131-I-metaiodobenzylguanidine or 111-indium diethylenetriamine pentaacetic acid octreotide and confirmed by MRI. \(^{A2,12,316,517}\)

NATURAL HISTORY

Little is known about natural history because of the rarity of cardiac pheochromocytomas. Presumably, it is that of pheochromocytomas and severe hypertension in general. Although pheochromocytomas are usually benign, at least one patient has been reported with widespread metastases. \(^{S10}\)

TECHNIQUE OF OPERATION

Preoperative preparation of the patient with \(\alpha\)- and \(\beta\)-adrenergic blocking agents is mandatory, and the anesthesiologist must be familiar with the intraoperative management of paroxysms of arterial hypertension and hypotension that may occur during the course of operation. Interestingly, these seem not to occur once CPB is established. Median sternotomy is probably the most useful incision, and CPB and cardioplegia are generally necessary. The tumor can be expected to be along the anterior surface of the heart and intimately related to the coronary arteries, including the left main coronary artery, or along the roof (superior aspect) of the left atrium and extending over the pulmonary veins and posterior left atrial wall, or in the area between the ascending aorta and pulmonary trunk. \(^{A2,94}\) The tumor usually cannot be enucleated, but must be dissected away from surrounding structures. It often has a large extracardiac collateral blood supply with potential risk of important hemorrhage. At times, a coronary artery or a portion of the left atrial wall must be included in the resection, and appropriate reconstruction will be necessary.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Usual care after a cardiac surgical procedure is appropriate (see Chapter 5).

RESULTS

Removing the tumor returns the patient to a normotensive state and results in cure, except in the unusual circumstance when the tumor is malignant. In a review of 26 cases collected from the literature, 25 patients underwent reconstruction within the native heart and one had successful transplantation. \(^{J1}\) Mortality was 24% (CL 15%-36%), with five patients (20%, CL 11%-32%) dying of hemorrhage.

INDICATIONS FOR OPERATION

Diagnosis is generally an indication for operation.
be involved. Right heart sarcomas tend to be bulky and infiltrative, cause heart failure, and metastasize early.\textsuperscript{b17} Left heart sarcomas tend to be more circumscribed and less infiltrative, cause heart failure early, and metastasize later.\textsuperscript{b17} Sarcomas tend to metastasize widely.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Presenting symptoms are nonspecific and include fever, malaise, and weight loss. Presence of a pericardial effusion is not uncommon. Heart failure is a late manifestation, and distant metastasis may already be present. Echocardiography, CT, and MRI are used for diagnosis.

**NATURAL HISTORY**

Prognosis is poor for untreated patients with cardiac sarcomas, many of whom have distant metastases when first seen.\textsuperscript{v3} For patients with angiosarcoma who had medical therapy but not surgical resection, Neragi-Miandoab and colleagues reported that 90% were dead within 12 months.\textsuperscript{v6}

**TECHNIQUE OF OPERATION**

The tumor is removed as completely as possible. Radical excision of portions of the atria and ventricles may be necessary. For tumors involving the right heart, resection may include the superior vena cava, entire right atrium, tricuspid valve, right coronary artery, and up to about 30% of the right ventricular muscle mass.\textsuperscript{v5} For sarcomas of the left heart, autotransplantation has been recommended to permit radical tumor resection and adequate reconstruction.\textsuperscript{b17,c14,v5} Under a clinical trial (ESPERO) at the M.D. Anderson Cancer Center and Methodist DeBakey Heart and Vascular Center in Houston, Texas, all patients with cardiac sarcomas and no overt heart failure are given neoadjuvant chemotherapy preoperatively to reduce tumor bulk and destroy tumor cells at the periphery of the tumor.\textsuperscript{v5}

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Usual postoperative care is given (see Chapter 5).

**RESULTS**

Among a series of 27 patients with cardiac sarcoma treated surgically by the Houston group, operative mortality was 7.4% (2 patients).\textsuperscript{b2} Chemotherapy was administered to 19. At a median follow-up of 22 months, 12 patients were alive and 7 were tumor free. Among 24 patients who underwent operation with curative intent, median survival was 24 months. Patients who underwent surgical resection, radiofrequency ablation, or radiation treatment for tumor recurrence \((n = 7)\) had a median survival of 47 months. Patients \((n = 7)\) with no further intervention for recurrent disease had a median survival of 25 months.

**INDICATIONS FOR OPERATION**

Because many patients with cardiac sarcomas have evidence of metastatic disease on presentation, and because persistent tumor is often present at the limits of the surgical resection, indications for radical surgical treatment are not clearly defined. Surgical treatment combined with chemotherapy should be considered for younger patients without clear evidence for metastatic disease.

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**Section IX  Carcinoid Heart Disease**

**DEFINITION**

Carcinoid heart disease is a manifestation of malignant carcinoid syndrome in which a unique form of fibrosis involves the endocardium, primarily of the right heart. \textit{Malignant carcinoid syndrome} is a symptom complex associated with carcinoid tumors of the gastrointestinal tract arising from argentaffin cells, which secrete large amounts of serotonin. Primary tumors are usually in the ileum, but may occur in the pancreas, biliary vessels, ovaries, and testes. The syndrome is characterized by flushing, telangiectasias, diarrhea, and bronchospasm and occurs in about 10% of patients with carcinoid tumors. Carcinoid heart disease occurs in approximately 50% of those who have the syndrome.\textsuperscript{b124}

**MORPHOLOGY**

Most patients with carcinoid heart disease have pathologic lesions limited to right-sided valves. These are glistening, white-yellow fibrous deposits, devoid of elastic fibers, located on the ventricular aspect of the tricuspid valve and downstream aspect of the pulmonary valve.\textsuperscript{b9,b13} The fibrous plaques result in constriction of the valve anulus and adherence of the valve leaflets to the right ventricular endocardium, in the case of tricuspid involvement, and the pulmonary trunk wall, in the case of pulmonary valve involvement. Thus, the dominant physiology is that of tricuspid regurgitation or pulmonary stenosis. The valve lesions morphologically resemble those resulting from appetite suppressants (fenfluramine and phentermine), because the lesions are not neoplasms and, in the case of carcinoid heart disease, not metastatic tumors.\textsuperscript{b14} In virtually all patients with carcinoid valve lesions, there are hepatic metastases from the primary gut tumor. (See “Carcinoid Tricuspid Valve Disease” under Morphology in Chapter 14 for a more detailed discussion.)

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Patients have the classic cutaneous flushing of carcinoid syndrome and usually display a hyperdynamic circulation, although they are generally not hypertensive. Nearly all have a systolic murmur and may also have cardiomegaly. In 74 patients investigated by Pellikka and colleagues, all had tricuspid valve involvement, and 90% had moderate or severe tricuspid regurgitation.\textsuperscript{v6} By echocardiography, the valve leaflets are shortened and thickened and on color Doppler have a characteristic “dagger-shaped” spectral profile. Patients with carcinoid heart disease have greater serum levels of serotonin and tachykinins than patients with the syndrome but without cardiac involvement. Severity of cardiac involvement, in addition, tends to correlate with both serum serotonin
levels and higher urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA).\textsuperscript{11}

**NATURAL HISTORY**

Survival in patients with carcinoid heart disease is lower than in patients with the syndrome but without cardiac involvement. Evolution of valve lesions may be rapid, leading to heart failure, although death is usually caused by progressive systemic disease.\textsuperscript{24}

**TECHNIQUE OF OPERATION**

Tricuspid valve replacement may provide palliation in some patients (see “Technique of Operation” in Chapter 14). Pulmonary valve replacement may also be beneficial in reducing right ventricular dysfunc-
tion.\textsuperscript{16,17} There are at least two reports of secondary fibrous carcinoid involvement of tissue valves used to replace tricuspid or pulmonary valves in patients with carcinoid syndrome.\textsuperscript{3,4} Balloon valvotomy may be palliative, but is likely to be followed by early recurrence of stenosis.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Usual cardiac postoperative care is given (see Chapter 5); additionally, levels of urinary 5-HIAA are monitored.

**RESULTS**

Robiolio and colleagues reviewed 47 carcinoid valve replacement cases. Thirty-day mortality was 56% for patients older than 60 years and 0% for those 60 years or younger. Two patients survived beyond a decade.\textsuperscript{16}

**INDICATIONS FOR OPERATION**

Precise indications for valve replacement cannot be stated. The underlying disease is progressive, and operative mortality for valve replacement mortality is high in older patients. Therefore, a young individual with low comorbidity and important heart failure would likely present the best candidate for a satisfactory outcome.

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Hypertrophic Obstructive Cardiomyopathy

**Definition**
Hypertrophic cardiomyopathy (HCM) is a genetic myocardial disorder characterized by left and/or right ventricular hypertrophy that is usually, but not always, asymmetric and is associated with microscopic evidence of myocardial fiber disarray and fibrosis.\(^{10,6,7}\) Degree of hypertrophy at any given site can vary substantially and influences clinical manifestations of the disease.

**Ventricular septal hypertrophy** is the most common type of asymmetric hypertrophy, with midventricular, apical, and other types occurring much less frequently.\(^{6}\) Forms interfering with left ventricular (LV) emptying, termed **hypertrophic obstructive cardiomyopathy** (HOCM) or (obsolete) **idiopathic hypertrophic subaortic stenosis** (IHSS), are of surgical importance and are characterized by a variable dynamic obstruction that is usually subaortic and is associated with abnormal **systolic anterior motion** (SAM) of the anterior leaflet of the mitral valve. The more commonly occurring nonobstructive forms are not amenable to surgical treatment except for cardiac transplantation (see Chapter 21). Prevalence of HCM in the general population is about 1 in 500 (0.2%).\(^{11}\)

**Historical Note**
Pathologic findings compatible with HOCM were described by two 19th-century French pathologists, Hallopeau and Liouville,\(^{11,15}\) and an early 20th-century German pathologist, Schmincke.\(^{7}\) In 1952, Davies described a family from Cardiff, Wales, with five of nine siblings affected and three dying suddenly who probably had this disease. Although these reports and the surgical report of Brock in 1957...
described diffuse muscular subaortic stenosis, the disease was first accurately categorized by Teare, a London pathologist, in 1958. Teare described both disproportionate thickening of the ventricular septum compared with the free wall and presence of myocardial fiber disarray in young people who died suddenly. These pathologic findings were rapidly confirmed and clinical features were further elucidated by Braunwald and colleagues, whereas Braunwald and colleagues called it idiopathic hypertrophic subaortic stenosis and Wigle and colleagues, muscular subaortic stenosis.

At that time, LV outflow tract obstruction was thought to be distinctive for the disease. That the anterior mitral leaflet contributed to the obstruction was first documented in 1964 by Fix and colleagues, who emphasized the importance of reduced LV compliance as the major determinant of cardiac dysfunction (‘inflow’ or diastolic obstruction) rather than outflow obstruction. Knowledge that nonobstructive HCM was much more common awaited introduction of echocardiography, which detected asymmetric septal hypertrophy (ASH), one of the hallmarks of the disease, as well as the presence or absence of SAM. During the early 1970s, ASH and SAM were thought to be specific for HCM but this is now known to be incorrect. Echocardiography not only established that HCM is relatively common, but also that it is usually genetically transmitted rather than sporadic.

Surgical awareness of the obstructive form of the disease began with Brock’s reports in 1957 and 1959. However, in his patients and in the first patient operated on at Mayo Clinic in February 1958, nothing was done surgically, because the nature of the disease was not understood. Credit for the first myotomy, consisting of a simple incision of the prominent anterior muscular ridge in the septum, probably belongs to Cleland. Myotomy was used by a number of other surgeons about this same time.

At Mayo Clinic, a left ventriculotomy was performed to allow adequate excision (myectomy) of muscle under direct vision. The few years the surgical approach to septal myectomy was modified in several ways. Dobell and Scott used a left atrial approach, exposing the hypertrophied septum by dividing the anterior mitral leaflet across its center, whereas Lillehei and Levy used a similar approach but detached the base of the anterior mitral leaflet near the anulus. Swan used a corkscrew to excise septal muscle from a limited LV approach. Julian and colleagues used a “fish mouth” LV incision that detached the lower part of the free wall from the septum and gave excellent exposure of the subaortic septal bulge, which was then excised. Cooley and colleagues developed an approach through the right ventricle used first by Harken, in which septal muscle was shaved off the right ventricular side, judging septal thickness by means of a finger inserted into the LV through the aortic valve.

None of these techniques is currently in use. Simple myotomy using an aortic approach was used for a time by the Toronto group. Later, they modified the procedure to include excision of muscle (myectomy) as advocated by Morrow. Other procedures have also been used, including mitral valve replacement by Cooley and colleagues, use of an LV-aortic valved conduit to bypass the obstruction, and a modified Konno procedure preserving the aortic valve (see “Modified Konno Operation” under Technique of Operation in Section II of Chapter 47).

MORPHOGENESIS AND MORPHOLOGY

Morphogenesis

HCM is caused by a missense mutation in one of at least 11 genes that encode the proteins of the cardiac sarcomere. These include mutations in the β-myosin heavy-chain gene (chromosome 14q11-q12), in cardiac troponin-T (chromosome 1), and in α-tropomyosin (chromosome 15q2). It is transmitted as an autosomal dominant trait, although nonfamilial cases probably occur as well.

Morphology

Muscular hypertrophy present in HCM involves the interventricular septum and LV, and is variable in its location and severity.

Ventricular Septum

In classic HOCM, hypertrophy is maximal in the cephalad portion of the ventricular septum (Fig. 19-1). Point of maximal thickening lies just apical (caudal) to the free edge of the anterior mitral leaflet in its open position. This muscular prominence (mound) tapers off gradually toward the LV-aortic junction and toward the apex. At the point opposite the free edge of the anterior mitral leaflet, LV endocardium is often thickened by a localized plaque of fibrous tissue that lies at right angles to the long axis of the outflow tract. Because it is present in both nonobstructive and obstructive forms of HCM, this plaque is presumably related to contact between the anterior mitral leaflet and septal bulge in diastole rather than systole, with the leaflet snapping open rapidly at the onset of diastole (in part because of high left atrial pressure) and contacting the ventricular septal prominence.

Ventricular septal hypertrophy is not always maximal in its anterior basal parts. Occasionally, it may be maximal at a site below the anterior mitral leaflet adjacent to the papillary muscles, producing midventricular hypertrophy leading to obstruction, to which the papillary muscles and free-wall hypertrophy contribute (Fig. 19-2). There is no SAM or mitral regurgitation. Apical LV aneurysm in the presence of normal coronary arteries occasionally occurs with midventricular hypertrophy. Hypertrophy may be confined to the posterior or apical septum. Localized apical hypertrophy is apparently most common among the Japanese. Occasionally the entire septum may be of uniform thickness.

Dynamic Morphology of Septum and Mitral Valve

When septal hypertrophy is classic, obstruction is sited in the LV outflow tract between the hypertrophied ventricular septum and anterior mitral leaflet. In systole the posterior mitral leaflet closes against the body of the elongated anterior leaflet at about the junction of the middle and free-edge thirds (rather than near the free edge as in the normal heart).
Chapter 19  Hypertrophic Obstructive Cardiomyopathy

Figure 19-1  Ventricular septal hypertrophy in hypertrophic obstructive cardiomyopathy. Longitudinal section of heart from a 32-year-old woman who died suddenly while receiving propranolol therapy. Hemodynamic investigation had confirmed presence of subaortic obstruction and mitral regurgitation, partially resulting from an abnormal mitral valve (insertion of anomalous papillary muscle [arrow] onto the ventricular surface of the anterior mitral leaflet). Note asymmetric hypertrophy with grossly thickened ventricular septum and anterior mitral leaflet, which is very thickened and fibrosed from repeated mitral leaflet–septal contact. There was microscopic evidence of extensive myocardial fiber disarray involving both septum and free wall of the left ventricle. (From Wigle and colleagues.  

The free-edge portion of the anterior mitral leaflet beyond the point of coaptation hinges (angulates) on the remainder of the leaflet in a cephalad direction toward the aortic anulus (Fig. 19-3). This brings the free edge of the anterior mitral leaflet in contact with the ventricular septum. This SAM of the anterior leaflet is a constant feature of classic HOCM; degree of movement correlates with severity of obstruction, as does diameter of the LV outflow tract at this point. Ventricular ejection is rapid and early, mostly within the first half of systole. SAM is temporally related to peak LV outflow gradient and to cessation of flow in the ascending aorta. The mechanism of SAM is probably multifactorial. Most likely, SAM is secondary to forward (anterior) displacement of the elongated mitral valve relative to the septum during systole, and to subsequent movement of the distal portion of the mitral valve apparatus. In association with marked septal hypertrophy opposite the mitral leaflet and rapid and early ventricular ejection, the Venturi effect of the high-velocity stream of blood carries the protruding edge of the anterior mitral leaflet toward the aortic anulus in early systole. As a secondary event, the higher pressure below the anterior leaflet then forces it further into the outflow tract. SAM is absent in nonobstructive HCM and when the obstruction is at a lower level. SAM can occur in transposition of the great arteries with intact ventricular septum (see “Left Ventricular Outflow Tract Obstruction” under Morphology in Chapter 52) and rarely in other disease states. SAM may also appear after mitral valve repair.

Left Ventricular Free Wall
In obstructive HCM with ASH, free-wall hypertrophy is more marked than in nonobstructive forms and is fairly uniform, particularly in the anterolateral and apical portions. There is, however, less thickening of the posterior free wall in almost all varieties of HCM. Thus, the ratio between the thick upper anterior part of the ventricular septum and the thinner posterior wall beneath the posterior mitral leaflet (the portion through which the beam passes in M-mode

Figure 19-2  Midventricular hypertrophy in hypertrophic obstructive cardiomyopathy. Cross-sectional slices of heart from a patient shown to have midventricular obstruction by hemodynamics, angiography, and echocardiography. Obstruction was at the level of the papillary muscles, where there was massive hypertrophy (second slice from left). Slice at left is from base of the heart; two slices at right are from the apex. The apex was the site of extensive myocardial infarction and aneurysm formation that was evidenced by a dyskinetic apical chamber on angiography and by persistent ST-segment elevation in leads V₄ to V₆ on the electrocardiogram. Coronary arteries showed no important luminal narrowing. The patient died of intractable ventricular arrhythmias. (From Wigle and colleagues.  

The free-edge portion of the anterior mitral leaflet beyond the point of coaptation hinges (angulates) on the remainder of the leaflet in a cephalad direction toward the aortic anulus (Fig. 19-3). This brings the free edge of the anterior mitral leaflet in contact with the ventricular septum. This SAM of the anterior leaflet is a constant feature of classic HOCM; degree of movement correlates with severity of obstruction, as does diameter of the LV outflow tract at this point. Ventricular ejection is rapid and early, mostly within the first half of systole. SAM is temporally related to peak LV outflow gradient and to cessation of flow in the ascending aorta. The mechanism of SAM is probably multifactorial. Most likely, SAM is secondary to forward (anterior) displacement of the elongated mitral valve relative to the septum during systole, and to subsequent movement of the distal portion of the mitral valve apparatus. In association with marked septal hypertrophy opposite the mitral leaflet and rapid and early ventricular ejection, the Venturi effect of the high-velocity stream of blood carries the protruding edge of the anterior mitral leaflet toward the aortic anulus in early systole. As a secondary event, the higher pressure below the anterior leaflet then forces it further into the outflow tract. SAM is absent in nonobstructive HCM and when the obstruction is at a lower level. SAM can occur in transposition of the great arteries with intact ventricular septum (see “Left Ventricular Outflow Tract Obstruction” under Morphology in Chapter 52) and rarely in other disease states. SAM may also appear after mitral valve repair.

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Fig. 19-3  Proposed mechanism of systolic anterior motion of anterior mitral leaflet in hypertrophic obstructive cardiomyopathy.  
A, At onset of systole, coaptation point (arrow) is in body of anterior and posterior leaflets.  
B-C, During early systole (B) and midsystole (C), there is anterior and basal movement of the residual length of the anterior leaflet (thick arrow), with septal contact and failure of leaflet coaptation (thin arrow) and subsequent mitral regurgitation directed posteriorly into the left atrium (stippled area).  (From Grigg and colleagues.)

Fig. 19-4  Left ventricular (LV) cineangiogram in right anterior oblique projection in hypertrophic obstructive cardiomyopathy. Note characteristic deformity of LV cavity, with septal muscle encroaching on anterior margin of outflow tract and the grossly hypertrophied papillary muscles contributing to virtual elimination of the mid-LV cavity in systole.  
A, Diastole. Dashed line crossing LV outflow area represents free-wall portion of mitral anulus, delineated by contrast medium trapped behind opened posterior leaflet.  
B, Systole. Lower dashed line outlines a radiolucent filling defect caused by contact between mitral leaflets and septum.
shape is characteristic of patients younger than age 40 and is rare in patients older than 65.1,2 When ventricular hypertrophy is located in the midportion of the ventricle, a dumbbell-shaped cavity results3; when it is confined to the apex, there may be complete obliteration of the lower half of the cavity and a spade-shaped basal portion.4 LV apical aneurysms are present in approximately 2% of patients with HCM and occur over a wide age range.5,6,10

Rarely the LV may become dilated in the late stages of HOCM. This dilatation may result from transmural myocardial infarction (MI)7,8 or severe progression of the disease process, with or without heart failure.9,10 Prognosis of patients with progressive LV wall thinning is poor, and concomitant cardiac failure is usually refractory to treatment.11,12 Most patients show an “hourglass” contour of the cardiac border, with midventricular hypertrophy and intracavitary gradients.

Histopathology of Left Ventricle
Microscopic findings in the hypertrophied ventricular septum are distinctive.13,14 Increased wall thickness is mainly caused by increased fibrous tissue, particularly in the ventricular septum but also in the free wall.15 Increase in muscle cell diameter and number of cell layers also contributes, with cell diameters being largest in layers closest to the cavity, perhaps because this is the site of greatest wall stress.11,13

In addition, numerous foci of disarrayed muscle cells are interspersed between areas of hypertrophied but normally arranged (parallel) cells.16,17 In areas of disarray, muscle cells are wider and shorter than those present in hypertrophied muscle in other diseases, with increased cellular branching, extensive side-to-side intercellular junctions, widened Z bands, and formation of new sarcomeres. There are also abnormalities in orientation of myofibrils.18,19 In obstructive forms of HCM, muscle cell disarray is confined to the ventricular septum, whereas in nonobstructive forms it may also occur in the LV free wall.20,21

Using a quantitative histologic method to determine extent of myocardial fiber disarray, Maron and Roberts found that the average degree of cell disarray in the ventricular septum of patients with HCM was 30%, compared with 1.5% in hearts with congenital or acquired cardiac disease or in normal hearts, and that when more than 5% of the relevant areas of the tissue section were involved, cell disarray was both highly sensitive (90%) and specific (93%) for HCM.22 By contrast, Bulkley and colleagues concluded that myocardial fiber disarray found in HCM was qualitatively and quantitatively similar in the LV of hearts with aortic atresia and a patent mitral valve and in the right ventricle of hearts with pulmonary atresia and intact ventricular septum.23 Thus, it is unlikely that cell disarray is a morphologic manifestation of a genetically transmitted myocardial defect in HCM24,25,26, rather, it is likely the result of uncoordinated muscular contraction occurring in these conditions.27,28

Histologic ventricular abnormalities in HCM lead to more forceful LV contraction and rapid early ventricular emptying. In addition, reduced distensibility (compliance) and impaired relaxation result in a prolonged early filling phase and a decrease in rate and volume of the rapid phase of LV filling. Consequently, there is a compensatory increase in the contribution of atrial systole to overall LV filling.29,30,31

Left Atrium
The left atrium is often dilated and thick walled as a result of decreased compliance of the LV and presence of mitral regurgitation.

Mitrail Valve
In obstructive forms of HCM, the mitral valve is positioned closer to the ventricular septum than in the normal heart.32 Mitral valve leaflets are disproportionately elongated and thickened, particularly the leading edge of the anterior leaflet.33,34 This is presumably the result of SAM. The mitral anulus forcefully constricts during systole, and this purse-string action gathers the mitral leaflets into folds.35,36

A further consequence of SAM is production of mitral regurgitation in mid- or late systole as the anterior leaflet moves forward (see Fig. 19-3). Studies by Bonow and by Wigle and colleagues indicate a direct relation between magnitude of the pressure gradient and degree of mitral regurgitation.37,38,39 It is likely that severity of mitral regurgitation, magnitude of the pressure gradient, and degree of prolongation of LV ejection time are determined by time of onset and duration of mitral leaflet–septal contact.37,38

Mitrail regurgitation occurs independently of SAM in about 20% of patients with HOCM.40,41,42 It can result from mitral valve prolapse, chordal rupture, anomalous attachment of a papillary muscle to the anterior leaflet, extensive anterior leaflet fibrosis resulting from repeated mitral leaflet–septal contact, congenital abnormalities, rheumatic disease, or mitral anular calcification.43,44,45 Presence of mitral regurgitation likely contributes to the exercise intolerance often present in patients with HOCM.46 Mitral anular calcification is frequently present in older patients with HOCM.47,48

Right Ventricle
The right ventricular chamber is distorted by the hypertrophied ventricular septum, which projects into the right ventricular outflow tract. This hypertrophy may cause an important pressure gradient in the right ventricular outflow tract and, in long-standing cases, hypertrophy of the free wall. Right ventricular hypertrophy may also occur secondary to pulmonary hypertension from long-standing left-sided heart failure and elevated left atrial pressure. Unverferth and colleagues demonstrated an important increase in amount of fibrous tissue in the right ventricular free wall in HCM, as well as an increase in myocyte cell diameter in the subendocardial layer.49

Coronary Arteries
In HCM, coronary arteries are larger in diameter than normal. Important coronary arteriosclerosis is present in about 5% of patients.49,50 Spray and colleagues and Maron and colleagues noted wall thickening and luminal narrowing of the intramural coronary arterial branches, located primarily in the ventricular septum and also occasionally in the left and right ventricular free wall in about half of patients with HCM.42,51 Muscular bridging of the left anterior descending coronary artery (LAD) during part of its course is more common in HCM than in normal hearts. The LAD may become totally occluded during systole at these sites52 or may have an irregular
sawtooth appearance.\textsuperscript{817} Septal perforating arteries may be obliterated or severely narrowed during systole. Hemodynamic effect of these changes is not known, although Maron and colleagues and Waller and colleagues have reported that transmural myocardial infarction occurs in HCM in the absence of arteriosclerotic coronary artery disease.\textsuperscript{59,63} Using thallium perfusion imaging and computed tomography, O’Gara and colleagues demonstrated that myocardial ischemia can occur in HCM both at rest and after exercise.\textsuperscript{61} This could be caused by systolic arterial compression or spasm, narrowing of intramural branches, inadequate capillary density, or reduction in diastolic coronary flow from impaired ventricular relaxation.

**Associated Lesions**

There is a specific association between HCM and diffuse lentiginosis.\textsuperscript{510} No evidence indicates that the latter is inherited.\textsuperscript{529} Association with essential hypertension noted in Brock’s original report is probably coincidental, although Wei and colleagues suggest that a “hypertrophic cardiomyopathy” with features indistinguishable from some forms of HCM can occur in a number of other disease states including severe-standing hypertension and severe aortic valvar stenosis.\textsuperscript{814,92} Similarly, there may be a coincidental association of HCM with other congenital or acquired cardiac diseases such as atrial septal defect and rheumatic heart disease. With HOCM, functional impairment of von Willebrand factor (a plasma glycoprotein required for normal hemostasis) is frequent and is closely and independently related to the magnitude of outflow obstruction.\textsuperscript{1,2} A resting peak gradient of 15 mmHg is sufficient to impair function of this glycoprotein and may result in abnormal spontaneous bleeding.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

HOCM symptoms and signs are usually such that diagnosis can be made with confidence on clinical grounds. Subaortic or midventricular obstruction may be latent (provokable), labile, or persistent (obstruction at rest).\textsuperscript{81,96} In contrast, in nonobstructive HCM there may be no symptoms or signs, particularly in mild forms. In the text that follows, only obstructive HCM (HOCM) is discussed.

**Symptoms**

Symptoms associated with HOCM can occur at any age from infancy to beyond 70 years. They include angina, effort dyspnea, syncope, and dizziness on exertion, singly or in combination. However, these symptoms may not be related directly to the magnitude of LV outflow gradient. Rather, they are caused by a complex interaction of diastolic dysfunction, arrhythmias, myocardial ischemia, and outflow gradient.\textsuperscript{815}

Palpitation may occur, usually from atrial fibrillation, which may initially be paroxysmal but is permanent in about 10% of patients in the later stages of the disease. Onset of atrial fibrillation is usually heralded by a sudden increase in dyspnea and sometimes by heart failure and hypotension because of the rapid rate and loss of the atrial component of ventricular filling.\textsuperscript{82} Almost half of patients presenting with atrial fibrillation have a history of systemic embolism. Arrhythmia may also be caused by ventricular premature beats or bouts of ventricular tachycardia or supraventricular tachycardia, and can result in sudden death.\textsuperscript{534,54}

Later stages of HOCM are associated with severe and progressive heart failure with paroxysmal nocturnal dyspnea, orthopnea, and pulmonary edema. Rarely, ascites and peripheral edema develop in association with tricuspid regurgitation.

**Signs**

The three cardinal signs of HOCM are (1) late-onset systolic ejection murmur between the left sternal edge and apex, (2) bifid arterial pulse, and (3) palpable left atrial contraction.\textsuperscript{85}

The physical signs in typical cases of HOCM differ in important respects from other forms of aortic outflow obstruction. The pulse is jerky (bifid) with a rapid upstroke, in contrast to the anacrotic pulse of valvar aortic stenosis. An abnormal jugular a wave is frequently present, and occasionally, a short, low-pitched diastolic flow murmur that is enhanced by inspiration; both are the result of vigorous atrial contraction.\textsuperscript{812} The thrusting, overactive LV impulse is frequently double because of transmission of the forceful atrial contraction, which may also be audible as a fourth heart sound. Frequently, there is a third sound at the apex. Splitting of the second heart sound may be paradoxical, but this feature, as well as a gallop rhythm, is characteristically variable because of dynamic and variable obstruction. A mid-systolic murmur that is roughly proportional in intensity to the degree of obstruction is maximal between the left sternal edge and apex of the heart rather than in the aortic area, although it radiates to the base; a thrill may be present. The murmur increases in intensity after a Valsalva maneuver (or inhalation of amyl nitrite), because both increase the degree of obstruction. When important mitral regurgitation is present, the murmur is maximal at the apex and pansystolic. There is no aortic ejection click. Valvar calcification and an aortic diastolic murmur are also absent (except in occasional cases in which the valve is abnormal). Infants and young children presenting with severe HOCM may be cyanotic from reversal of shunt flow at the atrial level.\textsuperscript{876}

**Ventricular Function**

Although in early stages of HCM, LV systolic function is usually normal or occasionally supranormal, with high ejec tion fraction in both the obstructive and nonobstructive forms of the disease,\textsuperscript{96} in HOCM (i.e., in later stages), impaired systolic function of both left and right ventricles occurs, primarily as a result of myocardial fibrosis.\textsuperscript{82,73,96} Fibrosis can result from fibrous transformation of loose intra cellular connective tissue located between the myocardial fibers,\textsuperscript{73,97} or from myocardial ischemia and infarction caused by small-vessel or arteriosclerotic coronary artery disease.\textsuperscript{59,91} Myocardial fibrosis may result in thinning of the wall, reduction or loss of outflow obstruction, reduced ejection fraction, and increased end-systolic volume.\textsuperscript{96}

Diastolic dysfunction was initially attributed to decreased ventricular compliance.\textsuperscript{811,96} However, it now appears that impaired relaxation is the more important cause.\textsuperscript{96,97} Increased chamber stiffness increases diastolic pressure with respect to volume (dP/dV), and the diastolic pressure-volume curve is shifted upward and to the left.\textsuperscript{96}
Chapter 19  Hypertrophic Obstructive Cardiomyopathy

Electrocardiography

The electrocardiogram (ECG) in HOCM characteristically shows an LV strain pattern, although Q waves may be present, and rarely, minimal changes indicative of LV hypertrophy despite an important gradient. Occasionally the ECG shows complete right or left bundle branch block and more often left anterior hemiblock. Giant negative T waves in V1-V6 are typical of isolated apical hypertrophy. ECG features of left atrial enlargement are often noted, but those of right atrial enlargement less often.

Chest Radiography

Chest radiography shows mild to moderate cardiomegaly more often in HOCM than in other forms of aortic outflow obstruction. The aorta is typically small. The raised left atrial pressure may be reflected in the lung fields by evidence of pulmonary venous hypertension or frank interstitial edema.

Echocardiography

Transthoracic echocardiography (TTE) is the most important diagnostic study. Diagnosis can usually be established by M-mode echocardiography because, with rare exceptions, patients with familial HOCM have ASH, and all those with obstruction should demonstrate SAM, although this may appear only on provocation (e.g., after Valsalva maneuver). Standard echocardiography combined with Doppler color flow interrogation can be used to identify systolic and diastolic ventricular dysfunction, degree and direction of mitral regurgitation, presence of additional mitral valve abnormalities, and size of the left atrium. Transesophageal echocardiography (TEE) with Doppler color flow interrogation is invaluable for defining extent and level of outflow obstruction and abnormalities of the mitral valve (Fig. 19-5). It should be used preoperatively for planning the operative procedure and intraoperatively to assess its effectiveness (Fig. 19-6).

Exercise Echocardiography

Exercise echocardiography may identify LV outflow obstruction in symptomatic patients who would not otherwise be regarded as candidates for interventional treatment. Maron and colleagues reported on 320 patients with HCM judged to be eligible for exercise testing, of whom 201 underwent standard exercise testing with echocardiography; 119 had LV outflow tract gradients at rest of 50 mmHg or more and were not tested. In the 201 patients, LV outflow tract gradient increased from 4 ± 9 (median = 0) mmHg at rest to 45 ± 49 (median = 30) mmHg after exercise. In 106 patients (52%), gradients of 30 mmHg or more developed, including 76 (38%) that were 50 mmHg or more. Only a minority of

Figure 19-5 Transesophageal echocardiogram (frontal long-axis plane) demonstrating mechanism of mitral leaflet–septal contact and failure of mitral leaflet coaptation in midsystole. A, During diastole, mitral leaflets open. B-C, In early systole an abnormal coaptation point (arrow) is seen in body of anterior and posterior leaflets. D, During midsystole, anterior motion of both anterior and posterior leaflets occurs. E, At mid-late systole, anterior leaflet–septal contact is seen, resulting from anterior and basal movement (arrow) of anterior mitral leaflet. F, Frame during mid-late systole shows failure of coaptation of mitral leaflets (arrow). Key: LA, Left atrium; LV, left ventricle. (From Grigg and colleagues.)
The tip should be positioned near the base of the LV close to the mitral valve to avoid apical entrapment, which can produce a falsely high LV pressure.

LV end-diastolic pressure is usually increased, often greatly, because of transmission of a large left atrial wave (Fig. 19-7). Central and peripheral arterial pulse contours show a rapidly ascending limb with a short upstroke (0.06 to 0.085) but a total ejection time greater than 0.335. A secondary systolic atrial wave results in the characteristic “spike and dome” (bifid) pulse contour initially described by Benchimol and colleagues.

The beat following a ventricular ectopic beat shows an abnormal response—a reduced arterial pulse pressure (and exaggerated spike-and-dome contour) secondary to increased obstruction generated by the ectopic beat. Obstruction is increased by any maneuver that increases LV contractility or decreases LV preload or afterload. Whenever the obstruction increases, pulse pressure decreases and total LV ejection time increases.

Figure 19-6  Intraoperative transesophageal echocardiogram (frontal long-axis plane) before (upper panels) and after (lower panels) transaortic septal myectomy. Upper left panel, Systolic frame demonstrating anterior leaflet-septal contact with failure of mitral leaflet coaptation. Upper right panel, Same frame with Doppler color flow imaging demonstrating turbulent flow in aortic outflow tract and large jet of posteriorly directed mitral regurgitation arising from gap between the two leaflets. Lower left panel, Systolic frame demonstrating a widened left ventricular outflow tract after myectomy and abolition of systolic anterior motion of mitral valve. Note diminution in width of ventricular septum. Lower right panel, Same frame with Doppler color flow imaging demonstrating nonturbulent left ventricular outflow with marked reduction in severity of mitral regurgitation, with only a small residual jet. (From Grigg and colleagues.)

Cardiac Catheterization and Cineangiography

The diagnostic accuracy of echocardiography has substantially reduced the need for invasive studies in patients with HOCM. Cardiac catheterization and cineangiography are generally reserved for patients in whom echocardiographic studies are inconclusive, those in whom arteriosclerotic coronary artery disease is likely to be present, and those for whom surgical treatment (septal myectomy, dual-chamber pacemaker insertion, or cardiac transplantation) is being considered.

Right-sided heart catheterization will show any infundibular stenosis (occasionally severe) and elevation of pulmonary artery pressure, which may also be substantial because of high left atrial pressure. Retrograde left-sided heart catheterization will quantify and localize the obstruction. The catheter tip should be positioned near the base of the LV close to the mitral valve to avoid apical entrapment, which can produce a falsely high LV pressure. LV end-diastolic pressure is usually increased, often greatly, because of transmission of a large left atrial wave (Fig. 19-7). Central and peripheral arterial pulse contours show a rapidly ascending limb with a short upstroke (0.06 to 0.085) but a total ejection time greater than 0.335. A secondary systolic atrial wave results in the characteristic “spike and dome” (bifid) pulse contour initially described by Benchimol and colleagues. The beat following a ventricular ectopic beat shows an abnormal response—a reduced arterial pulse pressure (and exaggerated spike-and-dome contour) secondary to increased obstruction generated by the ectopic beat. Obstruction is increased by any maneuver that increases LV contractility or decreases LV preload or afterload. Whenever the obstruction increases, pulse pressure decreases and total LV ejection time increases.

This dynamic characteristic of the obstruction can be confirmed by various provocative maneuvers such as isoproterenol administration, exercise, and Valsalva maneuver, which...
increase the gradient, and by methoxamine administration, which decreases it.

Systolic LV outflow gradient often is not increased during exercise but becomes dramatically increased almost immediately after exercise.\(^3\) The increase usually becomes maximal 3 to 5 minutes into the recovery period. Presumably, increased systemic venous return prevents substantial reduction of LV volume (and increase in the gradient) during exercise despite increased myocardial contractility, heart rate, and cardiac output and a reduced systemic vascular resistance. After exercise, decreased venous return allows a reduction in LV volume and an increase in systolic gradient.\(^3\)

LV cineangiography is best performed in the left lateral view because in this position the cardiac apex moves caudally and does not overshadow the mitral area.

The prominent characteristic septal bulge can be seen to form the anterior boundary of the outflow tract and the anterior mitral leaflet to form its posterior boundary. SAM can usually be demonstrated when obstruction is present (Fig. 19-8).

Degree of mitral regurgitation can be assessed from the LV cineangiogram. However, multiple ectopic beats can make quantitation difficult. Coronary angiography should be added to the procedure in patients older than age 30 years in whom coronary artery occlusive disease is suspected or known to be present.

NATURAL HISTORY

In familial HCM, isolated ASH, identified by M-mode echocardiography, is an important part of the clinical spectrum and has the same genetic implications as HOCM. It is uncertain whether isolated ASH, an asymptomatic disease, develops into clinical obstructive cardiomyopathy (HOCM); if so, this sequence is uncommon after age 20 years.\(^1\)

HCM can present at any age from early infancy to the sixth or seventh decade. Echocardiographic studies of patients with HCM, including those with isolated ASH, suggest that obstruction is present in only about 20%. Infants and young children presenting with symptomatic HOCM represent the more severe end of the spectrum, with gross LV hypertrophy, frequent episodes of heart failure, and a high prevalence of sudden death.\(^1\) Progression of disease may be more rapid in children and young adults.\(^6\)

The natural history of HCM is typically variable. Although the clinical course is often stable over long periods, adverse events such heart failure, syncope, sudden cardiac death, and peripheral embolization can occur.\(^2\) Sudden onset of heart failure is frequently precipitated by atrial fibrillation, which

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**Figure 19-7** Left ventricular (LV) and aortic pressure tracings in hypertrophic obstructive cardiomyopathy (HOCM). Peak systolic gradient is 60 mmHg. Aortic pressure pulse shows typical double contour (“spike and dome”). LV end-diastolic pressure is elevated in association with transmission of an a wave from the left atrium (arrow). The beat after an ectopic beat demonstrates reduced aortic pulse pressure characteristic of HOCM (center of tracing).

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**Figure 19-8** Left ventricular cineangiogram in left lateral position showing systolic anterior motion of anterior mitral leaflet. A, Isovolumetric contraction. Anterior (a) and posterior (p) mitral leaflets are apposed in relatively normal systolic position, causing only slight narrowing low in left ventricular outflow tract despite prominent septal muscle (s) anteriorly. Aortic valve is still closed. B, Systolic ejection phase. Apposed free edges of mitral leaflets have risen to maximal level of obstruction, with anterior leaflet almost meeting the septal muscle. Despite severe obstruction (systolic gradient of 100 mmHg), there is no detectable mitral regurgitation.
may be associated with subsequent embolism. In patients with HOCM, correlation between symptomatic class and degree of obstruction has generally not been close, although in the multicenter trial reported by Shah and colleagues, there were no asymptomatic patients once the gradient exceeded 100 mmHg.\textsuperscript{51} Frank and Braunwald documented a substantially higher gradient in patients in New York Heart Association (NYHA) classes III and IV compared with those without symptoms.\textsuperscript{50} In the experience of Wigle and colleagues, presyncope and syncope on exertion are encountered most frequently in patients with HOCM.\textsuperscript{56}

Annual HCM-related mortality reported from referral centers has ranged from 4% to 6% in children and 2% to 4% in adults.\textsuperscript{52,53,54,56} (Figure 19-9). In contrast, studies involving largely unselected patients with HCM report annual mortality of 0.5% to 1.5%, similar to that for the adult general population.\textsuperscript{59,52,52,56}

Sudden cardiac death is common in patients with HCM.\textsuperscript{52} Risk factors for sudden death include a basal (resting) peak instantaneous gradient of at least 30 mmHg,\textsuperscript{54} young age, syncope, family history of malignancy, myocardial ischemia (particularly in the young), sustained ventricular tachycardia on electrophysiologic testing, and ventricular tachycardia on ambulatory monitoring.\textsuperscript{56} HCM is the most common association with unexplained sudden death in otherwise apparently healthy competitive athletes.\textsuperscript{52} Midventricular obstruction is an independent predictor of adverse outcomes especially for the combined endpoint of sudden death and potentially lethal arrhythmic events.\textsuperscript{55}

Neurologic death from cerebral embolism occurs in patients with permanent or paroxysmal atrial fibrillation or, infrequently, as a result of infective endocarditis on aortic and mitral valves.\textsuperscript{59} In the multicenter study by Shah and colleagues in patients with obstruction, but not operated on and followed for an average of 5.2 years, only one died from heart failure and two from infective endocarditis, but 23 from sudden cardiac death.\textsuperscript{510}

**TECHNIQUE OF OPERATION**

**Myectomy by Aortic Approach**

A full or partial upper median sternotomy is used, and cardiopulmonary bypass (CPB) is established in standard fashion (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). During cooling, a left atrial drainage catheter is inserted through a purse-string suture in the right superior pulmonary vein near its junction with the left atrium. A catheter can also be placed into the coronary sinus through a purse-string suture in the wall of the right atrium for retrograde delivery of cardioplegic solution (see “Technique of Retrograde Infusion” in Chapter 3). The distal ascending aorta is clamped, and cardioplegic solution is infused through a needle in the ascending aorta (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). The aorta is then opened through a transverse aortotomy or through an oblique incision that extends into the non-coronary sinus of Valsalva (Fig. 19-10, A). Stay sutures are applied to the edges of the aortotomy or to the aortic valve commissures to improve exposure. If additional myocardial protection is necessary, the coronary ostia can be cannulated and directly perfused with cardioplegic solution (see “Perfusion of Individual Coronary Arteries” in Chapter 3).

The right aortic cusp is retracted anteriorly against the sinus wall. Hypertrophied septum can be seen bulging down into the anterior aspect of the LV outflow tract (Fig. 19-10, B). A narrow ribbon retractor can be placed into the LV outflow tract and depressed posteriorly to avoid injury to the chordae tendineae and anterior leaflet of the mitral valve. Using a No. 15 (small rounded) scalpel blade, an incision is made deep into the septum, exactly beneath the nadir of the right coronary cusp and parallel to the long axis of the LV outflow tract. A second parallel incision in the septum is made as far leftward as possible without damaging the mitral valve (Fig. 19-10, C). As suggested by Morrow,\textsuperscript{545} a sponge stick can be pressed against the right ventricular free wall to depress the ventricular septum and bring it into better view through the aortotomy. Both incisions are then deepened and carried toward the LV apex as far as possible—often beyond visibility, because no structures can be damaged in this area. The two vertical incisions are then connected by a transverse incision beginning several mm below the right coronary cusp. This may prevent prolapse of the right coronary cusp and development of aortic regurgitation. With continuing pressure on the sponge stick, this transverse incision is extended downward into the ventricle until a thick, rectangular piece of septum has been excised (Fig. 19-10, D). In patients with important

![Figure 19-9](image-url) Freedom from hypertrophic cardiomyopathy (HCM)-related death among 273 patients with a left ventricular outflow gradient of at least 30 mmHg under basal conditions and 828 patients without obstruction at entry. (From Maron and colleagues.\textsuperscript{54})

**Table 19-1**

<table>
<thead>
<tr>
<th>No. at Risk</th>
<th>Obstruction</th>
<th>No obstruction</th>
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<tbody>
<tr>
<td>828</td>
<td>273</td>
<td>594</td>
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<td>594</td>
<td>178</td>
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<td>201</td>
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<td>201</td>
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</table>

**Note:** P = .001
hypertrophy of the adjacent left anterolateral free wall, a third incision is made beginning below the commissure between left and right coronary cusps and is directed toward the base of the anterolateral papillary muscle. Septal tissue between this incision and the primary trough already created is excised to further increase the cross-sectional area of the LV outflow tract (Fig. 19-10, E). Care is taken to remove any small pieces of muscle from the LV cavity; the left index finger is then passed through the valve into the cavity. If palpation of the septum confirms that the excision has traversed the entire length of the muscular obstruction (Fig. 19-10, F), operation is considered to be complete. The aortotomy is closed, and CPB is discontinued (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

In pediatric patients, HOCM has a more variable morphologic spectrum. The major site of obstruction may be subaortic, although it often occurs at the midventricular or apical level. Obstruction of the right ventricular outflow tract also occurs. Within the LV, hypertrophied muscle may extend onto the base of the anterior leaflet of the mitral valve, and

Figure 19-10  Technique of transaortic septal myectomy. A, Aorta is opened through oblique incision extending into noncoronary sinus of Valsalva (dashed line). B, Right aortic cusp is retracted against the aortic wall, exposing the hypertrophied septum. Dashed lines indicate initial incisions into the septum. C, Two parallel incisions are made in the septum: (1) beneath nadir of right coronary cusp and (2) as far leftward as possible. These incisions are joined by a transverse incision (dashed line), which is made several millimeters below the edge of the right aortic cusp. D, Rectangular channel created by septal myectomy.

Continued
these fibromuscular attachments may contribute to SAM of the anterior leaflet. When present, they should be carefully incised at both margins of the base of the anterior leaflet during the transaortic myectomy to reduce or eliminate abnormal SAM of the anterior leaflet.

**Adjuncts to Conventional Myectomy**

*Intraoperative TEE* facilitates performing septal myectomy by determining accurately the location and thickness of hypertrophied septum, detecting other lesions, assisting assessment of adequacy of the myectomy and correction of mitral regurgitation, and identifying complications such as ventricular septal perforation. Among 50 patients who underwent septal myectomy and in whom intraoperative echocardiography was used, 10 (20%; CL 14%-28%) required a second period of CPB for further resection of muscle because of persisting LV outflow tract gradients greater than 50 mmHg or for correcting more than moderate mitral regurgitation.

If adequate myectomy has been performed, there will be little or no residual gradient, SAM, or mitral regurgitation. *Direct measurements of LV and ascending aortic pressures* should be made after discontinuing CPB under stable hemodynamic conditions. If a residual gradient of more than 10 to 15 mmHg is present, CPB should be reestablished and additional muscle resected.

*Extended myectomy and reconstruction of the subvalvar mitral apparatus* have been proposed by Messmer. The septal myectomy is deeply extended into the LV cavity, wider...
toward the apex than the base, thus providing access to the base of both papillary muscles. These are mobilized down to the apex, and all hypertrophied portions and muscular trabeculae are resected. In theory, mobilization of malpositioned papillary muscles from the adjacent myocardium permits the mitral valve leaflets to be deflected away from the LV outflow tract during systole. A similar technique has been reported by Maron and colleagues for managing outflow obstruction in the midventricular region that results from muscular apposition created by anomalous chordae tendinae or anomalous insertion of a papillary muscle directly into the anterior mitral leaflet without interposition of chordae tendinae. In the latter instance, the papillary muscle is incised and separated from the ventricular septum or free wall down to its base. If an accessory muscle is present in the LV outflow tract, it is excised by amputating it at its base and severing the fibrous attachments to the anterior mitral leaflet.

Plication of the anterior leaflet of the mitral valve with myectomy, first proposed by McIntosh and colleagues, has been performed in patients judged at operation to be at increased risk for a suboptimal hemodynamic result because of morphology of the mitral valve (increased mobility, size, or length of anterior leaflet with respect to LV outflow tract dimension) and potential for its anterior leaflet to protrude into the myectomy trough during systole. Plication can be performed through the aortic valve either in the horizontal direction or vertically (tip of leaflet to base) using several interrupted polypropylene sutures.

Anterior leaflet extension by insertion of a pericardial patch into the body of the anterior leaflet has been employed by some groups. This maneuver increases leaflet stiffness, causes lateral displacement of the secondary chordae tendinae, and functions hemodynamically as a spinnaker sail to eliminate SAM. The effectiveness of leaflet plication and extension in reducing LV outflow tract obstruction and SAM has not been evaluated in large clinical trials.

Apical myectomy has been proposed for treatment of severely symptomatic patients with apical HCM and for patients with midventricular obstruction. Through an incision in the apex of the left ventricle lateral to the left anterior descending coronary artery, excision of ventricular muscle at the apex and midventricular levels is performed with the objective of increasing the LV end-diastolic volume and improving LV compliance. Postoperative hemodynamic studies in 14 of a series of 44 patients reported by Schaff and colleagues using this technique, showed a significant (P = .002 or less) decrease in LV end-diastolic pressure, increase in LV diastolic volume index, and increase in stroke volume. Five-year survival was 81%.

Modified Konno Operation
When echocardiography or initial visual examination through the aortic valve shows that muscular obstruction is deeper (more toward the apex) in the LV outflow tract than usual, or when there is residual muscular obstruction inferiorly after creating a trough, a modified Konno operation can be performed (see “Modified Konno Operation” under Technique of Operation in Section II of Chapter 47). The modified Konno operation may occasionally be selected preoperatively as the preferred procedure because of severity and location of obstruction.

Mitrail Valve Replacement
The role of mitral valve replacement in managing patients with HOCM remains incompletely defined. Cooley and colleagues have shown that excising the anterior mitral leaflet relieves LV outflow tract obstruction in most patients. McIntosh and colleagues showed that in comparing patients undergoing mitral valve replacement, septal myectomy, or septal myectomy combined with plication of the anterior mitral leaflet, the greatest reductions in resting and provable outflow tract gradients and in LV end-diastolic pressure occurred in those who had mitral valve replacement. Mitral valve replacement may be necessary for patients who have intrinsic disease of the mitral valve that is not typically associated with HOCM. This includes patients with rheumatic or severe myxomatous or degenerative disease that is not amenable to repair. A concomitant septal myectomy should be performed in most patients.

If mitral valve replacement is performed, all chordal attachments between papillary muscles and mitral valve leaflets must be severed (see Fig. 19-10, F and G). The entire anterior leaflet of the mitral valve must be excised. If hypertrophied and contributing to obstruction, the papillary muscles are excised. The small size and at times abnormal shape of the LV cavity require use of a low-profile prosthesis, most often a mechanical valve.

Mitrail Valve Repair
Other structural abnormalities of the mitral valve besides those typically associated with HOCM exist in approximately 7% of patients undergoing surgical treatment of HOCM. Mitral valve repair is feasible in 50% to 60% of these patients using conventional reparative techniques. Anuloplasty rings should be avoided, however, to prevent SAM. If anuloplasty is necessary, flexible or rigid bands on the posterior leaflet are preferred.

SPECIAL FEATURES OF POSTOPERATIVE CARE
The patient is cared for with the principles and protocols described in Chapter 5. Marked LV hypertrophy reduces ventricular compliance to such an extent that left atrial pressures of 16 to 18 mmHg may be required early postoperatively for adequate preload. Digitalis glycosides and the β-adrenergic receptor agonist isoproterenol should be avoided because they increase myocardial contractility and may increase residual outflow tract gradient. Hypovolemia and nitroglycerin, which can reduce LV volume and exaggerate any residual gradient, should also be avoided. Atrial fibrillation may be poorly tolerated, so measures should be taken to reduce its probability of occurrence and to treat it aggressively if it develops. This can be best accomplished by use of β-adrenergic receptor blocking agents (e.g., propranolol), calcium antagonists (e.g., verapamil, diltiazem), or amiodarone.

RESULTS
Early (Hospital) Death
In the larger surgical series of patients treated in the 1980s and early 1990s, hospital mortality ranged from 0% to 6%. Mortality has remained somewhat higher with concomitant coronary artery bypass grafting and valve
PART IV  Other Cardiac Conditions

Modes of Death
Cardiac failure, sudden death, ventricular arrhythmias, and stroke are the most common cardiovascular modes of death after discharge from the hospital.

Incremental Risk Factors for Premature Death
Older age at operation is a risk factor for early and late death. However, many elderly patients not only survive, but also exhibit marked hemodynamic and symptomatic improvement. Addition of mitral valve replacement or repair to myotomy or myectomy is a risk factor for late death. In separate series, female gender, preoperative syncope, increased NYHA functional class, documented coronary artery disease, preoperative atrial fibrillation, concomitant procedures, mitral valve replacement, development of complete heart block, and persisting outflow tract gradients greater than 15 mmHg were incremental risk factors for late death.

Myocardial Changes
The effect of surgical reduction of LV outflow tract obstruction on cardiac structure and function has been demonstrated. Deb and colleagues demonstrated a significant decrease in LV mass and mass index assessed by TTE in 60 patients following septal myectomy. This favorable remodeling occurred early after operation and persisted beyond 2 years. Among 150 patients followed for a median of 1.8 years and for up to 20 years after septal myectomy, substantial improvement in LV diastolic filling as determined by mitral inflow Doppler velocity signals was observed. Menon and colleagues reported a significant (P < .0001) decrease in echocardiographically determined mean left atrial volume index among 32 young patients (mean age 12.5 years) after septal myectomy. This reduction correlated closely with decrease in severity of mitral regurgitation (P = .04) Cannon and colleagues noted a reduction in oxygen consumption and corresponding reduction in coronary blood flow, and a change from lactate production during pacing to lactate consumption, in the anterior portion of the LV and septum. The
changes were more marked in patients with high coronary flow reserve before reoperation.

Conduction Disturbances

Complete heart block occurs in from 2.5% to 10% of patients.\textsuperscript{18,15,41,44,58,59,60,61,62} When complete right bundle branch block is present preoperatively, creating left bundle branch block (LBBB) at operation results in complete heart block.\textsuperscript{3,5} Complete LBBB develops in approximately 50% of patients postoperatively.\textsuperscript{18,5,62} In a recently reported series of 325 patients undergoing isolated septal myectomy, pacemakers were required in 7 (3%) with normal preoperative conduction, in 15 (30%) with preexisting conduction abnormality, and in 10 (77%) with right bundle branch block.\textsuperscript{18} In this series, new permanent pacemakers were implanted in 19 additional patients during follow-up, which averaged 3.6 ± 2.8 years and extended to 8 years. Freedom from pacemaker insertion at 8 years was 79%.

Perioperative Myocardial Infarction

Perioperative myocardial infarction occurs occasionally at sites remote from the myotomy and can occur without associated coronary arterial occlusive disease.\textsuperscript{59} With current techniques for intraoperative myocardial preservation, occurrence of myocardial infarction is low.

Iatrogenic Defects

Ventricular septal defect (VSD) is created in up to 3% of patients treated by transaortic myotomy or myectomy.\textsuperscript{16,44,75} In recently reported series from experienced centers, the frequency is less than 1%.\textsuperscript{58,61,10} McIntosh and colleagues believe that an iatrogenic VSD is more likely to occur when the septum is relatively thin (<18 mm).\textsuperscript{31} VSD may not be detected until some weeks after operation and could then be the result of septal infarction rather than surgical perforation.\textsuperscript{52} A VSD may contribute to hospital mortality and may be large enough to require subsequent repair.\textsuperscript{16,3,5}

Aortic valve regurgitation can occur after operations for HOCM. It occurred postoperatively in 5% of 115 patients (CL 3.1%-8.3%) reported by Mohr and colleagues and in 4% of 525 patients (CL 3.1%-5.1%) operated on exclusively through the aortic root by Brown and colleagues.\textsuperscript{16,44} In the latter series, regurgitation developed within 6 months of operation in more than half the patients. Sasson and colleagues, using pulsed or color Doppler echocardiography to quantify severity of aortic regurgitation, found the prevalence of aortic regurgitation to be 54% in 52 patients who were studied a mean of 7.8 years postoperatively.\textsuperscript{52} Clinically evident aortic regurgitation was present in only 12% of these patients. The authors noted that although initially trivial, regurgitation may progress over time, but it was well tolerated in all patients who were studied. In the experience of Brown and colleagues, a small aortic anulus (≤21 mm in diameter) and a low mitral–septal contact lesion increased the probability of postoperative regurgitation, probably in both cases the result of increased operative difficulty and increased retraction and possible injury of aortic valve cusps.\textsuperscript{16} Loss of support of the right coronary cusp as a result of excising septal muscle beneath it may result in aortic regurgitation,\textsuperscript{52} as may altered velocity, direction, and dynamics of the turbulent jet of blood in the outflow tract.\textsuperscript{52} These observations emphasize the importance of considering alternative approaches to the obstruction, or mitral valve replacement in patients in whom the aortic anulus is small or the area of obstruction is difficult to expose through the aortic root. Avoiding resection of the first few mm of ventricular muscle beneath the right coronary cusp may prevent subsequent cusp prolapse and aortic regurgitation.

Postoperative Pressure Gradients

Adequate myectomy substantially reduces preoperative gradients,\textsuperscript{58,44,3,5,61,52,59,62} although on provocation a mild gradient can be demonstrated in about 25% of patients.\textsuperscript{56,58,52} In those in whom a gradient is present preoperatively only on provocation, these maneuvers do not produce a gradient postoperatively.\textsuperscript{56} In addition, operation almost always abolishes abnormal postectopic response and abnormal arterial pulse contour. In patients with several postoperative evaluations extending over many years, residual gradient either remains the same or diminishes (Fig. 19-13, A).\textsuperscript{56,3,51,18}

\begin{figure} 
\centering 
\includegraphics[width=\textwidth]{fig19-13.png} 
\caption{Effectiveness of isolated septal myectomy as assessed longitudinally by echocardiography. Dot on y axis is preoperative value, and dashed line leads to immediate post-myectomy value at time zero. Dots are grouped “independent” point estimates, and solid line enclosed within 68% confidence limits (equivalent to ±1 standard error) is average response corrected for repeated measures. A, Peak left ventricular outflow tract (LVOT) gradient. B, Systolic anterior motion (SAM) of septal leaflet of mitral valve. (From Smedira and colleagues.\textsuperscript{51})} 
\end{figure}
When gradients and symptoms persist after inadequate myectomy, reoperation is advised. The procedure can be a repeat myectomy through the aortic root, a modified Konno procedure preserving the aortic valve, or—particularly when the ventricular septum is less than 18 mm thick on echocardiographic assessment—mitral valve replacement.\textsuperscript{M31,M41}

Systolic Anterior Motion of the Mitral Valve

Both echocardiography and cineangiography show reduction or abolition of SAM of the mitral valve in most patients, and this is generally sustained (see Figs. 19–6, 19–13, B).\textsuperscript{G8,S18,W6} In addition, grooves created by myectomy and reduced thickness of the myectomy site are demonstrable by these techniques\textsuperscript{S5} and may result in enlargement of the LV outflow tract.\textsuperscript{B9,S23}

Mitrail Regurgitation

Mitrail regurgitation is usually abolished or substantially reduced after adequate myotomy or myectomy (see Fig. 19–6).\textsuperscript{L9,G8,N9} Persistent important mitral regurgitation usually suggests a coexisting myotic lesion such as mitral valve prolapse, spontaneous chordal rupture, or damage from infective endocarditis.\textsuperscript{N16}

Symptomatic Status

Many reports indicate striking symptomatic improvement in patients who have undergone adequate myotomy or myectomy.\textsuperscript{B18,H7,M16,M29,M44,S9} Most patients promptly become completely asymptomatic or complain of mild effort dyspnea only, and syncope is usually abolished.\textsuperscript{M44} Approximately 80% to 90% of patients are in NYHA functional class I or II postoperatively.\textsuperscript{B18,H7,M44,S6,S8,S18} No strong evidence indicates that late recurrence of symptoms is related to recurrence of obstruction. Patients who die late from arrhythmia or cerebral embolization are usually asymptomatic before the event, and in those dying in heart failure, deterioration is frequently rapid. The longer the follow-up, the greater the number of patients dying in heart failure from progression of the disease process (impaired diastolic relaxation).

Atrial fibrillation adversely affects symptoms as well as long-term survival.\textsuperscript{W15} Surgical relief of obstruction in HOCM does not consistently abolish chronic atrial fibrillation or permit successful cardioversion. When this rhythm occurs as a new feature in later stages of the disease, there is further symptomatic deterioration and, if anticoagulants are not given, a high probability of thromboembolism. Although surgical and catheter-based ablation procedures for this atrial fibrillation have been performed,\textsuperscript{M27,S30} the combined Cleveland, Rio de Janeiro, Venice, and San Francisco experience suggests that atrial fibrillation recurrence after these procedures is frequent.\textsuperscript{K3}

Left Ventricular Function and Structure

Preoperative resting ejection fraction, greatly increased in patients with HOCM (76% ± 9%), is reduced postoperatively ($P < .001$) to 67% ± 18%, a figure that lies well within the range of normal.\textsuperscript{B6} Preoperatively, during exercise, ejection fraction falls to within the normal range (71% ± 14%) and postoperatively falls slightly (66% ± 18%). These data do not suggest that important damage to the LV results from a transaortic myectomy. LV cavity size and wall thickness are decreased, as are left atrial pressure and volume.\textsuperscript{M43,N2,W16}

INDICATIONS FOR OPERATION

Septal myectomy should be considered for any patient who remains symptomatic (NYHA class III or IV) after appropriate medical therapy ($\beta$-adrenergic receptor blockade, calcium antagonists, disopyramide), septal ablation (see “Special Indications and Controversies”), pacemaker therapy, and who has an important LV subaortic gradient (≥50 mmHg) at rest or after physiologically based provocation with exercise, caused bySAM with septal contact.\textsuperscript{M37} In the extensive experience of Wigle and colleagues, successful operation (total relief of obstruction at rest or on provocation) provides substantially more hemodynamic and symptomatic benefit than any currently available medical therapy.\textsuperscript{N6} Increased age and severe symptoms are not contraindications to operation.

Atrial fibrillation is also an indication for operation. Elimination of the obstruction and coexisting mitral regurgitation can result in a decrease in left atrial size, particularly in younger patients.\textsuperscript{M39} This size reduction may be an effective form of antiarrhythmic therapy for these individuals.\textsuperscript{W6} A maze procedure can also be used to treat the atrial fibrillation if it remains refractory to drug treatment (see Chapter 16).

These indications may be extended to include less symptomatic patients with severe gradients, particularly if there is substantial coexisting mitral regurgitation or a history of syncope or unexplained cardiac arrest.\textsuperscript{B7} as well as to asymptomatic younger patients with gradients greater than 100 mmHg. Septectomy can be justified because of low operative risk and potential to reduce risk of sudden death.

Because most patients with HOCM achieve satisfactory relief of LV outflow tract obstruction and relief of symptoms with sepal myectomy, and because of the disadvantages of a prosthetic mitral valve, mitral valve replacement is reserved for specific situations. These include a ventricular septum that is thin (<18 mm) or has unusal morphology,\textsuperscript{M29,M31} inability to achieve an adequate myectomy,\textsuperscript{M29} structural abnormalities of the mitral valve that are not amenable to repair and are associated with moderate or severe mitral regurgitation, and recurrence or persistence of ventricular outflow obstruction after previous myectomy.\textsuperscript{K1,K31,K4} Mitrail valve replacement may be appropriate therapy for midventricular obstruction when extended myectomy is ineffective or substantial mitral regurgitation persists after adequate myectomy.\textsuperscript{K7} There is general agreement, even among its advocates, that mitral valve replacement should be reserved for severely symptomatic patients with a substantial (≥50 mmHg) resting LV outflow gradient who fulfill these criteria.\textsuperscript{K10}

Because coronary artery bypass grafting alone does not relieve symptoms in patients with HOCM and coronary artery occlusive disease,\textsuperscript{N15,S27} myectomy and bypass grafting are indicated when the two conditions coexist.

SPECIAL SITUATIONS AND CONTROVERSIES

Alternative Therapies

Percutaneous Transluminal Septal Myocardial Ablation

Ablation of septal myocardium by percutaneous transluminal infusion of alcohol into the appropriate septal branches of the
LAD results in infarction and localized thinning of the basal septal myocardium, enlargement of the LV outflow tract, and reduction of the outflow gradient.\textsuperscript{51,56} No randomized trials comparing alcohol septal ablation with septal myectomy have been performed. Zeng and colleagues conducted a meta-analysis of three studies with adequate data to compare the two methods of treatment and demonstrated similar early mortality, reduced intraventricular septal thickness, increased LV end-diastolic dimension, and short-term improvement in NYHA functional class.\textsuperscript{21} Septal ablation was associated with less reduction in the LV outflow tract gradient and greater need for permanent pacing (21\% vs. 4.4\%) than was surgical myotomy.

A study from Toronto General Hospital comparing 48 patients undergoing myectomy with 54 having septal ablation demonstrated substantial clinical improvement in both groups.\textsuperscript{82} However, after propensity adjustment, patients treated with alcohol ablation had higher postprocedure resting ($P = .002$) and provocable ($P = .004$) outflow tract gradients, more SAM ($P = .01$), and higher NYHA classification ($P = .05$) at most recent follow-up. Substantially more patients achieved the defined optimal outcome after myectomy (survival, NYHA functional class I, no postprocedure pacemaker, and follow-up resting LV outflow gradient of <20 mmHg) than after septal ablation (73\% vs. 22\%, $P = .001$). A high prevalence of SAM (78\%) was also noted among 37 patients from Massachusetts General Hospital who had septal ablation.\textsuperscript{78} Patients with persistent SAM had more anterior malposition of the mitral valve and less reduction in mitral regurgitation than those without SAM.

Sorajja and colleagues from Mayo Clinic observed a procedural complication in 27\% (death 1.5\%, CL 0.5\%-3.5\%; sustained ventricular arrhythmias 3\%, CL 1.5\%-5.4\%; tamponade 3\%, CL 1.5\%-5.4\%; pacemaker implantation 20\%, CL 16\%-24\%) of 134 patients treated with alcohol septal ablation.\textsuperscript{21} This was more than combined complications of 5\% (death, tamponade, ventricular arrhythmia, pacemaker implantation) among an age- and sex-matched cohort of patients who underwent myectomy ($P = .0001$). Four-year survival was similar in the two groups, but survival free of severe symptoms was significantly lower for patients having septal ablation who were 65 years of age or younger (Fig. 19-14).

Myectomy can be successfully performed after failed alcohol ablation, but with a higher risk of heart block than in cases where only surgery is performed. Otherwise, alcohol ablation does not appear to adversely affect surgical outcome.\textsuperscript{21}

### Table 19-1 Factors Favoring Three Therapeutic Options in Patients with Hypertrophic Obstructive Cardiomyopathy and Drug-Refractory Severe Symptoms\* 

<table>
<thead>
<tr>
<th>Septal Myectomy</th>
<th>Alcohol Septal Ablation</th>
<th>Dual-Chamber Pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;55 years (and children)</td>
<td>Age ≥55 years</td>
<td>Not candidate for septal myectomy or alcohol ablation</td>
</tr>
<tr>
<td>Obstruction due at least in part to anomalies of subvalvular apparatus</td>
<td>Unfavorable surgical candidate with important comorbidity</td>
<td></td>
</tr>
<tr>
<td>Intrinsic mitral valve disease (severe mitral regurgitation)</td>
<td>Patient unwillingness to undergo surgery</td>
<td></td>
</tr>
<tr>
<td>Acute gradient reduction required</td>
<td>No access to surgical center</td>
<td></td>
</tr>
<tr>
<td>Presence of coexisting diseases: coronary artery disease, fixed aortic stenosis, atrial fibrillation (for Maze)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Particularly high gradients and extreme left ventricular hypertrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary anatomy not amenable to ablation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous alcohol ablation unsuccessful</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\*New York Heart Association functional classes III/IV.

\textsuperscript{546} From Maron and colleagues.\textsuperscript{546}
In general, alcohol ablation should be reserved for specific patient subgroups such as the elderly, those with significant comorbidity and relative contraindications to myectomy, and those with a strong preference for avoiding operation (Table 19-1).11,30,31

**Dual-Chamber Pacing**

Dual-chamber (DDD) pacing decreases the subaortic pressure gradient and relieves associated symptoms in some patients with HOCM.11,30,31 The mechanism by which the gradient is decreased is uncertain but may be related to decreased septal motion, which results in increased LV outflow tract area and reduced SAM of the anterior mitral leaflet, late activation of the basal septum, or decreased LV contractility.17,36 Not all patients respond favorably to pacing.11,30,31 Two studies with follow-up extending to 10 and 12 years have demonstrated sustained improvement in symptoms and reduction of the LV outflow tract gradient in most patients.11,36 In the study by Topilski and colleagues,17 positive results were attributed to periodic assessment and optimization of pacemaker function. DDD pacing may be of particular value in the elderly and other patients who are not candidates for myectomy or septal ablation (see Table 19-1).

**Cardioverter-Defibrillator**

Patients with HOCM and unexplained syncope, cardiac arrest, and ventricular tachycardia or fibrillation should be considered for implantation of a cardioverter-defibrillator in combination with myectomy or other surgical procedures.44 Implantation may be indicated in some patients with non-obstructive HCM who have a history of cardiac arrest or unexplained syncope and in whom physiologic testing is positive.44,36

**Cardiac Transplantation**

Cardiac transplantation should be considered for suitable candidates with HOCM who have not responded to maximal medical and surgical therapy. These patients usually have intractable symptoms of heart failure associated with dilated ventricular cavities.315

**Left Ventricular–Aortic Conduit**

A valved conduit from the apex of the LV to the thoracic or abdominal aorta has been inserted in patients with HOCM.11,31,36,38 This procedure should be used only when other methods of surgical treatment are infeasible.

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Cardiomyopathy is a cardiac muscle disease process that leads to clinical myocardial dysfunction. The disease process results in morphologic changes in the heart that are typically classified as (1) dilated cardiomyopathy, (2) ischemic cardiomyopathy, (3) hypertrophic cardiomyopathy, (4) restrictive cardiomyopathy, and (5) arrhythmogenic right ventricular (RV) dysplasia. Clinical manifestations, predictors of survival and functional outcome, and therapeutic objectives focus on the clinical and pathophysiologic condition termed heart failure.

Section I Heart Failure

DEFINITION

Heart failure is a clinical syndrome that represents a complication or common final pathway of many heart diseases in which defective cardiac filling (diastolic heart failure) or impaired contraction (systolic heart failure) or emptying results in the heart’s inability to pump a sufficient amount of blood to support tissue metabolism, or to be able to do so only with elevated filling pressures. It is commonly characterized by secondary organ abnormalities in the skeletal muscles (fatigue), lungs (dyspnea on exertion and sometimes at rest), and kidneys (salt and fluid retention).

HISTORICAL NOTE

William Withering drew attention to the use of foxglove, Digitalis purpurea, in his classic treatise An Account of the Foxglove and Some of Its Medical Uses: With Practical Remarks on Dropsey and Other Diseases in 1785. He began using an old family remedy for dropsey—swelling of the limbs—and determined that the active ingredient of the herbal concoction was derived from foxglove leaves. After 10 years’ experience, he published use of digitalis in treating dropsy, anasarca, and hydrops pectoris. Withering advised digitalis primarily as a diuretic, assuming this was its principal action. He also recognized a powerful action on the heart, quieting and slowing its rate. Cushey, writing about digitalis in 1925, noted that much literature was published regarding its actions until 1810, thereafter, clinical use of digitalis remained unchanged for 100 years.

William Heberden, writing in 1802 about diagnosis and treatment of dropsy, stated “A dropsey is very rarely an original distemper, but is generally a symptom of some other, which is too often incurable; and hence arises its extreme danger.” He recommended removing “stagnating water” by purging and diuretic salts. He knew of digitalis and used it in his practice.

Bertin made an important distinction in 1833 between hypertrophy and dilatation of the heart. He noted that dilatation does not constantly accompany thickening (hypertrophy) of the myocardium. He proposed classifying hypertrophy using “simple” to describe a heart whose walls were thickened without dilatation of chambers, “eccentric” to describe increased wall thickness with dilatation of chambers, and “concentric” to describe increased wall thickness and diminished cavity size.

In 1870, J. Milner Fothergill won the Hastings Gold Medal of the British Medical Association for an essay about digitalis. His text on heart disease and treatment provides a glimpse of heart failure treatment in 1872. He stated, “The treatment of [cardiac] dilatation taxes all the powers that can be brought to bear on it, and the success which attends our efforts is very limited indeed.” He recommended “rest, nutritious and easily-digestible diet, … and a residence in a hospital ward for a few weeks.” In addition to rest and abstaining from all exertion, he recommended treatment with digitalis.

When William Osler published The Principles and Practice of Medicine in 1892, treatment of heart failure included “complete bed rest, a carefully regulated diet, and use of aromatic spirits of ammonia, sulphuric ether, and stimulants.” Digitalis was used more selectively. “Morphia” (morphine) was used. Even “strychnia” (strychnine) was given. Cautious use of nitroglycerine was also recommended.

Understanding of heart failure advanced in the 20th century. Paul D. White used the term congestive heart failure to refer to insufficiency of the myocardium in his classic text Heart Disease, published in 1931. Mechanisms and causes of heart failure became more refined. Treatment consisted of:

- Rest
- Digitalis
- Diuretic drug therapy
- Other drugs, including cathartics and hypnotics
- Other measures, including venesection

Diuretics that were useful at that time were theobromine, mercury, certain salts, and parathormone.

By the 1950s, rapid advances were being made in treating diseases of the circulation. Heart failure treatment included not only rest but intermittent exercise to prevent phlebothrombosis and enhance efficacy of diuretic therapy. Dietary sodium restriction was understood. Digitalis was available as powdered leaf and in several purified compounds and was the mainstay of heart failure treatment. Mercurial diuretics were the most effective. These drugs were given parenterally and acted by diminishing reabsorption of chloride by the renal tubules. Their action was enhanced by intravenous administration of aminophylline. Chlorothiazide became available for oral use and was thought to be an effective diuretic. Oxygen therapy was found to be useful. Other measures were still in use, such as sedation with morphine, venesection, thoracentesis, puncture of legs, and radiiodine to induce hypothyroidism.

Loop diuretics were introduced in the late 1960s. For the first time, efficacious diuretic agents were available. Ethacrynic acid, the first of the loop diuretics, is a phenoxyacetic acid derivative; furosemide is a sulfonamide derivative. These drugs selectively inhibit sodium chloride reabsorption in the thick ascending limb of the loop of Henle. Other sulfonamide derivatives were subsequently introduced. These diuretics have become the basis for treating heart failure.

MORPHOLOGY AND MORPHOGENESIS

Cardiac Remodeling

Cardiac remodeling is the central feature of the failing heart. One of the principal mechanisms by which the heart
The basic cellular feature of cardiac remodeling is myocyte hypertrophy, which includes both an increase in myocyte size and presence of additional sarcomeres, whose qualitative aspects differ according to the inciting pathologic conditions. Early stages of myocardial hypertrophy are characterized by increases in number and size of mitochondria in cardiac myocytes and in number of myofibrils. The myocardial cell, therefore, is larger and longer.

Transition from compensatory hypertrophy to heart failure is related to alterations in cell organization and changes in coronary blood flow to the increased cell mass of the hypertrophied ventricle. Myocardial capillary density and coronary reserve are reduced, resulting in myocardial ischemia that is most pronounced in the subendocardium. Ischemic myocyte injury associated with replacement fibrosis impairs systolic and diastolic function and accelerates heart failure. At a more advanced stage of hypertrophy, subtle changes of cellular organization and contour occur. Long-standing hypertrophy disrupts both cellular organization and Z-band architecture. Late stages of hypertrophy are characterized by loss of contractile elements with breakdown of Z bands, loss of normal parallel arrangement of sarcomeres, deposition of fibrous tissue, and tortuosity of T tubules.

When the remodeling process leads to segmental or global ventricular dilatation, the increased curvature results in increased wall tension, as predicted by the Laplace relationship. Increased wall tension induces increased myocardial oxygen consumption, impairs subendocardial blood flow, and decreases arrhythmia thresholds. Increasing degree of remodeling has been correlated with worsening prognosis.

Fetal Gene Activation

Growth factors present in the embryonic heart but dormant in the normal adult heart are reactivated by myocyte hypertrophy. In the embryonic heart, growth factors provide the stimulus for normal cell division and heart growth. Withdrawal of growth factors inhibits the cell cycle and favors repair in the normal adult heart. The fetal gene repertoire responds to myocyte hypertrophy with induction of β myosin heavy chain (MHC), atrial natriuretic factor, and repression of α-MHC, among others. Loss of α-MHC content contributes directly to reduced contractility in heart failure. Excitation-contraction coupling is compromised by alterations in the phosphorylation status of troponin-I; and defects in calcium ATPase and calcium release channels impair contractility and promote β-adrenergic desensitization.

The environment of continuous growth signals promoted by the fetal gene profile produces cell dysfunction and eventually cell death, likely related to apoptotic mechanisms. Alterations in the extracellular matrix of the myocardium include replacement fibrosis.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Pathophysiology

Heart failure begins after an event produces an initial decline in pumping capacity of the heart. Once the injurious event is initiated, three major forces can contribute to chronic heart failure: intrinsic myocardial damage, abnormal load on one or both ventricles, and extrinsic forces.

The major causes of intrinsic myocardial damage include myocardial infarction secondary to ischemic heart disease, inherited conditions that affect the contractile apparatus, infiltrative myocardial diseases, autoimmune injury, infection, metabolic abnormalities (e.g., hyperthyroidism), and toxic agents (e.g., alcohol, certain chemotherapeutic agents). Abnormal loading conditions may result from chronic pressure overload (e.g., chronic hypertension, aortic stenosis) or volume overload (e.g., mitral regurgitation, aortic regurgitation, intracardiac shunts, extracardiac fistulae between arterial and venous circulations). Extrinsic forces include constrictive pericarditis, severe anemia, and substrate-inducing chronic tachycardia.

These conditions initially evoke a variety of compensatory mechanisms that, in the short term, restore cardiovascular function to a normal homeostatic range in which the patient is asymptomatic. Such compensation is termed adaptive. Over time, however, sustained activation of these compensatory systems becomes maladaptive and can lead to secondary damage of ventricular myocardium, worsening ventricular remodeling, and eventually cardiac decompensation and death. Changes in configuration of the ventricular chamber that are also detrimental to cardiac function include dilatation, change in shape (increased sphericity), thinning of the wall, and inflow valve regurgitation.

Cardiorenal-Hemodynamic Mechanisms

A common early manifestation of heart failure is excessive salt and water retention resulting from abnormalities of renal blood flow attendant reduction of cardiac output and vasoconstriction. Sympathetic nervous system up-regulation increases cardiac afterload and heart rate and decreases renal perfusion. Reduced renal perfusion alerts receptors in renal arterioles, activating the renin-angiotensin-aldosterone system. Renal and tissue renin stimulates production of angiotensin I. Angiotensin converting enzyme (ACE) catalyzes conversion of angiotensin I to angiotensin II. Angiotensin II and aldosterone blood levels are increased, causing vasoconstriction and retention of salt and water. Angiotensin II induces vasoconstriction of efferent arterioles, increasing glomerular filtration pressure despite reduced renal blood flow. This increase in sympathetic activity is initially compensatory for reduction in renal blood flow, but over time becomes maladaptive, accelerating cardiac remodeling.

Neurohormonal Mechanisms

As cardiac output and tissue perfusion are reduced, complex neurohormonal responses are evoked for maintaining arterial perfusion (Fig. 20-1). This compensatory (adaptive) mechanism is initially beneficial in maintaining tissue perfusion as cardiac output declines, but the process actually increases hemodynamic burden and oxygen requirements of the heart, eventually becoming detrimental (maladaptive). Circulating levels of norepinephrine may be markedly increased, and there is increased activity of adrenergic neurons that cause vasoconstriction and increase afterload of the failing ventricle. Over time, density of adrenergic receptors and concentration of norepinephrine in the myocardium are reduced. These changes are accompanied by reduced activity of adenylate cyclase, which lowers intracellular concentrations
Figure 20-1 The facets of heart failure; physiologic responses. Key: ACE, Angiotensin-converting enzyme; RAS, renin-angiotensin system; TNF, tumor necrosis factor.

Heart failure may progress as a result of overexpression of compensatory biologically active molecules that exert toxic effects on the myocardium. A variety of molecules have been implicated as sufficiently toxic to contribute to heart failure, including norepinephrine, angiotensin II, endothelin, aldosterone, and tumor necrosis factor. These molecules are of neuroendocrine origin, but may also be produced by a variety of cell types within the heart, including the myocyte itself.

Symptoms and Signs
Heart failure can be an acute decompensation or a chronic progressive disease. It is usually associated with decline in...
cardiac output. The consequence of elevated left ventricular (LV) preload and pulmonary capillary pressure is dyspnea. Cardiac remodeling is generally accepted as a determinant of the clinical course of heart failure. An approach to classification has been proposed that reflects the progressive nature of the clinical syndrome.

Evolution of the disease is identified by four stages of heart failure (Box 20-1). This classification complements the New York Heart Association (NYHA) functional classification, which gauges severity of symptoms primarily in stages B and C. The classification suggests that patients with heart failure are expected to advance from one stage to the next unless progression of the disease is slowed or stopped by treatment.

### NATURAL HISTORY

Heart failure is estimated to affect more than 5 million people in the United States alone and accounts for 1 to 3 million hospitalizations per year, or about 5% to 10% of all hospital admissions. The number of individuals with heart failure is increasing, with 400,000 to 700,000 new cases diagnosed each year, and the frequency is expected to increase two to three times during the next decade. About 3% of the adult population is treated for heart failure. Occurrence of heart failure increases with age; 6% to 10% of people older than age 65 are affected, and it is the most common cardiac diagnosis in this patient population.

Heart failure results in nearly 300,000 deaths per year in the United States, 60% sudden. Sudden death may be completely unexpected (one third of patients), a consequence of rapid deterioration (one third of patients), or a result of progression of chronic heart failure (one third of patients). About one third of patients die within 1 year of initial heart failure diagnosis, with nearly 80% dead within 6 years.

Cost of treating patients with heart failure is enormous, estimated at more than $40 billion per year, or more than 5% of the healthcare budget. Of that total, about $20 billion goes directly for medical costs, $500 million of which is spent on drugs for treating heart failure.

### TREATMENT OF HEART FAILURE

When a specific treatable medical disorder is responsible for heart failure, specific treatment of the underlying condition is a critical component of initial therapy (see Section VII).

#### Pharmacologic Therapy

Standard guidelines for evaluating and treating heart failure have been published. A fundamental goal is to slow or reverse ventricular remodeling. Intense medical therapy, which has evolved over the last 20 years, demonstrably improves survival. ACE inhibitors, new-generation β-blockers, and aldosterone improve survival, attributed in part to their reverse remodeling effects.

Current treatment of heart failure, based on various pathophysiological theories, recognizes that no single model explains all aspects of the heart failure syndrome and therefore attempts to use all clinical models to develop effective therapeutic strategies. Most patients with symptomatic LV dysfunction should be routinely managed with a combination of four categories of drugs: a diuretic, an ACE inhibitor, a β-adrenergic blocker, and digitalis. Diuretics and spironolactone are used to treat congestion and fluid retention related to cardiorenal mechanisms. Short-term intravenous inotropic support, intravenous vasodilators, or both, are used to treat cardiocirculatory mechanisms. Long-term inotropic support is achieved using digoxin. Intermediate and long-term strategies are directed at neurohormonal mechanisms using carvedilol, a β1-, β2-blocker with antioxidant properties, and ACE inhibitors. When ACE inhibitors are not tolerated, angiotensin receptor blockers may be effective.

#### Pacing Therapy for Conduction Abnormalities

Worsening of LV systolic function is frequently accompanied by impaired electromechanical coupling, which further diminishes systolic function. About 20% to 30% of patients with symptomatic heart failure have a prolonged P-R interval or an intraventricular conduction disorder characterized by wide QRS (left bundle branch block) and a discoordinate contraction pattern. Prolonged P-R interval may result in early contraction of the atria and mitral regurgitation during the diastolic phase, reducing ventricular filling. Proper timing of the P wave relative to mitral valve closure by cardiac pacing may provide more appropriate ventricular filling time.

Prolonged QRS and delay of conduction may result in contraction of the base of the heart well in advance of the LV lateral wall and apex. This may cause paradoxical septal motion and mitral valve regurgitation. Biventricular pacing (also termed cardiac resynchronization therapy) allows simultaneous electrical stimulation of the RV and LV using an implantable pacing system. A discoordinate contraction pattern of the ventricles may be resynchronized by pacing the lateral wall of the LV synchronous with pacing the apex of the RV. Optimal aortic pulse pressure occurs when the peak of left atrial pressure coincides with start of the LV contraction as a result of optimal preload mechanisms. In addition
to optimizing left atrial–to-LV mechanical timing, favorable response to both LV and biventricular stimulation may result from improved synchrony of RV and LV contraction.A10

**Implantable Cardioverter-Defibrillator Therapy**

In patients with advanced heart failure, the potential for fatal ventricular arrhythmias has prompted consideration of implantable cardioverter-defibrillator (ICD) therapy over chronic anti-arrhythmia drugs.

**RESULTS**

**Pharmacologic Therapy**

The effect of various therapeutic interventions has been evaluated in a number of clinical trials in patients with LV systolic dysfunction. Both ACE inhibitors and β-blockers, acting individually or synergistically, reduce morbidity and mortality in heart failure patients treated with diuretics and digoxin. Agents such as ACE inhibitors that inhibit neurohormonal activation relieve symptoms, reduce hospitalizations, and prolong survival.35 An increasing dose of ACE inhibitor or adding spironolactone to an ACE inhibitor may further improve prognosis. The optimal dose of β-blockers is unknown. Digoxin continues to be a mainstay of heart failure treatment and has been shown to decrease heart failure–related hospitalizations, but there is no evidence that it decreases mortality. It is not known whether digoxin is effective when added to a β-blocker.

**Pacing Therapy for Conduction Abnormalities**

Shortening of the P-R interval correlates with improved functional class and increased oxygen consumption.A3 Resynchronization therapy with biventricular pacing has been shown to improve symptoms in patients with moderate to advanced heart failure.1,3 Several randomized multicenter trials have examined its effects on functional status, quality of life, and hemodynamics in patients with dilated cardiomyopathy. These studies have demonstrated clinical improvement correlated with narrowing of the paced QRS complex, decrease in interventricular conduction delay, and a trend toward increase in duration of ventricular filling.6,8,2 Clinical benefits appear to be maintained over 12 months in patients with both sinus rhythm and atrial fibrillation.1,1,4 Biventricular pacing incorporating antitachycardia options or an ICD appear to be the future direction of pacing therapy.3,13

**Implantable Cardioverter-Defibrillator Therapy**

Large prospective, randomized multicenter trials have identified patient populations for whom ICD therapy provides survival benefit even in the absence of prior cardiac arrest or sustained ventricular tachycardia.82

**INDICATIONS**

**Pacing Therapy for Conduction Abnormalities**

The 2008 American College of Cardiology (ACC)/American Heart Association (AHA) Practice Guidelines recommend the following indications for cardiac resynchronization therapy (CRT) in patients with severe systolic heart failure.82

**Class I**

1. For patients who have LV ejection fraction (LVEF) of 35% or less, a QRS duration of 0.12 seconds or more, and sinus rhythm, CRT with or without an ICD is indicated for treatment of NYHA functional class III or ambulatory class IV heart failure symptoms with optimal recommended medical therapy. (Level of Evidence: A)

2. For patients who have LVEF of 35% or less, with NYHA functional class III or ambulatory class IV symptoms, who are receiving optimal recommended medical therapy and have frequent dependence on ventricular pacing, CRT is reasonable. (Level of Evidence: C)

3. For patients with LVEF of 35% or less, with NYHA functional class I or II symptoms, who are receiving optimal recommended medical therapy and are undergoing implantation of a permanent pacemaker or ICD with anticipated frequent ventricular pacing, CRT may be considered. (Level of Evidence: C)

4. CRT is not indicated for asymptomatic patients with reduced LVEF in the absence of other indications for pacing. (Level of Evidence: B)

**Class III**

1. CRT is not indicated for patients whose functional status and life expectancy are limited predominantly by chronic noncardiac conditions. (Level of Evidence: C)

**Implantable Cardioverter-Defibrillator Therapy**

The 2008 ACC/AHA Practice Guidelines indicate the following indications for ICD therapy in patients with severe systolic heart failure.82

**Class I**

1. LVEF less than 35% due to prior myocardial infarction (MI) who are at least 40 days post-MI and are in NYHA functional class II or III (Level of Evidence: A)

2. Nonischemic dilated cardiomyopathy who have an LVEF of 35% or less and are in NYHA functional class II or III (Level of Evidence: B)

3. LV dysfunction due to prior MI who are at least 40 days post-MI, have an LVEF less than 30%, and are in NYHA functional class I (Level of Evidence: A)

4. Nonsustained ventricular tachycardia (VT) due to prior MI, LVEF less than 40%, and inducible ventricular fibrillation (VF) or sustained VT at electrophysiological study (Level of Evidence: B)
**Class IIa**

ICD implantation is reasonable for patients:

1. With unexplained syncope, significant LV dysfunction, and nonischemic dilated cardiomyopathy (Level of Evidence: C)
2. Who are nonhospitalized and awaiting transplantation (Level of Evidence: C)
3. With cardiac sarcoidosis, giant cell myocarditis, or Chagas disease (Level of Evidence: C)

**Class IIb**

ICD therapy may be considered in patients with:

1. Nonischemic heart disease who have an LVEF of 35% or less and are in NYHA functional class I (Level of Evidence: C)
2. A familial cardiomyopathy associated with sudden death (Level of Evidence: C)
3. LV noncompaction (Level of Evidence: C)

**Class III**

ICD therapy is not indicated for patients:

1. Who do not have a reasonable expectation of survival with an acceptable functional status for at least 1 year, even if they meet ICD implantation criteria specified in the Class I, IIa, and IIb recommendations above (Level of Evidence: C)
2. With drug-refractory heart failure who are not candidates for cardiac transplantation or CRT (Level of Evidence: C)

---

**Mitral Valve Repair**

In an earlier era of cardiac surgery (1980s and early 1990s), mitral valve surgery was generally considered ill advised for patients with severe mitral regurgitation in the setting of markedly depressed LV function. It was hypothesized that the sudden increase in ventricular afterload by transforming a regurgitant mitral valve into a competent one would induce acute failure of an already dysfunctional LV. Over the last 15 years, results of mitral valve repair or replacement in this setting have progressively improved.

**Partial Left Ventriclectomy**

In 1996, Batista introduced the concept of surgically reversing the remodeling process in dilated cardiomyopathy with a procedure termed *partial left ventriculectomy.* The basis for the operation was the Laplace law, which relates wall tension to chamber radius. It was reasoned that reduction of LV size would improve cardiac function. Theoretically, reduction in LV volume reduces wall tension and improves contractility, with restoration of a more normal volume/mass relationship. Initially, only LV posterior wall was removed. Later, resection was sometimes extended to include the papillary muscles and mitral valve.

Although it is true that reducing chamber radius will reduce wall stress for a given pressure, it is not obvious from this explanation alone that volume reduction will increase the heart’s pumping capacity. The potential limitation of this procedure is that it removes functioning, though weakened, myocardium. Systolic wall stress is reduced, and LVEF may improve with reduction of ventricular chamber radius, but it may be associated with a deleterious effect on diastolic compliance that neutralizes any beneficial effect and may actually reduce net ventricular pumping capacity.

**Alternative Therapies**

**Dynamic Cardiomyoplasty**

Dynamic cardiomyoplasty is use of an electrically stimulated skeletal muscle that is wrapped around part of the heart to augment or restore contractility of the ventricles. It was introduced experimentally by Kantrowitz and McKinnon in 1959 and developed for use in humans by Carpenter and Chachques in 1958. Although it is true that reducing chamber radius will reduce wall stress for a given pressure, it is not obvious from this explanation alone that volume reduction will increase the heart’s pumping capacity. The potential limitation of this procedure is that it removes functioning, though weakened, myocardium. Systolic wall stress is reduced, and LVEF may improve with reduction of ventricular chamber radius, but it may be associated with a deleterious effect on diastolic compliance that neutralizes any beneficial effect and may actually reduce net ventricular pumping capacity.

**Ventricular Shape Change and Constraint Devices**

Chaudhry and colleagues used a prosthetic jacket of knitted polyester mesh to provide passive LV constraint in a canine heart-failure model produced by intracoronary microembolization. The prosthetic jacket prevented progressive LV remodeling and abolished functional mitral valve regurgitation. This led to the Acorn Cardiac Support Device (Fig. 20-2) for use in humans (Acorn Cardiovascular, St. Paul, Minn.).

**Direct Cardiac or Aortic Compression Devices**

Devices to assist the failing heart by direct compression of the heart (to shift end-systolic pressure–volume relationship) or aorta have been designed to avoid blood–foreign surface interaction of the assist device.
Less than 25% of patients have familial disease.\textsuperscript{M1} Several families have been described in which some members have dilated cardiomyopathy, and in some of these the inheritance is X-linked.\textsuperscript{B8} In these, onset seems to be early (second and third decades) in men and late (sixth decade) in women. Most asymptomatic relatives of patients with dilated cardiomyopathy and LV enlargement have histopathologic and immunopathologic findings similar to those of patients with established disease.\textsuperscript{M1,M6}

Dilated cardiomyopathy is characterized pathophysiologically by impaired ventricular systolic function.\textsuperscript{B14,B15,B16,G3} However, particularly late in the disease, decreased LV compliance may develop. Both end-diastolic and end-systolic ventricular volumes are increased.

All forms of cardiomyopathy may have a nonspecific prodromal phase lasting weeks or months that suggests an infectious process.\textsuperscript{K11} Then symptoms of left, right, or biventricular failure develop and progress to chronic heart failure.\textsuperscript{S6}

**Chest Radiography**

Chest radiography may be normal or show cardiomegaly, which can be extreme.

**Two-Dimensional Echocardiography**

Two-dimensional echocardiography has become standard for evaluating ventricular function.\textsuperscript{B6,J3,L3} It is excellent for diagnosing systolic dysfunction characterized by segmental or global reduction of systolic wall motion. As many as one third of patients with heart failure, however, have normal systolic function. This implicates diastolic dysfunction as a major pathophysiologic abnormality in these patients. Doppler color flow interrogation is a practical, noninvasive method for diagnosing and following patients with diastolic dysfunction.\textsuperscript{N2} Methods used to evaluate it are based on analysis and interpretation of flow velocity across the mitral valve.

**Cardiac Catheterization**

Cardiac catheterization usually reveals nonspecific findings. Right, left, or biventricular ejection fractions are reduced, and the diastolic pressure contour often has the square root sign characteristic of pericardial constriction. Endomyocardial biopsy may be useful in excluding other conditions in patients believed to have dilated cardiomyopathy. However, positive diagnosis of dilated cardiomyopathy from biopsy is rarely possible.\textsuperscript{O2}

**NATURAL HISTORY**

Approximately 5 to 8 of every 1,000,000 people are diagnosed with dilated cardiomyopathy each year. It can develop at any age but is more common among patients aged 20 to 60 years. Some 10% of patients are diagnosed after age 65. It occurs three times more frequently in males and blacks than in females and whites. About 80% of patients are dead within 10 years of onset.\textsuperscript{F11} Despite heterogeneity of its etiology, there is considerable correspondence among different estimates of survival with this condition.

The course is variable, with some patients dying within 1 to 2 years of the evident onset of disease; a few have an even
more fulminating course. Cardiac autoantibodies may play a functional role, and their removal may induce hemodynamic improvement. A few patients recover spontaneously, most commonly when cardiomyopathy is related to acute myocarditis. Spontaneous recovery is increasingly recognized following prolonged periods of support with LV assist devices (LVAD; see Chapter 22). Mode of death is usually chronic cardiac failure. Occasionally, death is due to intractable ventricular arrhythmias and sometimes is sudden (see Section I). Important risk factors for death include marked cardiomegaly, ventricular arrhythmias, pulmonary hypertension, and elevated right atrial pressure. Thromboembolism is particularly common when the LV is greatly dilated and in patients with atrial fibrillation.

TECHNIQUE OF OPERATION

Cardiac Transplantation

Cardiac transplantation is widely used as a treatment for end-stage dilated cardiomyopathy. Technique of operation is described in Chapter 21.

Mitral Valve Repair

Mitral regurgitation in cardiomyopathy has two major mechanistic components: anular dilatation as part of overall LV enlargement, and abnormal separation of the papillary muscles (Fig. 20-3). Details of mitral anuloplasty and management of the subvalvar apparatus are discussed in Chapters 10 and 11.

Partial Left Ventriculectomy

Partial left ventriculectomy consists of full-thickness LV free-wall resection between the papillary muscles, extending from the mitral anulus to LV apex. In the presence of mitral regurgitation, the mitral valve is repaired or replaced, usually through the ventriculectomy incision.

Alternative Therapies

Dynamic Cardiomyoplasty

The latissimus dorsi muscle is transferred as a muscle flap through a window in the chest wall made by partial removal of a rib. It is used as a wrap around the heart for reinforcement or as a substitute for a defect in the ventricular wall. Electrodes are implanted on the muscle flap and connected to an electrical stimulator, which paces contractions synchronously with myocardial contraction.

A variation of dynamic cardiomyoplasty is an auxiliary blood pump formed from a pedicled graft of latissimus dorsi muscle (skeletal muscle ventricle) connected to the circulation in a cardiac assist configuration. It has shown some promise in experimental heart failure. Adaptive conditioning by electrical stimulation enables the skeletal muscle to perform a portion of cardiac work without fatigue. Such skeletal muscle pumps have been able to maintain blood pressure greater than 80 mmHg for up to 4 years in dogs, without compromising viability of the working muscle. Although this work is experimental, clinical application for cardiac assist may eventually become feasible.

Ventricular Shape Change and Constraint Devices

The LV is a conical structure, whereas the RV is a crescent-shaped chamber wrapped to the right side of the LV. In the presence of systolic heart failure, progressive ventricular enlargement distorts the normal shape as well as the Frank-Starling pressure-volume relationship. The dilated ventricle also increases wall stress based on the Laplace law relating radius, pressure, and wall tension. All these pathologic phenomena could theoretically be abated by surgical techniques or devices that prevent further ventricular enlargement.

Animal studies showing that native pericardium provides constraint to deformation of the ventricles provided the physiologic concept behind cardiomyoplasty and passive ventricular constraint. Although dynamic cardiomyoplasty was originally touted as a procedure to augment systolic ventricular contraction, subsequent clinical studies demonstrated that the constraining effect of the muscle wrap was the primary
beneficial effect.\textsuperscript{K1} In the late 1990s, application of the cardiac constraining principle stimulated development of multiple devices designed to change LV shape or restrain ventricular dilatation in heart failure.

**Direct Cardiac or Aortic Compression Devices**

Direct cardiac or aortic compression devices have the advantages of simplicity of application during unstable circulatory conditions and ease of removal after recovery from heart failure or at transplantation. The CardioSupport system (Cardio Technologies Inc., Pine Brook, N.J.) is a cufflike structure that surrounds both ventricles from apex to atrioventricular groove. It is applied under negative pressure (−200 mmHg) to provide a vacuum seal. Compression bladders are inflated and deflated in synchrony with cardiac contraction, timed from epicardial electrocardiogram (ECG) electrodes.

The Heart Booster (Abiomed, Danvers, Mass.) is a cufflike device consisting of several parallel compression tubes covering both ventricles and held in place with surgical adhesive. A hydraulic drive system fills and empties the compression tubes. Both of these compression systems are in the development phase.

The Kantrowitz CardioVad (LVAD Technology Inc., Detroit, Mich.) is an experimental system operating on the principle of diastolic augmentation, like an intra-aortic balloon catheter and pump. The blood pump is an inflatable bladder sutured into the wall of the descending thoracic aorta via left thoracotomy, with the patient on cardiopulmonary bypass (CPB). There is direct blood contact with the textured surface of the inflatable bladder, which is expected to become covered with pseudointima. The pump is worn externally and provides a stroke volume of up to 60 mL via a transcutaneous tube.\textsuperscript{12}

The C-Pulse (Sunshine Heart Inc., Sydney, Australia) is a counterpulsation device that is wrapped externally around the ascending aorta, avoiding direct blood contact. The inflatable cuff and a sensing wire are attached to an external pneumatic driver that inflates and deflates the cuff in sequence with the ECG signal to provide timed counterpulsation. Implantation is performed via median sternotomy and does not require CPB. The system can be turned on and off by the patient as required. This device is intended for use in ambulatory patients with advanced NYHA class III or early class IV symptoms.

**RESULTS**

**Cardiac Transplantation**

Results of transplantation are detailed in Chapter 21.

**Mitral Valve Repair**

Bolling and colleagues reported a hospital mortality of less than 2% and 1-year survival of 82% following mitral valve anuloplasty using an undersized flexible ring in the presence of severe LV systolic dysfunction, with preoperative LVEF ranging from 8% to 25%.\textsuperscript{811} Patients experienced improved NYHA class, LVEF, and exercise oxygen consumption, and reduced end-systolic and end-diastolic volumes. Perhaps the most persuasive evidence supporting the safety of mitral valve repair or replacement in the setting of severely depressed LV function came as an offshoot of the multi-institutional ACORN trial for the Acorn cardiac constraining device.\textsuperscript{B5} One arm of the study included patients with poor ventricular function, dilated cardiomyopathy, and severe mitral regurgitation. Hospital mortality among patients undergoing mitral valve repair or replacement with or without a constraining device was 1.6%, and 12- and 24-month cumulative survival was 86% and 85%, respectively. Mitral valve surgery was associated with reduced LV end-diastolic and end-systolic volumes, decreased LV mass, increased LVEF, and decreased sphericity. Postoperative functional mitral regurgitation remained stable over midterm follow-up, with more than 80% of patients having 0 or 1+ mitral regurgitation at 6 to 18 months.

These and other reports indicate that in the present era, with optimal myocardial protection and appropriate preoperative management of heart failure, patients can undergo mitral valve repair in the presence of severe LV dysfunction (LVEFs as low as 10%) with low anticipated hospital mortality. Nevertheless, long-term benefit remains controversial. A retrospective analysis by Wu and colleagues failed to demonstrate a survival benefit conferred by mitral valve anuloplasty.\textsuperscript{S6}

**Partial Left Ventriculectomy**

Batista and colleagues reported clinical improvement following partial left ventriculectomy in patients with dilated cardiomyopathy and advanced heart failure.\textsuperscript{B6} Batista was joined by other colleagues to report a combined series of patients having partial left ventriculectomy to treat advanced heart failure.\textsuperscript{B5} Although the procedure initially generated considerable enthusiasm as an alternative to cardiac transplantation, surgical mortality was considerably higher than after transplantation, and subsequent composite freedom from death, need for ventricular assist support, and cardiac transplantation was low at 2 years.\textsuperscript{F7,S12,S14} Franco-Cereceda and colleagues at Cleveland Clinic noted that perioperative mortality was low (3.2%; CL 1.0%-7.5% of 62 patients), but a ventricular assist device was required in 18% (CL 13%-24%) of cases; survival at 3 years was 64%.\textsuperscript{F7} LVEF showed only small initial improvement that declined with time, and failure (relisting for transplant, NYHA class IV symptoms, or death) was common (74%) during the first 3 years after operation.\textsuperscript{F7,S8,S12} The challenge in part appeared to be patient selection.

Frazier and colleagues reported a combined institutional series of 42 patients with dilated cardiomyopathy treated by partial left ventriculectomy.\textsuperscript{F9} Cardiac output and LVEF improved minimally. Changes in myocyte hypertrophy and fibrosis were postulated to be related to clinical results. Lundehemer and colleagues\textsuperscript{L6} showed the healed scar was 4 cm wide and reached 2 to 12 mm beyond the surgical suture line. In addition, myocardial fibers were misaligned. Konertz and colleagues\textsuperscript{K1} reported 49 patients with 5 early deaths (10%: CL 6%-17%).\textsuperscript{K8} Functional improvement was better in patients with ischemic etiology (88% NYHA functional class I or II) than idiopathic dilated cardiomyopathy (56% NYHA class I or II). These authors proposed use of stress echocardiography to identify patients with segmental wall motion abnormalities who would be better treated by an infarct exclusion operation, reserving partial left ventriculectomy for patients with a global wall motion abnormality. They also proposed evaluating ventricular function in response to dobutamine infusion as a means of predicting improved function after partial ventriculectomy.
Thus, initial enthusiasm for partial left ventriculectomy was dampened by mixed results after operation, with a high prevalence of early failure. Despite the lack of current interest in this procedure, good functional results can be obtained in some patients.

**Alternative Therapies**

**Dynamic Cardiomyoplasty**

Long-term studies of patients having cardiomyoplasty have shown improvement in quality of life and functional class following dynamic cardiomyoplasty. However, clinical improvement has not correlated with changes in LVEF or cardiac output. Kass and colleagues suggested that benefits derived from cardiomyoplasty may be primarily due to passive constraint of the heart rather than to an active squeezing assist effect. There have been late deaths from ventricular arrhythmias, mainly ventricular fibrillation, so antiarrhythmic drugs or implantable cardioverter-defibrillators are needed. Consequently, dynamic cardiomyoplasty has not found a place in routine treatment of cardiac failure.

**Ventricular Shape Change and Constraint Devices**

In a multi-institutional randomized trial in the United States, the Acorn Cardiac Support Device implanted via median sternotomy was compared with continued optimal medical therapy for patients with dilated cardiomyopathy and NYHA class III heart failure. Compared with the medical group, the cardiac support device group had greater reduction in LV end-systolic and end-diastolic volumes and greater improvement in LV sphericity and quality-of-life measures. Nevertheless, both groups had similar LVEFs, occurrence of repeat hospitalizations, and mortality.

Other constraining devices that have entered clinical trials, but without current U.S. Food and Drug Administration (FDA) approval, include the Myosplint device (Myocor, Maple Grove, Minn.), which alters the LV short axis into two bilobed spheres, producing a reduction in wall stress; and the Paracor device, a nitinol mesh coated with polyurethane that is slipped over the heart via a small thoracotomy.

**Direct Cardiac or Aortic Compression Devices**

The CardioSupport system, which provides epicardial compression, has been used in experimental animals for up to 7 days without adverse events. Initial feasibility studies of the C-Pulse device in patients demonstrated predictable augmentation of coronary flow and reduction of LV afterload, decrease in heart failure symptoms, and improved cardiac performance. A multicenter trial to assess safety and performance is in progress.

**INDICATIONS FOR OPERATION**

**Cardiac Transplantation**

Indications for cardiac transplantation are presented in Chapter 21.

**Mitral Valve Repair**

Isolated mitral valve repair is not advisable in the setting of deteriorating cardiac performance requiring inotropic support or overt cardiogenic shock. A high operative mortality would be expected under these circumstances. These patients, if unresponsive to other measures, are better served by a strategy utilizing mechanical circulatory support (see Chapter 22) or cardiac transplantation (see Chapter 21).

In the absence of acute cardiac decompensation or chronic inotrope dependence, surgical mitral valve repair can be considered in patients who remain symptomatic despite optimal medical therapy when mitral regurgitation is severe. However, because long-term studies have not yet demonstrated a survival and functional benefit from mitral valve surgery in this setting, consensus has not been reached regarding specific patient subsets who should undergo mitral valve surgery. More routine application of mitral valve repair in dilated cardiomyopathy with severe mitral regurgitation will depend on demonstration of survival benefit, a more favorable functional outcome, evidence of sustained competence or near competence of the mitral valve, evidence of hemodynamic benefit, and reverse remodeling following repair.

**Partial Left Ventriculectomy**

As originally described, partial left ventriculectomy was indicated for patients in NYHA class IV heart failure from dilated cardiomyopathy. Currently, in countries where cardiac transplantation is available, this procedure has been largely abandoned. However, in countries or regions without access to these more complex and expensive therapies, this procedure may be advisable for patients with marked LV dilatation (end-diastolic dimension of 7 cm or more) and class IV heart failure despite optimal medical therapy.

**Alternative Therapies**

**Dynamic Cardiomyoplasty**

Dynamic cardiomyoplasty is not indicated for routine treatment of heart failure.

**Ventricular Shape Change and Constraint Devices**

To date, no ventricular constraining device has received FDA approval in the United States, and supplemental trials are in progress.

**Direct Cardiac or Aortic Compression Devices**

These devices are intended for short-term use (<7 days) for any cause of cardiogenic shock.
Section V  Restrictive Cardiomyopathy

DEFINITION

Restrictive cardiomyopathy is a cardiac muscle disease that results in impaired ventricular diastolic function with loss of compliance and is usually accompanied by diffuse ventricular hypertrophy. The most common example of restrictive cardiomyopathy is endomyocardial fibrosis (or obliterator cardiomyopathy), a form of restrictive cardiomyopathy in which the pathologic process—chronic inflammation—is restricted to the endocardium.

HISTORICAL NOTE

This condition has been known to exist for many years, but its in vivo differentiation from chronic constrictive pericarditis became possible only when modern cardiac diagnostic methods became available. Endomyocardial fibrosis began to receive serious study during the late 1940s. D’Arbela, Brockington, and Davies and their colleagues identified the similarity between the tropical zone form of the disease (Davies endocardial fibrosis) and that of the temperate zone (Löffler endocarditis) during the 1960s and 1970s. Metras and colleagues have first reported by Prigent and Dubost and their colleagues in 1973. D8,P8

MORPHOLOGY

The ventricular walls are excessively rigid, resulting in restrictive filling and reduced left, right, or biventricular diastolic volume with normal or near-normal systolic function. Microscopically, fibrosis and myocyte hypertrophy are usually present. Often there is no morphologic suggestion as to etiology. However, restrictive cardiomyopathy may be secondary to amyloid infiltration and other processes, with or without eosinophilia.

Endomyocardial fibroelastosis consists of fibrous endocardial lesions involving primarily the inflow portions of right and left ventricles, along with the posterior wall and apex. The atrioventricular valves are often involved and regurgitant. The outflow tract of the ventricle is usually spared. The heart may be more or less normal in size or somewhat enlarged, but massive cardiomegaly is rare, as is ventricular hypertrophy. Although both ventricles are commonly involved, 40% of patients have purely LV involvement, and 10% purely RV involvement. Metras and colleagues have described a more localized form of the disease that affects only the LV papillary muscles and presents as isolated mitral regurgitation.

Microscopically, a thick layer of hyalinized fibrous tissue is usually seen in the endocardium. Calcification may be present, and thrombi may cover the inner portion of the involved ventricle. The myocardium is minimally affected. These changes may be associated with eosinophilia (Löffler syndrome). In addition to evidence of chronic inflammation, an anomalous lymphatic pattern has been observed, connected to the distal coronary circulation.

Endomyocardial fibrosis is of unknown etiology. There has been speculation as to the possible role of a diet high in bananas, malnutrition, and immunologic responses from various infections. About 50% of patients undergoing resection reveal molecular evidence of a number of infective-agent genomes of unknown importance to pathogenesis. In a subset of patients, antimyosin antibodies against specific myocardial proteins have been identified, and immunosuppressive therapy in such patients has been suggested. These antibodies against C-terminal sequences may mediate the disease in a similar fashion as Chagas disease.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

The primary physiologic abnormality in restrictive cardiomyopathy is severe impairment of ventricular compliance. Generally, ventricular systolic function is unimpaired. Pathophysiologically, this condition simulates chronic constrictive pericarditis to such an extent that the two conditions are separated hemodynamically with great difficulty.

Endomyocardial fibrosis is pathophysiologically complex. Early in this process, there are only scattered areas of fibrosis, with little hemodynamic effect. As progressively increasing endomyocardial fibrosis develops, with consequent restriction of ventricular filling, ventricular end-diastolic pressures elevate, as do pulmonary or systemic venous pressures, depending on which ventricle is involved. Involvement of the atrioventricular valves then adds valvar regurgitation to the already impaired hemodynamic state.

When endomyocardial fibrosis involves both ventricles, RV failure usually dominates the clinical picture, with liver enlargement, ascites, and peripheral edema in association with tricuspid regurgitation. There are often pleural and pericardial effusions. RV endomyocardial fibrosis is characterized by distinctive findings of right atrial enlargement, as well as hepatomegaly, ascites, and peripheral edema. With isolated LV involvement, there are features of LV failure and often mitral regurgitation. There is usually a third heart sound.

Chest radiography shows cardiomegaly, usually attributable to right atrial enlargement and pericardial effusion. Calcification may be seen diffusely within the ventricles. Echocardiography reveals enlarged atria, ventricular cavity obliteration, and at times, mitral and tricuspid regurgitation. Mitral and tricuspid valve Doppler inflow velocities reveal a restrictive pattern with short deceleration time. Magnetic resonance imaging is particularly valuable in detecting delayed endocardial enhancement. Cardiac catheterization confirms the diagnosis, with physiologic findings of cardiac restriction (see Section I of Chapter 23) dominating the findings. Angiography often reveals obliteration of the apex of the involved ventricle, which in the RV may mimic Ebstein anomaly. The LV may show an apical diverticulum.

NATURAL HISTORY

Generally, symptoms are of long duration, with death delayed for 5 to 20 years after abnormalities of cardiac function become apparent. However, the natural history of patients with restrictive cardiomyopathy has not been well defined.
Endomyocardial fibrosis tends to affect children and young adults. It occurs primarily in Uganda, Nigeria, and India. However, cases have been sporadically reported in many countries, including the United States. The natural history of patients with this type of cardiomyopathy is generally unfavorable, characterized by a slowly deteriorating course and death within 5 to 10 years, often within 1 to 2 years.

**TECHNIQUE OF OPERATION**

Resection of endocardial fibrosis is performed using CPB and cold cardioplegic myocardial protection (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2 and “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). In left-sided disease, the mitral valve and interior of the LV are exposed through the usual incision for valve repair or replacement in the right side of the left atrium (see “Technique of Operation” in Section I of Chapter 11). When exposure is unsatisfactory, an approach through the right atrium and across the atrial septum is used; only if no other approach is possible is a left ventriculotomy used. The thickened and fibrotic endocardium in the inlet and apical portions of the LV are excised. Endocardectomy is as extensive as needed, but no attempt is made to remove the fibrotic plaque in one block. Localizing the pathology to the inlet and apical portions in the ventricles facilitates the surgical procedure. Often the tensor apparatus of the mitral valve must be sacrificed as part of the excision, and the valve is often regurgitant preoperatively. Therefore, in most patients, mitral valve replacement is part of the procedure (see “Mitral Valve Replacement” under Technique of Operation in Section I of Chapter 11).

Approach is through the right atrium in cases of isolated RV involvement. The procedure described is carried out, often associated with tricuspid valve replacement. However, whenever possible, a 5-mm strip of endocardium is left on the ventricular septum along the anulus of the tricuspid valve, particularly in the region of the anteroseptal commissure, to avoid damage to the bundle of His.

**RESULTS**

In general, risk of death after operation has been 10% to 20%, and greater in patients with biventricular disease. Metras and colleagues have reported 4 hospital deaths (20%; CL 10%-33%) among 20 patients operated on in Côte d’Ivoire (Ivory Coast).

Functional results of operation are good. In most patients, the hemodynamic state of the LV returns to normal after surgical treatment of the left-sided form of the disease. However, in RV endomyocardial fibrosis, despite clinical improvement, the hemodynamic status of the ventricle usually remains abnormal. RV endocardectomy may be complicated by complete heart block, but Metras and colleagues have avoided this in most cases by being conservative with the endocardial resection beneath the tricuspid valve.

**INDICATIONS FOR OPERATION**

Operation is indicated for patients whose disability has progressed to NYHA class III or IV.

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**Box 20-2 Cardiomyopathies Associated with Specific Cardiac or Systemic Disorders**

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<tr>
<th>Ischemic</th>
<th>Valvar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive</td>
<td>Inflammatory</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>Chagas disease</td>
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<td>Duchenne</td>
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<td>Friedreich ataxia</td>
<td>Sensitivity and toxic reactions</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Radiation</td>
</tr>
<tr>
<td>Anthracyclines</td>
<td>Peripartum (pregnancy)</td>
</tr>
</tbody>
</table>

**Section VI Arrhythmogenic Right Ventricular Dysplasia**

This condition is discussed in Section 6 of Chapter 16.
REFERENCES

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B

D
PART IV Other Cardiac Conditions


F


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T


U


V


W


Section I: Cardiac Transplantation in Adults without Congenital Heart Disease

Definition

Historical Note

Immunologic Basis of Heart Transplantation

DETECTION OF NONSELF SPECIFICITY OF ANTIGEN RECEPTORS MAJOR HISTOCOMPATIBILITY COMPLEX MOLECULES ANTIGEN PROCESSING T LYMPHOCYTES ANTIGEN-PRESENTING CELLS B LYMPHOCYTES NATURAL KILLER CELLS CYTOKINES ADHESION MOLECULES ACTIVATION OF IMMUNE SYSTEM FOLLOWING CARDIAC TRANSPLANTATION B-Cell Activation Cellular Rejection Humoral Rejection

Clinical Features

RECIPIENT EVALUATION AND SELECTION Evaluation of Comorbid Conditions Age Pulmonary Vascular Resistance Renal Dysfunction Infection Prior Malignancy DONOR EVALUATION AND SELECTION Effect of Brain Death on Myocardial Function

IMMUNOLOGIC ASPECTS OF TRANSPLANT TESTING ABO Compatibility Tissue Typing Panel Reactive Antibodies Crossmatching Virtual Crossmatch

Technique of Operation

DONOR HEART PROCUREMENT ORTHOTOPIC CARDIAC TRANSPLANTATION Bilateral Technique Bicaval Technique

GENERAL INTRAOPERATIVE CONSIDERATIONS

Special Features of Postoperative Care

IMMUNOSUPPRESSIVE MODALITIES Adrenocortical Steroids Cyclosporine Tacrolimus Azathioprine Mycophenolate Mofetil Cyclophosphamide Methotrexate Sirolimus Antithymocyte Globulin Monoclonal Antibodies OKT3 (Anti-CD3) Anti-CD25 (Basiliximab, Daclizumab) Plasmapheresis Immunoabsorption Photopheresis Total Lymphoid Irradiation Results

The method for blood vessel anastomoses, Carrel reported transplantation of kidneys into experimental animals. Little was done in the years after these reports, and the next work on the subject was in two reports from Dederer working in Mann’s laboratory at Mayo Clinic in 1918 and 1920. His experiments were not successful, but Williamson later commented that Dederer’s short-term success in two members of the same litter of puppies “seems very suggestive that there are biological phenomena which may be instrumental in the failures that have so frequently been attributed to mechanical difficulties.” In 1926, Williamson reported further studies on renal transplantation. He noted that autologous kidney transplants functioned satisfactorily for months, but that renal allografts functioned for only days. Although Williamson described the histologic condition of failed renal allografts as representing a form of glomerular nephritis, he also concluded that “the failure of homogeneous kidney transplants seems attributable to a biological incompatibility between the donor and recipient.” In 1926, Williamson reported further studies on renal transplantation. He noted that autologous kidney transplants functioned satisfactorily for months, but that renal allografts functioned for only days. Although Williamson described the histologic condition of failed renal allografts as representing a form of glomerular nephritis, he also concluded that “the failure of homogeneous kidney transplants seems attributable to a biological incompatibility between the donor and recipient.” Work continued in Mann’s laboratory, but even by 1934, Wu and
Mann had not increased the understanding of failure of the transplanted kidney.\textsuperscript{91b}

Twenty-two years then elapsed before report of successful transplantation of the human kidney between identical twins.\textsuperscript{107,110} In the interim, the work of Medawar during World War II revolutionized the understanding of transplantation. Although antigens and antibodies were to some extent understood, at least to the point that they were involved in various types of infectious disease, Medawar was the first to develop concepts of immunology applicable to transplantation. His work was a result of the British government’s research program early in World War II directed toward devising new methods of skin coverage for children extensively burned by the bombings of the Battle of Britain in 1939. His first paper in 1944 described his classic experiments with skin transplants in rabbits.\textsuperscript{112} He found that reaction of the rabbit to transplantation of skin from another rabbit was very different from the benign reaction to transplantation of its own skin from one site to another, just as Williamson and others had found in the case of the kidney. Medawar determined that the skin transplant from another rabbit developed a cellular infiltrate that destroyed the transplant in 7 to 10 days. Medawar termed this process rejection, and it is the analog of cellulary mediated acute rejection of cardiac transplantation as it occurs today. In the same paper, he also described second-set rejection, which occurred when later a second transplant of skin was made to the same rabbit from the same donor rabbit. This second skin graft was destroyed in 5 to 6 days, more rapidly than in first-set rejection. Medawar deduced that preformed antibodies were responsible for second-set rejection, which may be somewhat analogous to humorally mediated hyperacute rejection occurring rarely after cardiac transplantation.

In this and a second classic paper, Medawar developed a number of fundamental concepts.\textsuperscript{118} He confirmed his deduction that rejection under some circumstances was mediated by cells (lymphocytes) and in others by humoral antibodies. He recognized that the observed phenomena were the result of enormous genetic diversity among individuals. He hypothesized that second-set rejection implied immunologic recollection of past events. Methods for preventing rejection soon began to be discussed and studied, and Medawar suggested in the early 1950s that the recently discovered corticosteroids may help prevent rejection. However, techniques of immunosuppression developed slowly, and in the interim, at Peter Bent Brigham Hospital in Boston in 1955, Merrill and colleagues performed the first successful human kidney transplant. Based on immunologic concepts developed by Medawar, they chose identical twins for this procedure.\textsuperscript{107,110} This successful case had been preceded at Brigham Hospital by extensive investigations and some clinical renal transplantation between genetically diverse individuals, with poor success. This work was summarized by Hume and colleagues in 1955.\textsuperscript{118}

In 1960, Merrill and colleagues reported successful transplantation with mild immunosuppression between nonidentical twins.\textsuperscript{110} It was not until 1962 that Murray and colleagues were able to report successful “kidney transplantation in modified recipients,” and in this experience are reported the beginnings of modern immunosuppressive therapy.\textsuperscript{118,119} Caine and Murray showed experimentally in 1961 that azathioprine prolonged the survival of kidney transplant recipients.\textsuperscript{118,119}

Subsequently, intensive study has considerably improved immunosuppression techniques, including development of cyclosporine and other agents.

When Shumway completed his training during the late 1950s at the University of Minnesota in the early era of cardiac surgery, he went to Stanford University and began developing an experimental program in cardiac transplantation. Lower and Shumway first reported successful experimental orthotopic cardiac transplantation in 1960, just at the time when renal transplantation was becoming established.\textsuperscript{110} This work was confirmed by Kondo and colleagues, who also achieved prolonged survival.\textsuperscript{110}

In 1964, Hardy and colleagues performed the first heart transplant into a human, using a chimpanzee heart.\textsuperscript{113,115} Hardy’s team had pursued laboratory investigations in cardiac transplantation for the previous 8 years.\textsuperscript{114,116,118,119,127} They had planned to use a human donor, but the selected recipient (a 68-year-old man in shock from end-stage ischemic cardiomyopathy with respiratory failure, obtundation, and a freshly amputated gangrenous leg) was too close to death to await a donor. Thus, Hardy and his team elected to use a chimpanzee donor (as a xenotransplant, a graft from an individual of a different species than the recipient), based on studies of chimpanzee renal transplants in humans.\textsuperscript{115} The xenotransplanted heart contracted well on cardiopulmonary bypass (CPB), but was apparently too small to support the circulation unassisted. The patient died approximately 1.5 hours after discontinuation of CPB.

The first human-to-human heart transplant (allograft) was performed in Cape Town, South Africa, by Christiaan Barnard on December 3, 1967.\textsuperscript{114} The recipient was Louis Washkansky, a 53-year-old ex-boxer with end-stage ischemic cardiomyopathy. Three days after the Cape Town operation, Adrian Kantrowitz performed the second human heart transplant in Brooklyn.\textsuperscript{115} The recipient was an 18-day-old neonate with Ebstein anomaly, refractory heart failure, and previous aortopulmonary shunt for severe cyanosis. The patient received the heart of an anencephalic infant, but died 5 hours later of cardiac failure and refractory acidosis. On January 2, 1968, Barnard performed the third human heart transplant on Philip Blaiberg, a 46-year-old dental surgeon with refractory heart failure, severe coronary artery disease, and a large left ventricular aneurysm. He became the first long-term survivor, living for 18 months. Norman Shumway performed the fourth heart transplant 4 days later, and this patient died 2 weeks later. After this, other heart transplants followed rapidly in a number of institutions. By the end of 1968, cardiac transplantation had been performed in 102 patients in 50 different institutions in 17 countries. The results were generally poor, with 60% mortality by the eighth postoperative day and a mean survival of only 29 days.\textsuperscript{127}

Although cardiac transplantation was then started in yet more centers around the world, few patients were more than short-term survivors. This resulted in reduced clinical use, so by the early 1970s, cardiac transplantation had largely disappeared from clinical practice. An exception to this was the program at Stanford, where clinical and experimental transplantation continued at a steady pace and generated a continuous stream of new information. The report of Caves and colleagues describing a method of transvenous endomyocardial biopsy was an important clinical advance because it allowed monitoring cardiac allograft rejection on a serial basis.\textsuperscript{127} As a result, in about 1980, cardiac transplantation...
began to reappear as a viable therapeutic modality. Another major reason for its greater success was the knowledge of immunosuppression that came from research and from experience with renal transplantation.

Cyclosporine A, introduced for immunosuppression in 1981, accelerated the evolution of cardiac transplantation from the experimental phase to a clinically useful treatment modality for patients with advanced heart failure. Cyclosporine is a fungal metabolite first isolated from Tolypocladium inflatum Gams in 1972. Its marked immunosuppressive properties were discovered by Borel in 1972. 

Distant heart procurement programs also increased activity and improved success in cardiac transplantation. Watson and colleagues in 1977 showed the feasibility of such programs, and he and Thomas reported good clinical results using distant donors.

Since 1980, published data on more than 80,000 cardiac transplantations from over 300 cardiac transplant programs have been reported in the voluntary registry of the International Society for Heart and Lung Transplantation (ISHLT). A declining number of cardiac transplantations have been reported internationally, from a high of nearly 5000 in 1995 to less than 4000 by 2006. Cardiac transplantation in the United States has remained stable at about 2200 per year. At the same time, the number of patients on waiting lists has grown to more than 4100.

**IMMUNOLOGIC BASIS OF HEART TRANSPLANTATION**

Detection of Nonself

Biological variation between individuals occurs at the macro level, cellular level, and molecular level. Analysis of the structure of proteins and the genes that code for them indicates that some molecules can be unique to each individual. Genetically determined differences in the amino acid sequence of proteins result in alteration of their three-dimensional structure and charge; it is variation in the protein peptide components that allows the immune system to distinguish cells originating from nonself. Although individual variability may not alter a protein’s function, molecules that vary in this fashion from one individual to another are said to be polymorphic. Protein polymorphism is not the only manner by which self can be distinguished from nonself, but it is the predominant feature that drives rejection in clinical cardiac transplantation.

The effector mechanisms by which cells of the immune system eliminate nonself are operative during allograft rejection and are part of the immune response that defends humans from invasion by infectious agents or toxins. Two components of the immune system, the innate immune system and the adaptive immune system, participate in responding to nonself molecules themselves.

**Specificity of Antigen Receptors**

A unique feature of the immune system is that each T lymphocyte carries only one type of antigen receptor on its surface, and each antigen receptor is specific for a single antigen (peptide). A lymphocyte contains an average of about 200,000 antigen receptors on its surface, all identical and specific for a single antigen. Given the huge number of foreign antigens an individual may encounter, survival depends on an adequate variety (repertoire) of lymphocyte antigen receptors to combat invasion by foreign (nonself) peptides.

The actual process by which an antigen receptor identifies a bound peptide as “nonself” is mysterious. Specific receptors apparently do not discriminate between self and nonself in terms of antigen recognition, but rather, self/nonself discrimination is a function of lymphocyte populations that contain a large number of antigen receptors. During the period of immunologic development, the process of selection takes place among T cells while they develop in the thymus, in which potential harmful lymphocytes that could react with self-antigen are usually eliminated. Certain disease states develop when this process is incomplete. A small population of lymphocytes are cross-reactive, their antigen receptors binding to more than one antigen.

**Major Histocompatibility Complex Molecules**

The proteins primarily involved in the immune response to organ transplantation are called major histocompatibility complex (MHC) antigens. T lymphocytes recognize only antigenic peptides contained within the MHC-binding groove on the surfaces of antigen-presenting cells. In each species, MHC antigens have unique names. Human MHC antigens are termed human leukocyte antigens (HLA). The MHC
consists of a group of genes on the short arm of chromosome 6 that code for a number of proteins expressed on the cell surface (Fig. 21-1). These genes are polymorphic in that individuals vary in the exact nucleotide sequence of the genes and therefore the specific amino acid sequence of the protein products. Therefore, for any individual MHC gene, there are likely to be multiple variations (also called alleles) of that gene distributed within a population of individuals.

In the context of transplantation, it is important to differentiate between donor and recipient MHC molecules. Donor MHC molecules are a source of antigen in that they are ingested by the recipient antigen-presenting cells and processed into peptides that are subsequently loaded into recipient MHC molecules for presentation to recipient T cells. The more extensive the difference in amino acid sequence between donor and recipient MHC molecules, the more likely it is that the donor MHC molecule will be broken into peptides that are recognized as nonself. In the special case of direct antigen presentation (see “T Lymphocytes” in later text), intact donor class II MHC molecules on donor antigen-presenting cells or donor endothelial cells within the transplanted heart may play an important role in T-cell activation.

The functions of MHC molecules are closely related to their three-dimensional structure and high degree of polymorphism. Within their three-dimensional structure, there is a distinct groove formed by two α helices that lie on top of a β-pleated sheet. This groove represents the domain in which peptides are processed when they are presented to a T cell. A T cell will respond only to an antigenic peptide contained in the MHC peptide-binding groove of an antigen-presenting cell. The polymorphism of the MHC molecule lies in and around the protein-binding groove, creating differences among individuals by different side grooves that may project into and out of the MHC groove for processed peptides.

The MHC complex proteins are broadly subdivided into groups called class I, class II, and class III. Class I and class II proteins are most commonly considered in the context of transplantation and have similar overall three-dimensional shapes.

The human MHC class I molecules routinely typed for solid organ transplantation are called A, B, and C. Class I molecules are expressed on the surface of virtually all nucleated cells, although with varying levels of expression. The highest surface density is found on lymphocytes, with lower expression on fibroblasts, muscle cells, and endothelial cells. However, certain cytokines such as interferon (IFN)-γ can increase the level of MHC expression on these other cells. This inducibility of MHC molecules likely plays an important role in initiating and perpetuating a rejection episode. As inflammatory mediators are released during a rejection episode, it is likely the level of MHC expression on donor vascular endothelial cells and muscle cells increases further, augmenting the antigenic stimulation.

MHC class I molecules consist of two polypeptide chains: a larger highly polymorphic α chain coded by a gene in the MHC complex on chromosome 6, and a smaller nonpolymorphic β chain called β2-microglobulin that is coded by a gene on chromosome 15 (Fig. 21-2). The α1 and α2 domains form a peptide-binding region in which they interact three dimensionally to form a platform of eight strands forming a β-pleated sheet flanked by two long α-helical regions forming the floor and walls of the peptide-binding groove. Within this region, peptide fragments of eight or nine amino acids present in the peptide-binding groove. The α3 domain is highly constant among class I MHC molecules, and the interaction between the α3 domain and that of β2-microglobulin helps maintain the correct confirmation of the MHC molecule for cell-surface stability. The α3 domain interacts with the CD8 molecule on the surface of T cells, which generally restricts the recognition of antigens displayed in the groove of class I HLA molecules to CD8+ T cells.

The primary class II molecules related to solid organ transplantation are called HLA-DR, HLA-DP, and HLA-DQ. These molecules are composed of an α chain and a β chain, each of which contains two domains designated α1 and α2 and β1 and β2, expressed as transmembrane proteins (Fig. 21-3). The α1 and α2 domains form the structure of the
antigenic peptide-binding groove. The $\beta_2$ domain interacts with CD4 molecules, which generally restricts the presentation of antigen in the groove of class II MHC molecules to CD4$^+$ T cells.

**Antigen Processing**

Two basic pathways exist for the processing of antigen that subsequently is displayed on the cell surface in the peptide-binding groove of a MHC molecule. The exogenous pathway involves proteins originating from outside the cell that present with MHC class II molecules (Fig. 21-4). This pathway is the principal vehicle for processing and presenting alloantigens following organ transplantation. It is initiated when the antigen binds to the surface of the antigen-presenting cell, which then internalizes the protein via receptor-mediated endocytosis or phagocytosis. Once the peptide (which may be either MHC class I or II) is loaded into the binding groove of the class II molecule, it is transported to the cell surface for presentation to T cells. Any protein from the donor organ can serve as an antigen.

The *endogenous pathway* involves proteins that originate inside the cell, in which proteins complex with MHC class I molecules and are presented to T cells (Fig. 21-5). This pathway appears to have a minor role in transplant rejection, and theoretically any cell (not just antigen-presenting cells) can use it in the presentation of internal peptides on MHC class I molecules. This pathway is typically used in the body’s defense against intracellular pathogens, such as viruses whose proteins can be degraded and presented on the cell surface, resulting in the cell’s destruction by cytotoxic CD8$^+$ T cells.

**T Lymphocytes**

T lymphocytes represent the most important component of the immune response to transplanted organs (Box 21-1). They are defined by presence of a CD3 molecule (part of the T-cell antigen receptor) on their surface and generally...
with either CD4 or CD8 surface molecules. The two basic subtypes of T lymphocytes are T helper (T\textsubscript{H}) cells and cytotoxic T cells. The T\textsubscript{H} lymphocyte expresses CD4 molecules on its surface and functions primarily to detect nonself antigens by means of its T-cell receptors. When activated, it can also recruit other cells (CD8\textsuperscript{+} T cells, other CD4\textsuperscript{+} T cells, B cells, phagocytes, neutrophils, and other inflammatory cells) into the immune response (Table 21-1).

Cytotoxic T lymphocytes differ from T\textsubscript{H} cells in that they express CD8 molecules on their surface. The cytotoxic T lymphocyte functions primarily as an effector cell that kills target cells (cells that express nonself antigens in the groove of a class I MHC molecule), and under special circumstances may suppress other cells (prevent their activation). The T-cell receptor allows the T lymphocyte to detect the presence of a nonself antigen by providing the capability of binding to antigen and MHC molecules in a specific manner. This receptor allows detection of nonself MHC antigens in the transplanted heart. Each T-lymphocyte clone has a T-cell receptor that is unique with respect to the receptors of other T-cell clones and has a unique T-cell genetic sequence. The pool of unique T cells constitutes the T-cell repertoire, which includes more than $10^{12}$ unique T-cell receptors in a given individual.

The portion of the T-cell receptor that interacts with the antigenic peptide–MHC complex is a heterodimer of two covalently linked polypeptide chains designated \( \alpha \) and \( \beta \) (Fig. 21-6). The \( \alpha \) and \( \beta \) chains each have a variable region (V-region) that contains a highly variable amino acid sequence.

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**Box 21-1 T-Cell Facts**

- The thymus is required for T-cell development.
- When mature, all T cells express CD3 surface molecules.
- Peripheral T cells express CD4 or CD8 molecules, but not both.
- CD4 and CD8 surface markers identify T-cell populations with different immunologic capabilities.
- T cells regulate antiviral and antifungal cellular immune responses.
- T cells regulate activation and differentiation of B cells and switching of antibody secretion from IgM to other classes.

*From Kirklin and colleagues.*

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**Table 21-1 T-Cell Types and Properties**

<table>
<thead>
<tr>
<th>Property</th>
<th>CD4\textsuperscript{+} (Helper)</th>
<th>CD8\textsuperscript{+} (Cytotoxic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specificity</td>
<td>Recognize antigen in association with class II MHC molecules expressed on antigen-presenting cells</td>
<td>Recognize antigen in association with class I MHC molecules</td>
</tr>
<tr>
<td>Function</td>
<td>Undergo activation by antigen-presenting cells and proliferate</td>
<td>Can kill virus-infected cells and cells expressing nonself antigens</td>
</tr>
<tr>
<td></td>
<td>Facilitate activation, proliferation, and differentiation of cytotoxic T cells</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Provide “help” for activating and differentiating B cells, and regulate antibody class switching</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Regulate inflammation by secretion of cytokines</td>
<td></td>
</tr>
<tr>
<td>Proportion of peripheral T-cell population</td>
<td>Two thirds</td>
<td>One third</td>
</tr>
<tr>
<td>Subtypes</td>
<td>T\textsubscript{H}1 and T\textsubscript{H}2, possibly others</td>
<td>Types 1 and 2</td>
</tr>
</tbody>
</table>

*From Kirklin and colleagues.*

Key: MHC, Major histocompatibility complex.
The α and β chains are associated with membrane-bound proteins called the CD3 complex. It is required for expression of T-cell receptor on the cell surface and is responsible for transduction of a membrane signal when the T-cell receptor complex interacts with antigen. Ability of a lymphocyte to respond to the presence of a specific antigen is termed recognition.

T cells recognize antigen only in the presence of self-MHC. T\(_{\text{H}}\) cells, which initiate the cellular response to transplant antigens, respond to antigen that is associated with an MHC complex on the cell surface through a process called antigen presentation. This process is limited to certain cell types called antigen-presenting cells. A presenting antigen must first be internalized within the antigen-presenting cell, broken down into 7 to 13 amino acid polypeptides, which are physically associated with MHC molecules, and exported to the cell surface as a complex. T\(_{\text{H}}\) cells respond only to those cells that express class II molecules on their surface. Cytotoxic T cells (CD8\(^{+}\)) respond to cells that have class I MHC molecules on their surface.

**Antigen-Presenting Cells**

Because cytotoxic T cells recognize antigens only on the surface of other cells that have class I MHC surface molecules, a functionally distinct class of cells has been identified that presents antigen to T lymphocytes. These antigen-presenting cells process antigens by breaking them down into individual peptides, inserting the peptides into the MHC molecule, and transporting them to the cell surface (Box 21-2). Cells that function as antigen-presenting cells are dendritic cells, macrophages, and B cells. Dendritic cells are the most efficient antigen-presenting cells because they have a large surface area, increasing the probability of contact with T lymphocytes. Dendritic cells are present throughout most lymphoid and nonlymphoid tissues and possess a high density of surface MHC class II molecules. Antigen-presenting cells also provide a second signal that is necessary for T-cell activation, which is the binding of another molecule on the surface of the T cell in addition to the binding of the T-cell receptor by an antigen-MHC complex.

**Box 21-2 Antigen-Presenting Cells**

- Derived from bone marrow
- Process peptides and present antigen to T cells
- Transport foreign antigens to lymph nodes for interaction with T cells
- Express adhesion molecules that facilitate T-cell receptor binding to the peptide/major histocompatibility complex
- Provide co-stimulatory “second signals” to activate the T cell

From Kirklin and colleagues.

**B Lymphocytes**

B lymphocytes arise from bone marrow and do not express CD4 or CD8 molecules on their surface. They use surface immunoglobulins rather than T-cell receptors for detecting antigen, and the end product of B-cell activation is differentiation into antibody-secreting plasma cells and memory B cells (B cells capable of generating an immune response when there is subsequent exposure to the same antigen). Immunoglobulins (antibodies) are produced by B cells that have differentiated into plasma cells. They consist of four polypeptide chains in two pairs, each consisting of a heavy chain and a shorter light chain (Fig. 21-7). The end of the molecule is called a variable region because the genes that code for the heavy and light chains are composed of segments that join together imprecisely. The other end of the heavy chain, called the constant region, contains sites for biologically important activity such as complement activation. The heavy chain constant regions form the basis for classifying immunoglobulins into isotypes IgG, IgA, IgM, IgD, and IgE.

**Natural Killer Cells**

Natural killer (NK) cells are structurally similar to T and B lymphocytes, but are not antigen specific and do not express either a T-cell receptor or immunoglobulin. These cells are called natural killer cells based on their ability to spontaneously lyse tumor cells in vitro. In vivo, they can lyse target...
cells without the requirement for prior immunization. They can lyse cell targets that lack surface expression of MHC molecules. NK cells represent about 15% of peripheral lymphoid cells.

Cytokines

Soluble molecules called cytokines play an important role in the immune response by stimulating secretion of proteins that alter the behavior or property of cells and facilitate recruitment of immunologic cells from distant locations. Unlike hormones, cytokines generally act locally and are not usually found in circulation in large quantities because of their short half-life. Although numerous cytokines have been identified that have diverse biological actions (Table 21-2), cytokines in transplantation are particularly important in mediating inflammatory processes and regulating T-cell responses. Cytokine production is one of the hallmarks of T-cell activation. Prominent cytokines in the immunologic response to transplantation include interleukin (IL)-2, IL-6, tumor necrosis factor (TNF), and IFN-γ.

Adhesion Molecules

Adhesion molecules are proteins formed within cells and secreted into the environment of these cells. They function to maintain structural integrity and position of body cells and promote adhesion of leukocytes to surrounding structures. Adhesion molecules include integrins (adhesion molecules that maintain cells in position by attaching one end of the integrin to the cytoskeleton of the cell and the other end to molecules of the extracellular matrix), selectins (adhesion molecules that mediate rolling of leukocytes along the vascular endothelium), and Ig superfamily adhesion molecules. Adhesion molecules mediate the initial interaction of T cells with antigens, their migration, and their retention within a transplanted organ.

Activation of Immune System Following Cardiac Transplantation

The inciting event is placing the donor heart into the recipient and perfusing it with native blood elements following aortic clamp removal. Within minutes, large quantities of donor cells, protein (some of which is soluble MHC molecules), and cellular fragments are carried to the spleen and lymph nodes, which are highly efficient in filtering antigen and trapping antigen within resident antigen-presenting cells. These cells enter the paracortex of the lymph node, which is populated by T cells, macrophages, and dendritic cells. If the T cells have a receptor capable of binding to MHC molecules containing a particular peptide, they will be activated, after which they interact with B cells, inducing the initial stages of B-cell activation. In addition, donor antigen-presenting cells migrate from the heart and encounter T cells as they circulate through the lymphoid tissues. Donor antigen-presenting cells also line the endothelial surfaces of the donor heart vasculature. Donor alloantigens containing foreign MHC complex molecules can be presented to the recipient T cells in two ways: directly and indirectly (Table 21-3). Direct recognition of donor antigens by T lymphocytes involves direct engagement between the recipient T-cell receptor and the donor antigen-presenting cell (also called passenger lymphocytes). Even though these antigen-presenting cells are nonspecific, the structural similarities are sufficient to allow binding with either helper or cytotoxic T lymphocytes, because both MHC class I and II molecules will be expressed. In this method of donor antigen presentation, the specific antigen presented in the groove of the complex is often unimportant because the donor antigen-presenting cell will be identified as nonspecific.

When shed MHC molecules from the donor organ are processed and presented by recipient antigen-presenting cells to recipient T cells, the process is termed indirect allorecognition. The exogenous pathway of processing and presenting alloantigens is generally operative in the indirect allorecognition process.

The presentation of donor antigen to T lymphocytes results in T-cell activation. T-cell activation occurs in concert with changes in the expression of various cell surface molecules, secretion of soluble factors, and a change in cell morphology. Once activated, the T* cell clone proliferates and releases cytokines that expand the immune response.

B-Cell Activation

B-cell activation begins with capture of antigen by immunoglobulin molecules on the B-cell surface. The antigen is then internalized, degraded, processed into peptides, and loaded into the groove of MHC class II molecules delivered to the cell surface.

When the B-cell encounters a CD4+ T cell that has the appropriate T-cell antigen receptor for binding to the antigen-MHC complex on the B-cell surface, the T cells engage in a process termed mutual activation. B-cell differentiation into immunoglobulin-producing plasma cells
requires antigen-specific signals through B-cell receptors
(immunoglobulin) expressed on the cell surface and antigen-
specific T-cell help in forming a co-stimulator signal and
cytokine stimulation.

**Cellular Rejection**

Cytotoxic T lymphocytes (CD8+) that are specific for graft antigens play an important role in the effector phase leading to acute rejection. Like T_{H1} cells, cytotoxic T cells are not activated with a single signal, but rather require the binding of multiple surface molecules that transmit additional signals through the cell membrane. This process requires engagement by allogenic histocompatibility molecules or by an antigenic peptide MHC complex, with an additional signal via a co-stimulator molecule such as CD28. This series of signals serves to activate cytotoxic T-lymphocyte precursors that then proliferate and differentiate into cytotoxic T

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**Table 21-2 Important Cytokines in Transplant Immunology**

<table>
<thead>
<tr>
<th>Source</th>
<th>Relevant Functional Activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-1</td>
<td>Monocytes, macrophages, endothelium, mesangial cells, fibroblasts, keratinocytes, most nucleated cells in response to injury</td>
</tr>
<tr>
<td>IL-2</td>
<td>Activated T cells, NK cells</td>
</tr>
<tr>
<td>IL-4</td>
<td>Activated T cells, mast cells</td>
</tr>
<tr>
<td>IL-5</td>
<td>Activated T cells, mast cells, eosinophils</td>
</tr>
<tr>
<td>IL-6</td>
<td>Probably most nucleated cells</td>
</tr>
<tr>
<td>IL-7</td>
<td>Bone marrow stromal cells, thymus</td>
</tr>
<tr>
<td>IL-8 and other chemokines</td>
<td>Activated T cells, monocytes, endothelial cells, hepatocytes, fibroblasts, epithelial cells, chondrocytes, keratinocytes, neutrophils</td>
</tr>
<tr>
<td>IL-10</td>
<td>Activated T cells, B cells, monocytes, macrophages, mast cell lines, keratinocytes</td>
</tr>
<tr>
<td>IL-12</td>
<td>Activated macrophages, activated B cells, dendritic cells, keratinocytes</td>
</tr>
<tr>
<td>IL-13</td>
<td>Activated T cells</td>
</tr>
<tr>
<td>IL-17</td>
<td>Activated T cells, mast cells</td>
</tr>
<tr>
<td>IL-23</td>
<td>Antigen-presenting cells</td>
</tr>
<tr>
<td>IFN-γ</td>
<td>Activated T cells, NK cells</td>
</tr>
<tr>
<td>TNF-α</td>
<td>Monocytes, macrophages, T cells, NK cells, Kupffer cells, microglia, B cells</td>
</tr>
<tr>
<td>TNF-β</td>
<td>Activated T cells and B cells</td>
</tr>
<tr>
<td>TGF-β</td>
<td>Platelets, activated macrophages, bone</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues. K14

Key: IFN, Interferon; IL, interleukin; MHC, Major histocompatibility complex; NK, natural killer; TGF, transforming growth factor; T_{H}, T helper; TNF, tumor necrosis factor.

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**Table 21-3 Characteristics of Responses to Alloantigens Presented via Direct and Indirect Pathways**

<table>
<thead>
<tr>
<th>Source</th>
<th>Direct</th>
<th>Indirect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen processing required</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Proportion of primary T-cell responders</td>
<td>1%-5%</td>
<td>1/10,000</td>
</tr>
<tr>
<td>Source of antigen-presenting cells</td>
<td>Donor</td>
<td>Recipient only unless there is a class II match between donor and recipient</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues. K14

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requires antigen-specific signals through B-cell receptors (immunoglobulin) expressed on the cell surface and antigen-specific T-cell help in forming a co-stimulator signal and cytokine stimulation.
lymphocytes in response to IL-2. Once a cytotoxic T lymphocyte receives the appropriate signals, it can administer a lethal hit to a target cell that results in cell death either through exocytosis (release of destructive granules into the target cell) or induction of apoptosis.

**Humoral Rejection**

*Humoral rejection* refers to production of antibodies or activation of complement in response to exposure to an alloantigen. B lymphocytes mediate the response, and antibodies can react with antigens in solution or on the cell surface. Antibodies associated with humoral rejection are generally IgM and IgG. Effector mechanisms associated with humoral responses include neutralization (blocking of relative sites or binding of receptors on a target cell), opsonization (antibodies acting as a “tag” that can be recognized by phagocytic cells), and complement activation. The most extreme form of humoral rejection is *hyperacute rejection*, mediated by preexisting antibodies that, upon entry into the donor heart vasculature following aortic clamp removal, rapidly bind to the vascular endothelium. These antibodies fix complement, which causes direct lyses of endothelial cells, and elaboration of complement components induces a massive infiltration of granulocytes. The subsequent massive cell necrosis and tissue swelling can lead to organ destruction within minutes.

### CLINICAL FEATURES

**Recipient Evaluation and Selection**

The general approach to patients referred for possible cardiac transplantation is listed in Box 21-3. If patients were selected primarily on the basis of highest expected posttransplant survival and quality of life at 1, 5, and 10 years, transplantation would be recommended for less ill patients whose survival is acceptable with medical or nontransplant surgical therapy. Alternatively, if transplantation were reserved only for patients closest to death from end-stage heart disease, the associated noncardiac organ dysfunction would drastically reduce patient and graft survival, compromising effective use of organs. Thus, some balance must be achieved between survival benefit to the recipient and maximal use of donor organs (in terms of organ survival).

Because of ongoing controversies, experts in the field have periodically convened to promote standardization of selection criteria. There is general consensus that the prognosis for survival and quality of life of patients with New York Heart Association (NYHA) class IV heart failure symptoms who do not improve with medical or surgical therapy are sufficiently poor that transplant should be considered. The major dilemma in decision making involves patients who are converted from class IV to class III/II by appropriate medical therapy. The decision-making process for this large group of patients is critically important because (1) the available supply of organs is inadequate to provide even a small fraction with transplantation, (2) allocation of a donor heart to a patient with a relatively better prognosis would deprive a more seriously ill patient with a short life expectancy (but preserved noncardiac organ function) the opportunity for transplantation at a time when his or her benefit would still be maximal, and (3) cardiac transplantation is not curative, is associated with its own chronic morbidity and survival limitation, and should therefore not be offered to patients with intermediate- or long-term survival approaching that of transplantation.

Identifying factors that predict mortality in ambulatory patients with advanced heart failure has been hampered by the complexity and variability of the heart failure syndrome, evolving nature of medical treatment for heart failure, retrospective nature of most studies, infrequent application of appropriate multivariable analysis, and almost uniform lack of patient-specific predictive models. Nevertheless, numerous risk factors have been identified (but poorly quantified) that are associated with adverse outcome in ambulatory patients with advanced heart failure (Box 21-4). Despite many clinical studies of heart failure, few variables consistently predict duration of survival (or freedom from rapid deterioration) in advanced heart failure patients undergoing transplant.

### Box 21-3  Approach to Potential Candidate for Heart Transplantation

- Address potentially reversible causes and components of heart failure
- Evaluate severity of heart failure and functional capacity
- Tailor medical therapy to improve symptoms and reduce mortality
- Assess risks of deterioration or sudden death
- Identify indications for transplantation
- Exclude contraindications to transplantation
- If heart transplantation is recommended, continue heart failure management with periodic reevaluation

Modified from Kirklin and colleagues.

### Box 21-4  Factors Associated with Increased Mortality in Heart Failure Patients

**Clinical**

- Heart disease etiology
- Heart disease duration
- History of syncope

**Hemodynamic**

- Lower left ventricular ejection fraction
- Lower right ventricular ejection fraction
- Higher pulmonary capillary wedge pressure
- Higher right atrial pressure
- Lower cardiac index
- Inotropic support required

**Functional Capacity**

- Higher New York Heart Association functional class
- Lower oxygen consumption at peak exercise \( V_{\text{O}_2 \text{ max}} \)
- Shorter distance covered during 6-minute walk

**Neurohumoral/Metabolic**

- Elevated plasma norepinephrine
- Elevated plasma renin activity
- Elevated atrial natriuretic peptide
- Leukocytosis
- Lower serum sodium

**Ventricular Arrhythmias**

- Noncardiac organ system function
- Renal dysfunction
- Elevated hepatic enzymes

Modified from Kirklin and colleagues.
Normal cardiac function is restored. A few programs have operated, and they have the potential for good quality of life if patients may be selected if their noncardiac organ systems are transplantable to patients younger than age 65. Older patients. Recipients older than age 60 years have a survival similar to younger patients.

In properly selected patients, heart transplantation are listed in part of their disease complex. The general contraindications to transplantation are listed in Box 21-6.

Evaluation of Comorbid Conditions

Noncardiac comorbidity may adversely affect longevity or quality of life after transplantation, independent of, or as a complex interaction with, graft function (Box 21-5). Of particular interest is the effect of chronic immunosuppression on natural history of these comorbid conditions. For many such conditions, there is a paucity of secure information upon which to base rational decisions about so-called relative contraindications, owing to the small numbers of patients available for analysis and reluctance to allocate a limited resource to those whose comorbid conditions constitute a major part of their disease complex. The general contraindications to heart transplantation are listed in Box 21-6.

**Age**

In the absence of other life-limiting noncardiac conditions, the appropriate upper age limit becomes an ethical rather than medical decision. In properly selected patients, recipients older than age 60 years have a survival similar to younger patients. Nonetheless, some programs limit heart transplantation to patients younger than age 65. Older patients may be selected if their noncardiac organ systems are normal, their cognitive function is totally intact, they have a strong will to live, their family support system is well developed, and they have the potential for good quality of life if normal cardiac function is restored. A few programs have addressed this issue by allocating only older donor hearts (>50 years) to elderly recipients.

**Pulmonary Vascular Resistance**

The critical feature of elevated pulmonary vascular resistance (Rp) is pulmonary systolic pressure at completion of CPB during the transplant operation. The donor right ventricle generally poorly tolerates a systolic afterload of more than about 50 mmHg, and overt right ventricular dysfunction usually occurs above a pressure of 55 to 60 mmHg, potentially resulting in acute right ventricular failure and death. Tolerance of the donor right ventricle to elevated afterload conditions (secondary to increased Rp) is partly a function of donor right ventricular reserves, ischemic/reperfusion injury, and possibly donor/recipient size ratio.

The majority of adult patients with advanced heart failure secondary to ischemic or dilated cardiomyopathy have a reactive component of elevated Rp that is directly responsive to left atrial (or pulmonary capillary wedge) pressure. When

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**Box 21-5 Patient Factors Associated with Increased Morbidity and Mortality after Cardiac Transplantation**

- Pulmonary hypertension (>6 Wood units not responsive to vasodilators or not decreasing to <3 to 4 Wood units, pulmonary artery systolic pressure > 70 mmHg, transpulmonary gradient > 15 mmHg)
- Infection, active, untreated: HIV positive
- End-organ disease, irreversible:
  - Hepatic
  - Renal
  - Pulmonary (FEV₁ < 1.5 L·sec⁻¹)
- Pulmonary infarction, recent
- Age > 60 years
- Diabetes mellitus with end-organ damage (without end-organ damage also increases risk)
- Peripheral arterial disease or cerebrovascular disease (risk related to severity)
- Gastrointestinal disease:
  - Chronic active hepatitis
  - Diverticulitis, recent
  - Peptic ulcer disease with active bleeding
- Obesity (>120% of ideal body weight)
- Malignancy (within 5 years, high risk; remote, less risk)
- Osteoporosis
- Psychiatric disorder:
  - Affective or schizophrenic
  - Personality disorder, including medical noncompliance
- Substance abuse:
  - Tobacco
  - Alcohol
  - Controlled drug
- Lack of social support

Modified from Renlund. Key: FEV₁, Forced expiratory volume in 1 second; HIV, human immunodeficiency virus; PA, pulmonary artery.

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**Box 21-6 Contraindications to Cardiac Transplantation**

**General Contraindications**

Presence of any noncardiac condition that would itself shorten life expectancy or increase risk of death from rejection or complications of immunosuppression.

**Specific Contraindications**

- Older age (>about 65 years)
- Active infection
- HIV positive
- Active peptic ulcer disease
- Chronic active hepatitis
- Recent diverticulitis
- Diabetes mellitus with end-organ damage
- Severe peripheral arterial or cerebrovascular disease
- Coexisting active neoplasm (within 5 years, high risk; removed, low risk)
- Morbid obesity (>140% of predicted ideal body weight)
- Creatinine clearance < 40 to 50 mL·min⁻¹, effective renal plasma flow < 200 mL·min⁻¹
- Bilirubin > 2.5 mg·dL⁻¹ when not due to reversible hepatic congestion, transaminases > 2 × normal
- Severe pulmonary dysfunction with FVC and FEV₁ less than about 40% of predicted, especially with intrinsic lung disease
- Pulmonary artery systolic pressure > 60 mmHg, mean transpulmonary gradient > 15 Wood units
- Acute pulmonary thromboembolism
- Severe osteoporosis
- Smoking within last 6 months
- High risk of life-threatening noncompliance:
  - Inability to make strong commitment to transplantation
  - Cognitive impairment severe enough to limit comprehension of medical regimen
  - History of marked depression or emotional instability
  - Psychiatric instability severe enough to jeopardize incentive for adherence to medical regimen
  - Recurring alcohol or drug abuse
  - Failure to establish stable address or telephone number
  - Previous demonstration of repeated noncompliance with medical therapy or follow-up
  - Lack of independent family or social support system

May be relative or absolute, depending on severity or program philosophy.

May be suitable for cardiac transplantation if inotropic support and hemodynamic management produce a creatinine level < 2 mg·dL⁻¹ and creatinine clearance > 50 mL·min⁻¹. Transplantation may also be advisable as combined heart–kidney transplant.

Requires liver biopsy to exclude cirrhosis or other intrinsic liver disease.

These apply only if the increased resistance is largely nonreactive (fixed).

Key: FEV₁, Forced expiratory volume in 1 second; FVC, forced vital capacity.
elevated Rp is primarily reactive, it falls rapidly after transplantation. If the donor heart left atrial pressure is normal, pulmonary artery systolic pressure, transpulmonary gradient, and Rp return to near-normal levels within 1 week of transplant, with little further change during the coming year.\textsuperscript{225}

It is generally recognized that operative risk progressively increases as Rp rises. Other risk factors interact with Rp to create a higher or lower risk for a given level of resistance. In general terms, an Rp greater than about 5 Wood units (WU) or a transpulmonary gradient (mean pulmonary artery pressure minus pulmonary capillary wedge pressure) above 14 mmHg that is unresponsive to pulmonary vasodilators and inotropic agents (used to test reversibility of pulmonary vascular hypertension) is a major contraindication to orthotopic cardiac transplantation.\textsuperscript{225} To define the reactive component of any elevation of pulmonary resistance, a standard part of the cardiac transplant evaluation is right heart catheterization to document cardiac and pulmonary pressures (and Rp).\textsuperscript{210} If Rp is elevated, a sustained favorable hemodynamic response (Rp < about 4 WU) to pulmonary vasodilator therapy (e.g., milrinone, prostaglandin E\textsubscript{1}, nitroprusside, nitroglycerin, nitric oxide) suggests a suitable risk for cardiac transplantation.

When Rp remains elevated and medical therapy (sometimes over days to several weeks on continuous intravenous [IV] infusions) fails to reduce pulmonary artery systolic pressure below about 60 mmHg, secure conclusions about pulmonary reactivity cannot be made. In that instance, implanting a left ventricular assist device may be warranted to force reduction of left atrial pressure and promote reversal of the reactive component.

Renal Dysfunction Multiple studies have shown that pre-existing renal dysfunction is a major risk factor for mortality after cardiac transplantation. A serum creatinine level of 2 mg·dL\textsuperscript{-1} and a creatinine clearance of less than 50 mL·min\textsuperscript{-1} portend a worse prognosis in adults following cardiac transplantation, particularly because of the necessity for cyclosporine or tacrolimus immunosuppression, with their associated nephrotoxic effects. A major dilemma often exists in estimating the likelihood that renal dysfunction is secondary to severe low cardiac output and aggressive diuretic therapy, or whether it is secondary to intrinsic renal disease. There is no specific level of serum creatinine or creatinine clearance that differentiates between these.

Effective renal plasma flow (ERPF), obtained by nuclear medicine techniques, is a useful adjunct to creatinine clearance. An ERPF of less than 200 mL·min\textsuperscript{-1} generally indicates important underlying intrinsic renal disease affecting the distribution of renal blood flow and likely represents a major risk factor for cardiac transplantation.

Infection Presence of active infection is a traditional absolute contraindication to cardiac transplantation if the infection is life threatening and not readily reversible with antibiotic therapy. Clearly, transplantation would be ill advised in the presence of an important pneumonia, central nervous system (CNS) infection, intraabdominal sepsis, or active bloodstream sepsis, because the likelihood of these infectious conditions progressing to a life-threatening state following the immunosuppression of transplantation would be high. However, certain infections, such as mediastinitis following implantation of a ventricular assist device, driveline infections, or in some cases, partially treated endocarditis,\textsuperscript{229} are consistent with good outcome following cardiac transplantation, albeit at a higher risk of posttransplant mediastinal infection and fatality.

Prior Malignancy All patients should be screened appropriately for malignancies by a chest radiograph, mammogram, prostate-specific antigen, abdominal ultrasound, and complete physical examination. A history of malignancy increases the risk of a subsequent fatal malignancy following cardiac transplantation.\textsuperscript{117} However, if there is no evidence of residual, recurrent, or metastatic disease for a sufficient period to consider the malignancy cured, cardiac transplantation should be considered. Although the suitable period differs among malignancies, in general, a malignancy-free interval of 5 years is considered long enough to proceed with transplantation. Rarely, patients with cardiac neoplasms may undergo successful transplantation if there is no evidence of metastases or extension of the cancer beyond the surgical resection areas necessary for transplantation (see Chapter 18). This is, however, a contentious subject because malignant cardiac neoplasms can metastasize during the waiting period for organ allocation.

Squamous cell or basal cell carcinoma of the skin represents a curable condition with a low probability of metastasis if completely excised. Thus, this malignancy, if completely excised, does not require an extended wait prior to cardiac transplantation.

Donor Evaluation and Selection

The donor becomes available when brain death has occurred, and criteria enumerated by the Ad Hoc Committee of the Harvard Medical School are generally used.\textsuperscript{226,24} The donor must be completely unresponsive, without reflexes or movements of breathing. Two flat electroencephalograms obtained 24 hours apart are sometimes required.

Once a potential donor has been identified, other criteria apply. The donor should be younger than about age 60 years (although occasionally hearts from older donors are used for elderly recipients) and without documented prior myocardial infarction. Coronary angiography is recommended in all potential donors older than age 45 years; the heart is generally not used for transplantation if there is important arteriosclerotic coronary obstruction. A history of smoking also prompts coronary angiography as part of the process of donor selection.

There should have been no prolonged episodes of profound hypotension or cardiac arrest after injury, because poor donor heart function after transplantation is likely to follow such an event. However, echocardiography often allows the heart to be used if ventricular performance is good. Important ventricular arrhythmias usually eliminate a donor.

Two-dimensional transthoracic or, occasionally, transesophageal echocardiography (TEE) is performed to evaluate cardiac morphology, ventricular performance, and cardiac valve function. The heart should have good contraction and be free of any segmental wall motion abnormalities. Global or regional hypokinesis and valvar heart disease preclude use of the heart. Severe left ventricular hypertrophy and cardiac contusion with wall motion abnormality disqualify the donor. Minor cardiac malformations such as patent foramen ovale or a small ventricular septal defect may be corrected and the heart used.

Any evidence of sepsis must be sought, and if found, the heart is rejected. Hearts from donors who are positive for
human immunodeficiency virus are not used. Hearts from donors who test positive for hepatitis C are not used unless the recipient is also positive. Active malignancy in the donor disqualifies use of the heart for transplantation except in cases of primary malignant brain tumor. Death resulting from carbon monoxide poisoning, with a carboxyhemoglobin level greater than 20%, eliminates the donor heart from use. History of IV drug abuse usually disqualifies the donor, but occasionally exceptions are made. There should not be a great disparity between size of donor and recipient, although donor hearts from males of about 75 kg or greater are usually suitable for larger recipients up to about 110 kg.

Findings on physical examination relative to the heart should be normal, and a 12-lead electrocardiogram is examined to exclude the possibility of preexisting Q-wave abnormalities and conduction defects. Nonspecific ST- and T-wave changes may be caused by head injury, hypothermia, and vasopressor agent, and do not per se contraindicate use of the heart. If there is any suggestion of hypotension or cardiac injury, serum cardiac enzymes are obtained and should be normal or at most mildly elevated.

Once this screening has been performed and the heart found acceptable, managing the donor becomes intense. Hypotension, hypothermia, and diabetes insipidus are frequent physiologic results of brain death and make careful attention to volume replacement essential, but excessive crystalloid infusion can produce right ventricular distension and lung damage from extravascular water. Active warming may be required to counteract hypothermia.

The decision to use a specific donor is based in part on the feasibility of keeping cardiac ischemic time to less than about 6 hours, because prolonged ischemic time is a risk factor for acute graft dysfunction.

**Effect of Brain Death on Myocardial Function**

The effect of brain death on the myocardium has been of considerable interest for two important reasons: (1) there is a low but important prevalence of primary graft failure following cardiac transplantation, and (2) many potential donor hearts are not used because of donor heart dysfunction. Successful strategies to improve dysfunctional donor hearts would increase the number of hearts available for transplantation.

Myocardial injury by catecholamine infusión and stress stimulation of the nervous system are central to understanding donor heart dysfunction. Epinephrine infusión can cause cardiac hypertrophy, and experimental catecholamine infusión produces a characteristic histologic appearance of myofibrillary degeneration, also known as **contraction band necrosis**. Its histologic features are distinct from coagulation necrosis, the predominant histologic pattern seen in acute myocardial infarction. In coagulation necrosis, myocardial cells die without obvious contraction bands, calcification appears late, and a predominant polymorphonuclear cell response occurs. Coagulation necrosis is not seen histologically for many hours or even days after the onset of the infarction. In contrast, myofibrillar degeneration is histologically detectable early after onset, and the myofibrils die in a hypercontracted state with obvious contraction bands.

This lesion can also be seen in humans when the mode of death involves considerable stress, such as physical assault in which death occurred from the assault but not from life-threatening injuries. This suggests an association between catecholamine release and myofibrillar degeneration. Experimental intracerebral and subarachnoid hemorrhages can also produce these myocardial lesions.

Brain death is frequently accompanied by massive release of endogenous catecholamines. In animal models, blood epinephrine and norepinephrine levels may increase 100- to 500-fold within 10 seconds of experimental brain injury, with a correlation between magnitude of catecholamine release and severity of injury. In humans, catecholamine levels after brain death have been highly variable, likely related to individual variability in neurohumoral response and the mechanism and rapidity of the catastrophic intracranial event. In Novitsky’s baboon model, rapid increase in intracranial pressure was accompanied by marked increases in mean arterial, pulmonary wedge, and central venous pressure within 15 minutes, and by a threefold to sevenfold increase in blood norepinephrine and epinephrine levels. A relationship between noradrenaline levels and increases in the plasma level of creatine kinase (CK)-MB has been demonstrated after acute head injury in man.

The physiologic response to this post–brain death catecholamine storm may result from the interplay between coronary vasoconstriction and repercussion in association with oxygen-derived free-radical generation. Oxidation products of catecholamines may induce myocardial injury, probably resulting from peroxidation of membrane phospholipids. Catecholamine storm may also induce myocardial injury by oxygen-derived free radicals generated by repercussion of myocardium that has been rendered ischemic by severe coronary vasoconstriction.

**Immunologic Aspects of Transplant Testing**

**ABO Compatibility**

The ABO blood group antigens are carbohydrate structures carried on glycoprotein and glycolipid components of cell surfaces and tissues throughout the body, most notably on the surface of erythrocytes. In the human heart, blood group antigens are confined to the vascular endothelium and mesothelial cells on the surface of the epicardium. In individuals who lack one or more of the ABO antigens, natural antibodies against the absent antigen appear during the first 6 months of life and are present permanently thereafter.

An accepted requirement for successful cardiac transplantation is identical or compatible blood groups between donor and recipient. If an allograft containing A or B blood antigens on its endothelial surfaces is transplanted into a recipient who has naturally occurring anti-A or anti-B antibody, hyperacute rejection or accelerated aggressive acute rejection will likely occur. When a donor and recipient display ABO incompatibility, circulating antidendor hemagglutinins rapidly bind to endothelial cells and promote platelet deposition, granulocyte activation, and thrombosis, resulting in hyperacute rejection. Although transplantation in the presence of ABO incompatibility (donor heart A into recipient blood group B or O, B into A or O, AB into A, B, or O) would be expected to produce universal hyperacute rejection, there are notable exceptions (see also “ABO-Incompatible Infant Heart Transplantation” in Section II). Considerable variability exists among individuals in the level of blood group antigen expression in tissues, such as on cardiac endothelium.

A specific exception to ABO incompatibility may be donors of A₂ blood group. Blood group A contains
subgroups A1 and A2. Subgroup A1 acts like blood group A in its propensity for producing hyperacute rejection when transplanted into an ABO-incompatible recipient. However, donor subgroup A2 may be less prone to producing hyperacute rejection because the A2 antigen is not readily displayed on the endothelial surfaces of the heart. Skin grafts from A2 donors are not hyperacutely rejected when transplanted into B or O recipients. A clinical trial of A2 kidneys transplanted into O recipients produced graft outcome similar to ABO-compatible transplants. The mechanism may relate in part to the two different galactosaminyltransferases produced by A1 and A2 genes, resulting in a qualitative difference in the type of core saccharide-based A antigens.

**Tissue Typing**

HLA antigens play a central role in the immune response, and the HLA genes are the most polymorphic known in the human genome. *Haplotype* refers to the set of genes on any one chromosome. Every individual has two haplotypes (one from each parent) for the genes on the short arm of chromosome 6 that code for the MHC complex. Each haplotype contains antigens determined by the HLA-A, HLA-B, HLA-C, HLA-DR, and other loci. The two haplotypes for an individual make up the HLA phenotype, which is the complete list of HLA antigens possessed by that individual. Studies of kidney graft survival have demonstrated a substantial survival benefit when the HLA antigens are matched between donor and recipient. Some benefit in freedom from rejection has also been demonstrated for heart transplantation related to the number of HLA mismatches.

Some studies suggest a higher probability of rejection with HLA-DR* S* and HLA-DQ mismatching in heart transplantation. However, because of the time limitations imposed by the current state of cardiac preservation during organ procurement and the scarcity of organs, donor hearts are currently not selected on the basis of prospective histocompatibility testing.

**Panel Reactive Antibodies**

In addition to HLA typing, the transplantation evaluation process includes routine examination of serum from a prospective transplant recipient for presence of circulating anti-HLA antibodies, also called *humoral sensitization*. Sensitization is established by documenting the presence of circulating anti-HLA antibodies by the panel reactive antibody (PRA) test. The most common cause of sensitization is pregnancy. Other common causes include prior blood transfusion, prior transplantation, or insertion of a ventricular assist device. Occasionally a patient will demonstrate a positive PRA with anti-HLA antibodies and no obvious sensitizing event. These antibodies may represent cross-reactivity between bacterial or viral epitopes and HLA antigens.

**Crossmatching**

The crossmatch at transplantation is typically the final test of immunologic compatibility between donor and recipient prior to making the decision to transplant. The goal of the crossmatch is to prevent hyperacute rejection and accelerated severe acute rejection during the first 5 to 7 days after transplantation. The crossmatch tests the reactivity of recipient sera (with its potential anti-HLA antibodies) against donor lymphocytes obtained from peripheral blood or lymph node. With current crossmatch techniques, hyperacute rejection is extremely rare. In practice, a pretransplant prospective crossmatch is often omitted when a recent PRA is 0% because of the very low probability of hyperacute or accelerated acute rejection in that setting and because of the additional time prior to transplantation needed to obtain a crossmatch. In that instance a retrospective crossmatch is usually obtained in the hours following transplantation to make a final determination of the presence of antidonor antibodies.

A positive complement-dependent lymphocytotoxic T-cell and B-cell crossmatch is a strong predictor of hyperacute or severe accelerated acute rejection. However, presence of a negative cytotoxic crossmatch does not guarantee protection against hyperacute or severe early rejection. It has been hypothesized that minimal clonal expansion of T* i * and T* i * subsets of T cells plus B cells is sufficient to produce a brief IgM (or IgM followed by IgG) response that is promptly down-regulated, and detectable levels of IgG may not be present (thus producing a negative crossmatch). However, with sustained stimulation following transplantation, B-cell clones expand and express increased affinity for the HLA antigen. Substantial clonal expansion then occurs with T1, T2, and B-cell proliferation and the production of antibody. Serum anti-HLA antibodies become predominantly IgG with sustained levels, and further antibody response is readily inducible with reexposure to even small amounts of these HLA antigens.

**Virtual Crossmatch**

With the current precision of flow cytometry technology in identifying circulating anti-HLA antibodies in potential recipients, many transplant centers omit formal crossmatching (with the considerable time requirement) in the presence of low PRAs, and rely instead on a comparison of HLA typing of the donor with identified anti-HLA antibodies in the recipient. If there are no donor antigens against which recipient antibodies are likely to react, it is generally safe to proceed with transplantation.

**TECHNIQUE OF OPERATION**

**Donor Heart Procurement**

Most donors are donating multiple organs including the heart. Therefore, the donor is prepared from neck to mid-thigh. Preferably, a central venous line and an arterial catheter are placed because marked hypotension may occur while mobilizing the abdominal organs.

A long midline incision is made from jugular notch to pubis. Volume replacement continues as needed because considerable bleeding from incisions is frequent as a result of the donor’s vasodilated state. After median sternotomy, a self-retaining retractor is inserted. While other organ procurement teams proceed, the pericardium is opened and usual stay sutures applied. The heart is examined for evidence of cardiac injury, congenital anomalies, coronary arteriosclerosis, or other acquired heart disease. The ascending aorta is dissected and mobilized as far as the brachiocephalic takeoff. The superior vena cava (SVC) is completely mobilized, including any pericardial reflection onto it. A purse-string suture is placed on the ascending aorta for cardioplegia infusion.

When cardectomy is ready to begin, 200 units · kg\(^{-1}\) of heparin are given, and the cardioplegia needle is inserted into
the ascending aorta and secured. In this setting, the cardioplegic solution is infused by gravity. Cold University of Wisconsin (UW) solution is commonly used as the myocardial preservation solution, but other intracellular- or extracellular-type solutions provide effective preservation.

If a central line is in place, it is withdrawn. The SVC is clamped and later divided as far distally as possible. The right or left superior pulmonary vein (or left atrium above the entrance of the left pulmonary veins if lung procurement is planned) is partially divided to permit escape of blood from the heart (Fig. 21-8). If lungs are also being harvested, the left atrium is incised for egress of pulmonary preservation solution, and later a cuff of left atrium is left around the right and left pulmonary veins for the lung allografts. The inferior vena cava (IVC) is divided, leaving part of it with the liver. After several cardiac ejections to completely empty the heart, the aorta is occluded just proximal to the brachiocephalic artery. Infusion of the cardioplegic solution is begun. Cardioplegic infusion pressure is monitored digitally while 1 to 2 L of solution is infused. Ice-cold saline or slush solution is poured into the pericardium.

Coronary sinus effluent is allowed to escape into the pericardial sac through the open IVC. Cardiectomy proceeds by dividing the right pulmonary veins at the pericardial reflection. The heart is retracted superiorly and to the right to expose the left pulmonary veins (Fig. 21-8, B), which are divided at the pericardial reflection. Downward traction alongside the aorta and pulmonary trunk exposes the maximal length of these vessels. The aorta is divided distal to the origin of the brachiocephalic artery (Fig. 21-8, C). The left pulmonary artery is divided at the pericardial reflection. The right pulmonary artery is divided. All that remains to be divided is connective tissue behind the left atrium at the pericardial reflection and lymphatic tissue, which lies between the left atrium and the tracheal bifurcation.

The heart is removed from the body and immersed in cold preservation solution. A few minutes are spent to trim the heart and prepare it for implantation. The right pulmonary veins are joined by incision, as are left pulmonary veins. The left atrium is opened posteriorly between the pulmonary veins to provide maximum length for the left atrial suture line. The aorta is separated from the pulmonary trunk. The pulmonary trunk is opened at its bifurcation to preserve maximum circumfer-ence that may be needed to match a dilated recipient vessel. The cardiac chambers are thoroughly irrigated with cold isotonic solution and inspected to ensure absence of debris or anatomic anomalies. The organ is placed in triple sterile plastic bags filled with preservation solution and transferred to an ice chest for transport.

Orthotopic Cardiac Transplantation

Biatrial Technique

In addition to the usual preparations for cardiac operations (see Chapters 2, 3, and 4), a large-gauge triple-lumen catheter is placed through the left internal jugular vein after anesthesia induction. The right internal jugular vein is left undisturbed if possible to preserve it as access for future endomyocardial biopsies. After endotracheal intubation, a TEE probe is placed for later monitoring during de-airing maneuvers and for assessing ventricular function. The heart is exposed through a median sternotomy. In the presence of previous cardiac operations, femoral artery and vein catheters are inserted percutaneously in case acute cardiac decompensation requires insertion of an intraaortic balloon pump or emergency institution of CPB.

When arrival of the donor heart is imminent, CPB is established with separate caval cannulation. Additional time is allotted if extensive dissection is necessary. The aorta is clamped and the caval tapes secured. The right atrium is incised just above the level of the entrance of the IVC, anterior to the sulcus terminalis. The incision is carried around to the IVC, leaving the cava below the cut surface of the right atrium. The interatrial septum is incised and carried superiorly until it meets the roof of the left atrium. The left atrial incision is then carried leftward, leaving a generous cuff of left atrium above the entrance of the left pulmonary veins. A cardiotomy sump is placed into the left atrium when the interatrial septum is incised, and the great arteries are divided proximally to expose the underlying left atrium. These arteries are accurately dissected free from one another to facilitate great vessel anastomoses.

The donor heart is removed from the ice chest, and fluid from the inner bag cultured. The roof of the left atrium is dissected free from the posterior aspect of the right and left pulmonary artery segments. The aorta is dissected from the pulmonary trunk, which is then divided just proximal to its bifurcation unless additional pulmonary artery is necessary for reconstruction. A cuff of left atrium is created by incising through the pulmonary vein orifices (Fig. 21-9, A). The right atrium is prepared by incising through the inferior vena caval orifice and extending the incision toward the base of the right atrial appendage approximately equidistant from the sulcus terminalis and the atrioventricular groove (Fig. 21-9, B).

During implantation, perfusate temperature is generally 28°C, with intermittent topical cooling using 4°C saline ice slush. No additional cardioplegic solution is infused. The left atrial anastomosis is constructed first using continuous 3-0 polypropylene suture (Fig. 21-9, C). When constructing it, the first few stitches are placed “at a distance” before lowering the donor heart into the pericardial space. The remainder of the entire left atrial anastomosis is constructed in an evert-ing fashion to provide endothelium-to-endothelium apposition, thereby reducing the chance of thrombus formation along the suture line. Construction of the far-leftward portion of the anastomosis along the left pulmonary veins is often facilitated by retracting the donor ascending aorta inferiorly with a traction suture. The right atrial anastomosis is also constructed with continuous 3-0 polypropylene suture. In the area over the interatrial septum, the suture lines are partially overlapping (Fig. 21-9, D). Each chamber is filled with cold saline before securing the suture lines.

The aortic anastomosis is constructed with continuous 4-0 polypropylene suture after the donor and recipient aortas are cut to appropriate length. A cardioplegia catheter to be used as a “needle vent” for aspirating air is placed in the donor ascending aorta. Air is evacuated from the heart through the aortic suture line, and the suture line secured. The aortic clamp is removed with strong suction on the needle vent.

This is a critical period during the operation because the donor heart is being reperfused after a prolonged period of global ischemia. It is useful to infuse one or two ampules of adenosine just prior to aortic clamp removal to facilitate maximal dilatation of the subendocardial arterioles during early reperfusion. In most instances, the donor heart will
Figure 21-8 Donor cardiectomy for orthotopic cardiac transplantation. A, Inferior vena cava is divided at its junction with right atrium. Most of the intrapericardial inferior vena cava is left behind attached to the liver, because nearly all these operations are for multiorgan procurement. Right pulmonary vein is incised to vent the left heart. (When lungs are being harvested, left atrioventricular groove is generously incised to provide egress of the pulmonary preservation solution). Aorta is occluded when the heart empties. Cold cardioplegic solution is administered through the catheter to the aortic root to achieve total electromechanical arrest. B, Heart is retracted superiorly, exposing pulmonary veins and left pulmonary artery. These are divided. C, Aorta, superior vena cava, and right pulmonary artery are divided at or above the pericardial reflection for maximal length on recipient great arteries. All that remains to be divided is connective tissue behind the left atrium at pericardial reflection. The heart is taken from the body and aorta and pulmonary trunk separated, atrial septum checked for defect, and cardiac valves and cardiac chambers inspected. It is packed in saline solution in triple sterile bags for transport.
Figure 21-9  Orthotopic cardiac transplantation, biatrial technique. A, Creating donor heart left atrial cuff by incising through pulmonary vein orifices. B, Creating donor heart right atrial cuff. Incision begins at orifice of inferior vena cava and extends toward right atrial appendage approximately halfway between sulcus terminalis and atrioventricular groove. C, Left atrial anastomosis is commenced.

begin rhythmic contractions within 1 to 3 minutes of clamp removal. If ventricular fibrillation or tachycardia occurs, the heart should be promptly defibrillated. An esmolol hydrochloride infusion is initiated temporarily if marked sinus tachycardia or frequent ventricular arrhythmias occur during early reperfusion. Esmolol is particularly useful in this setting because it reduces myocardial oxygen consumption when the heart is recovering from the period of ischemia, and its duration of action is very short; thus, its effects will have dissipated before discontinuation of CPB.

When a gentle sinus rhythm is established, preparations are made for the pulmonary artery anastomosis. (Some surgeons prefer to complete this anastomosis before removing the aortic clamp.) The pulmonary artery segments are cut to an appropriate length and the anastomosis constructed, usually with 4-0 or 5-0 polypropylene suture (Fig. 21-9, E).

The remainder of the operation is conducted as usual during rewarming, and CPB is gradually discontinued after thoroughly de-airing the heart through the aortic needle vent while examining it for residual air with TEE. Immediately before and after discontinuing CPB, the function of each ventricle is assessed with TEE, and appropriate interventions made if necessary to improve function.
Figure 21-9, cont’d  D, Right atrial anastomosis is commenced on interatrial septum. This suture line overlaps the atrial septal portion of the left atrial anastomosis. E, Aortic and pulmonary trunk anastomoses are completed. (From Kirklin and colleagues.14)

Bicaval Technique

Preparations for and initiation of CPB are identical to those for the biatrial technique. The SVC cannula should be placed 1 cm or more superior to the cavo–right atrial junction to facilitate the SVC anastomosis. If multiple implantation techniques are used at a given institution, clear communication to the donor procurement team is necessary to ensure the harvesting of all available donor SVC up to entrance of the brachiocephalic vein.

General conduct of the operation is the same as for the biatrial technique. Following aortic clamping, caval tapes are secured, and an incision made in the left atrium anterior to the right pulmonary veins as for mitral valve surgery. The incision is extended under the IVC and superiorly to the level of the right pulmonary artery. A cardiotomy sump is placed into the left atrium, and a generous cuff of right atrium adjacent to the IVC opening is retained. Within the right atrium, this cuff usually involves an incision through or immediately inferior to the coronary sinus orifice. With the cautery on a low setting, pericardial attachments are freed up from the IVC cuff, and this area is separated from the cut edge of the left atrium to facilitate implanting the donor heart.

Similarly, a cuff of right atrium adjacent to the entrance of the SVC is created, and its attachments to the underlying pulmonary trunk are divided to facilitate ease of later anastomosis. Commonly, implantable cardioverter-defibrillator leads are present in the recipient heart and are frequently densely adherent to the interior surface of the SVC. These should be freed up, mobilized, pulled as far as possible into the surgical field, and divided. This allows them to retract back into the upper SVC (where adhesions to the leads are uncommon) for ease of later extraction through the defibrillator pocket. The great arteries are divided proximally, and the remainder of the incisions along the inferior, superior, and left lateral aspects of the left atrium are as for the biatrial technique. A cuff of left atrium should be preserved above the entrance of the left pulmonary veins (Fig. 21-10, A).

Implantation begins with the left atrial anastomosis, which starts inferiorly, moving toward the left pulmonary veins (Fig. 21-10, B). Whenever possible, an everting suture technique should be used to promote direct endothelial apposition and avoid potential thrombus formation that might be more likely with an inverting anastomosis. When the suture line approaches the left atrial appendage in the donor heart, the geometry should be briefly reevaluated to ensure that the donor SVC will lie appropriately for the SVC anastomosis. If the recipient’s left atrium seems considerably larger than the donor’s, the base of the donor’s left atrial appendage can be incised slightly to lengthen it. When this suture line reaches the area of the right pulmonary veins, it is generally completed with the second arm of a 3-0 polypropylene suture. The left atrium is filled with cold saline solution and the suture line secured. Throughout implantation, cold saline slush is applied to the donor heart to minimize the tendency for metabolic activity.

The IVC anastomosis is constructed next, usually with 4-0 polypropylene suture. If the donor heart is considerably smaller than the recipient heart, it is particularly important to retain a sizeable cuff of right atrium near the IVC to prevent tension on that anastomosis.

Although various strategies have been used for the remainder of the anastomoses, we recommend proceeding with the aortic anastomosis next, after appropriately trimming lengths of donor and recipient aorta to allow nice geometric reconstruction of the new ascending aorta. Using continuous 4-0 polypropylene suture, a standard end-to-end anastomosis is constructed (Fig. 21-10, C). A double suture line technique, in which the first line is a continuous everting mattress suture followed by a simple running suture, is particularly hemostatic. Before securing the suture line, air is evacuated from the heart by vigorous expansion of the lungs, and the suture line is secured.

During rewarming, after a stable sinus rhythm has been established, the SVC anastomosis is constructed with
Figure 21-10 Orthotopic cardiac transplantation, bicaval technique. **A,** Right atrium is divided to create superior and inferior vena caval cuffs. Great vessels are divided as in biatrial method. **B,** Commencement of left atrial anastomosis. **C,** Completion of bicaval transplant technique, showing inferior vena caval, superior vena caval, aortic, and pulmonary trunk anastomoses. (From Kirklin and colleagues. 114)

Continuous 5-0 polypropylene suture. It is important to avoid excessive redundancy in creating the new SVC, because any kinking of the caval pathway can result in a venous pressure gradient. The pulmonary end-to-end anastomosis is constructed as in the biatrial technique.

**General Intraoperative Considerations**

In patients with a previous sternotomy, particularly with previous bypass surgery, the likelihood of acute severe cardiac decompensation is greatly increased if there is inadvertent injury to the patient’s saphenous or internal thoracic artery graft. In this situation, routine insertion of a percutaneous femoral artery catheter for arterial pressure monitoring is advantageous. Should decompensation occur, a guidewire for inserting an intraaortic balloon pump can be rapidly accomplished, or CPB established with a percutaneously inserted arterial cannula. In situations in which sternotomy is considered very high risk, a guidewire can also be placed in the femoral vein for percutaneous venous cannulation if necessary.

In preparing every donor heart prior to implantation, the area of the fossa ovalis should be specifically examined. If a patent foramen ovale is identified, it must be surgically closed. Failure to do so has resulted in severe hypoxemia and right-to-left shunting early after cardiac transplantation in a
situation of right ventricular dysfunction, particularly in the presence of elevated pulmonary artery pressure.56

Tricuspid regurgitation detected by Doppler echocardiography is common after orthotopic cardiac transplantation. This may relate to geometry of the newly constructed right atrium; an association has been suggested between larger relative size of the donor right atrium to the recipient’s and the likelihood of tricuspid regurgitation.51 Thus, consideration should be given to excising excess right atrial tissue, particularly on the lower side of the anastomosis, without jeopardizing the sinoatrial node. Less commonly, mitral valve regurgitation has been observed, associated with the “snowman” configuration formed by the donor-recipient left atrial anastomosis.51,55

During construction of the left atrial suture line, the orifice of the left pulmonary vein should be observed. Excessive protrusion of tissue from the suture line with an inverting technique can potentially obstruct pulmonary venous inflow and may also be thrombogenic. In extreme cases, surgically induced cor triatriatum secondary to anastomotic obstruction of pulmonary venous inlet has been reported.51,56

Sinus node dysfunction occasionally occurs. Therefore, specific attention to avoiding damage to the sinoatrial node is important during harvesting and implantation. The ligature on the SVC should be placed 1 to 2 cm above the superior cavo–right atrial junction. The incision in the donor right atrium should be kept well above the sulcus terminalis to avoid damaging the sinoatrial node while constructing the lower right atrial suture line.

Kinking of the pulmonary trunk may occur if the length of the newly constructed pulmonary trunk is redundant.14 Therefore, care must be taken to trim sufficient donor and recipient pulmonary trunk to avoid redundancy after constructing the anastomosis. The newly constructed pulmonary trunk is particularly vulnerable with an oversized donor heart relative to the size of the recipient’s pericardial space. Redundancy that results in kinking of the pulmonary trunk can produce an important gradient across the pulmonary anastomosis with resultant severe right ventricular hypertension.

Adverse neurologic events can occur. Mural thrombus may be potentiated by an excessively inverting suture line, particularly in the left atrium. Effective and complete deairing of the heart is extremely important to minimize the risk of cerebral embolism. When systemic vascular resistance is low following heart implantation, flow rates during CPB must be adequate. Although the precise level of perfusion pressure and flow rate that contribute to neurologic events has not been clearly defined, systemic mean perfusion pressure should be maintained at 40 mmHg or greater during rewarming, with a perfusion flow rate of 4.2 to 4.8 L·min⁻¹.

In the presence of important right ventricular dysfunction during rewarming, a second left atrial catheter is placed for infusion of inotropic agents, and prostaglandin E₁ and other vasodilator agents can be infused into the central venous lines. If this is not successful and pulmonary hypertension is present, nitric oxide55,58,11 can be used as an inhalational agent.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Usual care given to patients after cardiac surgery (see Chapter 5) is applied to patients who have received a cardiac transplant. Generally, subsystems function normally, and little or no special therapy is required. Cardiac function of the donor heart is usually good but is subject to influences of total denervation and consequences of myocardial ischemia attending explant and transplant. Cardiac denervation may temporarily lower heart rate; consequently, a chronotropic catecholamine agent may be indicated. Isoproterenol in doses of 0.01 to 0.1 µg·kg⁻¹·min⁻¹ or atrial pacing can be used to maintain an appropriate heart rate for patient age and size. Generally, the effects of β-adrenergic agents are unchanged.

Cardiac ischemia results in reduced diastolic compliance, so somewhat higher cardiac filling pressures may be required for optimal function. Impaired systolic function and contractility may also be observed, manifested by increased left atrial or pulmonary artery wedge pressure. Inotropic support is often required for 2 to 5 days, depending on function of the donor heart.

Acute distention and failure of the right ventricle resulting from excessive right ventricular afterload is occasionally observed, most commonly in the presence of preexisting recipient pulmonary hypertension or reactive pulmonary vasoconstriction from CPB or protamine administration. Various agents may dilate pulmonary vasculature, but the most effective combination appears to be milrinone at 0.3 to 1 µg·kg⁻¹·min⁻¹ and nitric oxide. Rarely, right ventricular mechanical support is required.

Aspirin, 325 mg daily, is given as soon as oral intake is begun and is continued indefinitely to counteract (at least in part) the tendency of the donor heart to develop coronary arteriosclerosis. Iron supplementation (ferrous sulfate 325 mg three times daily) is given until hematocrit is stable. A histamine H₂-receptor antagonist is administered routinely to counteract adverse effects of steroids on the gastric mucosa.

Immunosuppressive Modalities

Immunosuppressive modalities in transplantation are designed to reduce intensity of the immune response to a degree that allows acceptance of the allograft, yet provides sufficiently low toxicity to permit prolonged survival. Pharmacologic agents have evolved from general suppression of the recipient’s immunologic defenses to selective blockade of intracellular immune events that maximize graft acceptance while minimizing toxicity.

Three situations require specific combinations of immunosuppressive therapies: (1) initial high-dose immunosuppression to facilitate graft acceptance, minimize the chance of early rejection, and potentially favor induction of tolerance; (2) maintenance therapy for chronic acceptance of the allograft; and (3) augmented immunosuppression to reverse episodes of acute rejection. Specific immunotherapeutic modalities are being evaluated to prevent or reverse chronic rejection in the form of allograft vasculopathy.

The immune response to transplantation is highly dependent on T-cell activation and proliferation.59 The cellular events of T-cell activation are of great importance because many current immunosuppressive drugs target specific intracellular pathways of T-cell activation. A summary of modalities that interfere with specific phases of the allograft-induced immune response is given in Table 21-4.

Although there is considerable variability among institutions, the general strategy involves induction therapy
followed by maintenance therapy with initial “triple-drug” immunosuppression followed by gradual tapering or withdrawal of the steroid component. Induction therapy generally includes one of two approaches:

1. Daclizumab or basiliximab, which block IL-2 receptors
2. Antithymocyte globulin or OKT3, which targets the T-cell receptor and causes it to be removed from the cell surface or induces destruction of the entire cell through multiple mechanisms

Maintenance immunosuppression generally includes immunosuppressive agents from three general classes, comprising the triple-drug strategy:

1. Cyclosporine and tacrolimus interfere with calcium-mediated signaling via calcineurin, which blocks production and release of IL-2, which is essential for proliferation of cytotoxic T\(\text{H}\) cells.
2. Mycophenolate mofetil, azathioprine, methotrexate, and cyclophosphamide are often referred to as **anti-proliferative agents** because of their basic action of interfering with T-cell proliferation.
3. Adrenocorticosteroids, usually methylprednisolone or prednisone, have multiple mechanisms of action. In addition to an antiinflammatory effect, they inhibit transcription of multiple cytokines, impair macrophage function, and decrease circulating lymphocytes.

### Adrenocortical Steroids
Corticosteroids are generally administered intraoperatively before cardiac transplantation and constitute a portion of the maintenance strategy. Some centers continue at least low-dose prednisone therapy indefinitely, but an effective alternative strategy is to rapidly reduce and withdraw steroids in the early postoperative period. A summary of the important features and dosing of corticosteroids is found in **Box 21-7**.

#### Cyclosporine
Viability of heart transplantation as a therapeutic option for end-stage heart disease is directly linked to clinical availability of cyclosporine in 1979.\textsuperscript{533,617} Clinical features and dosing of cyclosporine are summarized in **Box 21-8**. Animal studies suggest that cyclosporine may be most effective when given before the antigenic challenge, a situation perhaps related to lower serum lymphokine concentration before onset of rejection. Absorption of cyclosporine is somewhat variable, but peak blood levels are achieved by about 3.5 hours. Bioavailability of the oral solution at steady state is about 30%. Approximately 90% of circulating cyclosporine is protein bound, and half-life is about 20 hours. Cyclosporine is eliminated primarily by the liver, with only about 6% by the kidneys. Cyclosporine blood concentration can be importantly affected by administration of other drugs, as summarized in **Table 21-5** and **Box 21-9**.

Renal toxicity, the major toxicity of cyclosporine, occurs in 25% to 38% of patients, manifested in the acute phase by

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### Table 21-4 Actions of Immunosuppressive Modalities

<table>
<thead>
<tr>
<th>Corticosteroids</th>
<th>Cyclosporine</th>
<th>Tacrolimus</th>
<th>Azathioprine</th>
<th>Mycophenolate Mofetil</th>
<th>Cyclophosphamide</th>
<th>Methotrexate</th>
<th>Actinomycin D</th>
<th>Sirolimus</th>
<th>ATG</th>
<th>OKT3</th>
<th>Basiliximab, Daclizumab</th>
<th>OKT4</th>
<th>Plasmapheresis</th>
<th>Photopheresis</th>
<th>TLI</th>
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<tr>
<td><strong>Inhibition of T-Cell Activation</strong></td>
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<td>Decreased APC effectiveness</td>
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<td>Inhibition of TCR/antigen binding</td>
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<td>Inhibition of accessory molecules</td>
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<td><strong>Inhibition of T-Cell Proliferation</strong></td>
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<td><strong>Inhibition of Smooth Muscle Proliferation</strong></td>
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<td><strong>Promotion of Suppressor Cells</strong></td>
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Data from Kirklin and colleagues.\textsuperscript{514} Key: ATG, Antithymocyte globulin; APC, antigen-presenting cell; IL, interleukin; TCR, T-cell receptor; TLI, total lymphoid irradiation.
Table 21-6 Nephrotoxicity of Cyclosporine

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Drug</th>
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<tbody>
<tr>
<td>Decreased metabolism (competition for cytochrome P450 system)</td>
<td>Erythromycin</td>
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<td>Ketoconazole</td>
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<td>Itraconazole</td>
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<td>Diltiazem</td>
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<td>Verapamil</td>
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<td>Nicardipine</td>
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<td>Cimetidine</td>
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</table>

Increased bioavailability (increased GI absorption) | Metoclopramide

From Kirklin and colleagues.634

Key: GI, Gastrointestinal.

Chapter 21 Cardiac Transplantation

Box 21-7 Corticosteroids

**Clinical Use**
- Maintenance immunosuppression
- Pulse therapy for acute rejection

**Mechanism**
- Antinflammatory action
- Inhibits IL-2 production by impairing gene transcription
- Suppresses antigen-presenting cell function, reduces adhesion molecule expression, inhibits leukocyte transmigration, inhibits lymphocyte proliferation

**Dose**
- **Maintenance Immunosuppression**
  - Individual protocols are highly variable. A standard regimen is an initial prednisone dose of 20-40 mg daily tapered to an every-other-day dose of approximately 0.1 to 0.2 mg·kg⁻¹ or no steroids by 6 months. Some programs use no maintenance corticosteroids.
  - Daily steroids (approximately 0.1 to 0.2 mg·kg⁻¹·day⁻¹) are maintained in the setting of recurrent rejection.

- **Treatment of Acute Rejection**
  - 500-1000 mg methylprednisolone IV daily for 3 days or prednisone 2-3 mg·kg⁻¹ PO for 3 days with or without rapid taper thereafter

**Target Levels**
- None available

**Adverse Effects**
- Diabetes, bone disorders, obesity, cushingoid changes, decreased wound healing, cataracts, peptic ulcer disease, hypertension, psychiatric disorders

From Kirklin and colleagues.634

*See Section II for pediatric treatment.

Key: IL, Interleukin; IV, intravenously; PO, orally.

Box 21-8 Cyclosporine

**Clinical Use**
- Chronic maintenance immunosuppression, usually combined with azathioprine or mycophenolate mofetil, with or without corticosteroids

**Mechanism**
- Calcineurin blockade, inhibition of interleukin (IL)-2 production, inhibition of T-cell proliferation

**Dose**
- Initial oral dose of 25-50 mg twice daily and, if renal function remains normal, rapidly increase over 3-4 days to achieve whole blood trough level of 300-400 ng·mL⁻¹

**Target Levels**
- 0-3 months posttransplant: 250-350 ng·mL⁻¹
- 3-6 months posttransplant: 200-300 ng·mL⁻¹
- 6-12 months posttransplant: 150-250 ng·mL⁻¹
- >12 months posttransplant: 50-150 ng·mL⁻¹

**Toxicity**
- Nephrotoxicity, neurotoxicity, hypertension, hypercholesterolemia, hepatotoxicity, hyperkalemia, renal tubular acidosis, hypermagnesemia, hyperuricemia, hypertrichosis, gingival hyperplasia

Box 21-9 Drugs That Decrease Cyclosporine Blood Levels by Induction of Cytochrome P450 System

- Rifampin
- Isoniazid
- Phenytoin
- Phenytoin
- Carbamazepine

From Kirklin and colleagues.634

Oliguria and elevated blood urea nitrogen and creatinine levels. These effects are largely initiated by renal arteriolar vasoconstriction, which occurs mainly at the level of the preglomerular arterioles.62,64 The intrarenal renin-angiotensin system may contribute to both nephrotoxic and hypertensive effects of cyclosporine, because cyclosporine stimulates renin synthesis and release from renal juxtaglomerular cells and afferent arteriolar vessel wall.62,63 Chronic cyclosporine nephrotoxicity is characterized by patchy glomerular sclerosis with interstitial fibrosis and thickening of capillary basement membranes. Once chronic renal damage has occurred, it is usually unresponsive to a decrease in cyclosporine dosage or drug withdrawal. Common drugs that increase nephrotoxicity of cyclosporine are listed in Table 21-6.

Less severe adverse side effects include reversible hepatotoxicity, fluid retention, hirsutism (20%-45%), gum hypertrophy (9%-16%), hypertension (53%), tremor (20%-50%), and rarely, late development of lymphoma (although this may result from overimmunosuppression with multiple agents).

**Tacrolimus**

Tacrolimus (initially called FK506) was first isolated in 1984 from the bacteria Streptomyces tsukubaensis.66 It was first used clinically in 1989 as replacement therapy for cyclosporine in liver transplantation.67 Tacrolimus is a macrolide compound unrelated to cyclosporine and with different binding sites. However, their basic immunosuppressive effects are similar. Tacrolimus gains its immunosuppressive effect by binding to a protein called FKBP-12, and it is the FKBP-12–tacrolimus complex that blocks calcineurin. In general, both the immunosuppressive effects and toxicity of tacrolimus exceed that of cyclosporine, possibly related to its binding affinity to FKBP, which is much greater than the binding affinity of cyclosporine to cyclophilin, the binding protein for cyclosporine.
Table 21-6  Drugs That Increase Cyclosporine Nephrotoxicity<br>

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal vasoconstriction and/or renal tubular injury</td>
<td>Amphotericin Aminoglycosides</td>
</tr>
<tr>
<td>Inhibition of cyclooxygenase, resulting in decreased renal prostaglandin synthesis and decreased renal vasodilatation, with potentiation of cyclosporine decrease in renal blood flow</td>
<td>Nonsteroidal antiinflammatory agents</td>
</tr>
<tr>
<td>Inhibition of creatinine secretion by renal tubules (potentiates similar action of cyclosporine)</td>
<td>Trimethoprim/sulfamethoxazole</td>
</tr>
<tr>
<td>Other mechanisms</td>
<td>Radiocontrast agents</td>
</tr>
<tr>
<td></td>
<td>Melphalan</td>
</tr>
<tr>
<td></td>
<td>Sirolimus</td>
</tr>
</tbody>
</table>

From Kirklin and colleagues.524  
*Drugs that act by increasing cyclosporine blood levels are not included in this table.*

A major side effect of tacrolimus that differs from cyclosporine is its marked tendency to induce diabetes. Unlike cyclosporine, gingival hyperplasia and hirsutism are rare with tacrolimus. Although unproven, there appears to be a higher propensity for lymphoproliferative malignancies with tacrolimus. Clinical features and dosing of tacrolimus are listed in Box 21-10.

Azathioprine

Azathioprine was thought to be only of historical interest when cyclosporine became available, but it was soon shown that triple-drug therapy was advantageous. Azathioprine again became part of the immunosuppression protocol along with cyclosporine and adrenocortical steroids. It is an imidazole derivative of 6-mercaptopurine. Mycophenolate mofetil has largely replaced azathioprine as the antiproliferative component of triple-drug immunosuppression. Clinical features and dosing of azathioprine are listed in Box 21-11.

Mycophenolate Mofetil

Mycophenolic acid, the immunologically active metabolite of mycophenolate mofetil, potently inhibits guanine synthesis, a critical enzyme in de novo synthesis of purines, by producing reversible noncompetitive inhibition of inosine monophosphate dehydrogenase. Blockade of this pathway for de novo DNA synthesis is unique to human lymphocytes, because most human cells can also synthesize purines for DNA through an alternative salvage purine pathway. Thus, human lymphocytes are uniquely susceptible to the action of mycophenolate mofetil.

Mycophenolate mofetil has greater antiproliferative potency than cyclosporine and has a potentially favorable effect on preventing allograft vaculopathy.103 Its clinical features and dosing are summarized in Box 21-12.

Cyclophosphamide

Cyclophosphamide is an alkylating agent derived from nitrogen mustard; it interferes with DNA replication by alkylating and cross-linking DNA strands. Both B cells and T cells are affected, with greater toxicity on B cells. This feature has prompted substitution of cyclophosphamide for other antiproliferative agents (mycophenolate mofetil or azathioprine) in the presence of antidonor antibodies and recurrent rejection. Its clinical features and dosage are listed in Box 21-13.

Methotrexate

Methotrexate is primarily an antineoplastic agent that has proved effective in treating leukemia, psoriasis, and adult rheumatoid arthritis. It is an analog of folic acid and binds competitively to the enzyme dihydrofolate reductase. This folic acid antagonist inhibits purine synthesis, resulting in inhibition of lymphocyte proliferation as well as other rapidly dividing cell lines. Methotrexate has important effects on both humoral and cellular immunity,126,121,158 and has been used as an effective adjunct to standard immunosuppression for recurrent or persistent acute rejection.519,116 Clinical features and dosing are summarized in Box 21-14.

Sirolimus

Sirolimus is a natural product of the actinomycete Streptomyces hygroscopicus, first isolated from a soil sample collected on Easter Island in 1965.38,55 Sirolimus is a macrolide antibiotic with a structure similar to tacrolimus but with a different mechanism of action. It belongs to a new class of immunosuppressive agents called target of rapamycin (TOR) inhibitors. TOR is a cytoplasmic enzyme that plays a critical role in converting signals from the T-cell surface to the cell nucleus for stimulation of growth and proliferation of
**Box 21-11  Azathioprine**

**Clinical Use**
Maintenance immunosuppression usually combined with either cyclosporine or tacrolimus, with or without steroids.

**Mechanism**
Impairs lymphocyte proliferation by inhibiting purine synthesis.

**Dose**
When used with cyclosporine or tacrolimus, maximum oral dose of 2-2.5 mg·kg⁻¹·day⁻¹. Dose reduced as necessary to maintain white blood cell count above 3000·mL⁻¹.

**Target Levels**
Blood levels not monitored.

**Adverse Effects**
Myelosuppression (leukopenia most common, rarely accompanied by thrombocytopenia and/or anemia). Bone marrow suppression effects may be additive with other myelosuppressive drugs. Hepatic toxicity, pancreatitis, alopecia (uncommon). Malignancies, especially cutaneous, may be more common with chronic therapy. Concomitant use of allopurinol, an inhibitor of xanthine oxidase, may increase myelosuppression. When using allopurinol, azathioprine dose should be reduced to 25% to 33% of pre-allopurinol dose.

From Kirklin and colleagues. ⁶³⁴

**Box 21-12  Mycophenolate Mofetil**

**Clinical Use**
Chronic maintenance immunosuppression with cyclosporine or tacrolimus, with or without corticosteroids. Replaces azathioprine in chronic immunosuppression regimen.

**Mechanism**
Hydrolyzed to mycophenolic acid, the active immunosuppressive component, which inhibits inosine monophosphate dehydrogenase, thereby inhibiting de novo purine synthesis. Selective inhibitory effects on T- and B-cell proliferation.

**Dose**
Begin at 500 mg IV or twice daily PO and progressively increase to a target dose of 1500-1750 mg twice daily if tolerated (gastrointestinal symptoms).

**Target Levels**
2-5 ng·mL⁻¹.

**Adverse Effects**
Gastrointestinal: nausea, vomiting, abdominal pain, diarrhea, loss of appetite, rarely gastric ulceration, gastritis, gastrointestinal bleeding, jaundice, pancreatitis. Leukopenia (uncommon), effects may be additive with other myelosuppressive agents.

From Kirklin and colleagues. ⁶³⁴

**Box 21-13  Cyclophosphamide**

**Clinical Use**
Maintenance immunosuppressive agent; may be substituted for azathioprine if antibody-mediated rejection suspected.

**Mechanism**
Inhibits lymphocyte proliferation by interfering with DNA replication. Inhibits B-cell response.

**Dose**
When used with cyclosporine or tacrolimus, maximum dose is generally 1-1.5 mg·kg⁻¹·day⁻¹. Dose is reduced as necessary to maintain white blood cell count above 3000·mL⁻¹.

**Target Levels**
Blood levels not monitored.

**Adverse Effects**
Myelosuppression with maximal effect at approximately 7-10 days. Bone marrow suppression effects may be additive with other myelosuppressive drugs. Hemorrhagic cystitis, alopecia, gastrointestinal distress, interstitial pneumonitis (rare).

From Kirklin and colleagues. ⁶³⁴

**Box 21-14  Methotrexate**

**Clinical Use**
Maintenance immunosuppressive agent may be substituted for azathioprine or added to mycophenolate in the presence of recurrent or persistent acute rejection.

**Mechanism**
Folic acid antagonist with antiproliferative effects on lymphocyte and other rapidly dividing cell lines.

**Dose**
Adults: 1-5 mg every 8-12 hours for 3 doses per week, generally administered for 3 to 12 weeks as adjunctive therapy.

**Target Levels**
Blood levels are not monitored.

**Adverse Effects**
Major toxicity is bone marrow suppression resulting in leukopenia, anemia, and thrombocytopenia. Other myelosuppressive agents such as azathioprine should be discontinued or reduced when administering methotrexate. Close monitoring of leukocyte counts is important because fatal infection associated with profound bone marrow suppression has occurred in cardiac transplant recipients. Most common side effects include gastrointestinal distress, hepatic toxicity, nephrotoxicity, stomatitis, and hypersensitivity pneumonitis.

From Kirklin and colleagues. ⁶³⁴
lymphocytes. TOR appears to play an important role in both cellular and humoral effector functions. Like cyclosporine and tacrolimus, sirolimus is a prodrug that binds to an immunophilin to exert its immunologic effects. In contrast to cyclosporine and tacrolimus, sirolimus inhibits neither calcineurin phosphates nor production of T-cell cytokines. Instead, it inhibits cell proliferation stimulated by growth factors. The net effect is selective blockade of cytokine signal-mediated cell division and proliferation with arrest of the cell cycle in the G1 phase. Thus, sirolimus acts synergistically with cyclosporine and tacrolimus.

Sirolimus can be combined with cyclosporine or tacrolimus in place of azathioprine or mycophenolate, or it can be added as a fourth agent to control recurrent or refractory rejection. In the presence of important renal dysfunction, it may be substituted for either cyclosporine or tacrolimus and used in combination with steroids and mycophenolate, although risk of rejection is likely increased with this combination. Caution should be observed in administering sirolimus in the first few weeks after transplantation because it may importantly impair wound healing. Its clinical features and toxicity are summarized in Box 21-15.

### Box 21-15 Sirolimus

#### Clinical Use
Maintenance immunosuppression as replacement for a calcineurin inhibitor or as a fourth agent

#### Mechanism
- Inhibition of TOR
- Inhibits T-cell differentiation and proliferation
- Inhibits B-cell activation and proliferation
- Inhibits mesenchymal cell proliferation
- Preserves T-cell apoptosis

#### Dose
2-5 mg · day⁻¹ PO

#### Target Levels
Whole blood trough level of 5-15 ng · mL⁻¹

#### Adverse Effects
- Hypercholesteremia
- Elevated triglycerides
- Thrombocytopenia (dose related)
- Interference with wound healing

Common adverse effects of sirolimus include thrombocytopenia and anaphylaxis. Its clinical features and dosing of ATG are summarized in Box 21-16.

### Box 21-16 Antithymocyte Globulin

#### Clinical Use
Antirejection prophylaxis (induction therapy), steroid-resistant or recurrent rejection, rejection with hemodynamic compromise

#### Mechanism
- Polyclonal anti-T-cell antibody preparation that blocks surface receptors (inhibits TCR/antigenic peptide interaction), impairs effectiveness of antigen-presenting cells, destroys T lymphocytes

#### Dose
Specifics regarding dosage, premedications, and hypersensitivity testing vary according to specific antithymocyte preparation.

#### Monitoring
- T-cell counts below 10% of pretreatment levels, but not routinely measured in many transplant centers

#### Adverse Effects
- Thrombocytopenia, arthralgias, edema, hives, fever, chills; vary according to preparation
- Rarely major systemic reactions, including hypotension, anaphylaxis, respiratory distress, serum sickness

From Kirklin and colleagues. Key: TCR, T-cell receptor.

Viral infections, particularly cytomegalovirus. Therefore, prophylactic valganciclovir should be administered following a course of ATG therapy.

The current available commercial preparation in the United States is a rabbit ATG (thymoglobulin). The reconstituted preparation contains 5 mg of thymoglobulin, of which greater than 90% is rabbit gamma immune globulin. The standard dose of 1.5 mg · kg⁻¹ · day⁻¹ is infused through a central venous catheter over 4 to 6 hours and administered for 5 to 14 days. Clinical features and dosing of ATG are summarized in Box 21-16.

#### Monoclonal Antibodies
Monoclonal antibodies offer a potential advantage over polyclonal preparations (which lack specificity) because their specificity provides a means by which certain cell surface molecules can be targeted. The mechanism by which immunosuppression and associated side effects occur depends on the target of the antibody and isotype and species used to generate the antibody. Monoclonal antibodies are typically derived from mice or rats, but some antibodies, such as the current anti-IL2 receptor drugs, are “humanized” in that the portions of the genes that do not code for the antigen-binding regions of the mouse monoclonal antibody have been removed and replaced with portions of a human antibody molecule. This tends to decrease the allergenic side effects of the monoclonal preparation.

#### OKT3 (Anti-CD3)
The CD3 antigen is present on essentially all mature T lymphocytes and is closely linked to the antigen recognition site of the T-cell receptor. Following engagement of the T-cell receptor to an antigen outside the cell, the CD3 complex transmits an intracellular signal that initiates T-cell activation.
**Box 21-17  OKT3**

**Clinical Use**
Antirejection prophylaxis (induction therapy), steroid-resistant or recurrent rejection, rejection with hemodynamic compromise

**Mechanism**
Monoclonal anti-CD3 antibody that blocks alloantigen recognition by modulating or depleting CD3 molecules from T-cell surfaces

**Dose**
2.5-5 mg IV daily, usually for 7-14 days

**Monitoring**
Measurement of T-cell markers, with a target suppression of CD3+ cells to an absolute cell count of <10 cells · mL−1 and less than 5% of total lymphocytes

**Adverse Effects**
Cytokine release syndrome: fever, chills, headache, nausea, myalgias, mild hypertension; rarely, bronchospasm and profound hypotension
Production of antimurine antibodies
Increased susceptibility to cytomegalovirus infection and posttransplant lymphoproliferative disorder, particularly with repeat or prolonged administration

From Kirklin and colleagues.

OKT3 is a murine monoclonal antibody specific for the portion of the CD3 complex involved in transmembrane signaling following binding of an antigen-MHC complex. Because CD3 is expressed only on T cells, administration of OKT3 depletes CD3 cells from the peripheral blood in 30 to 60 minutes. Although some of the cells undergo phagocytosis with subsequent removal by the reticuloendothelial system, many T lymphocytes undergo modulation, in which shedding or capping of the CD3 complex occurs without cell death. When OKT3 is discontinued and antibody level falls below therapeutic levels, T lymphocytes can reexpress the CD3 molecule on the T-cell receptor complex within a few hours. This phenomenon of rapid reappearance of CD3+ cells soon after discontinuation of therapy (which does not occur after treatment with polyclonal ATG), coupled with clinical observations of occasional acute rejection within 1 week of ending OKT3 therapy, have prompted some programs to routinely augment steroid doses for several days after completion of OKT3 therapy.

OKT3 is used primarily as induction therapy or in treating acute or refractory rejection. Its clinical features and dosing are summarized in Box 21-17.

**Anti-CD25 (Basiliximab, Daclizumab)** The two anti-CD25 antibodies currently available, basiliximab and daclizumab, are humanized IgG1 monoclonal antibodies that bind specifically to the α chain (Tac subunit) of the high-affinity IL-2 receptor on activated T lymphocytes. They contain approximately 90% human and 10% murine antibody sequences. These antibodies compete with the cytokine IL-2 for occupancy of the IL-2 receptor. Secretion of IL-2 by an activated T cell serves to recruit other T cells by stimulation and clonal expansion of a specific T-cell population. These anti–IL-2 receptor monoclonal antibodies are designed to be used with a calcineurin blocking agent (cyclosporine or tacrolimus) to decrease the amount of IL-2 that would be available for any unblocked IL-2 receptors. Clinical features and dosing of anti-CD25 monoclonal antibodies are presented in Box 21-18.

**Box 21-18  Anti-CD25 Monoclonal Antibodies**

**Clinical Use**
Anti-rejection prophylaxis (induction therapy)

**Mechanism**
Monoclonal anti-CD25 antibody against the interleukin (IL)-2 receptor on T lymphocytes

**Dose**
Basiliximab: administer 20 mg IV following completion of cardiopulmonary bypass. A repeat dose of 20 mg IV is administered on postoperative day 4.
Daclizumab: administer 1 mg · kg−1 IV within 24 hours before transplantation and every 14 days for 4 additional doses.

**Monitoring**
None is used clinically.

**Adverse Effects**
No serious adverse reactions have been reported.

From Kirklin and colleagues.

Plasmapheresis involves removing blood from the patient, separating plasma by centrifugation or membrane filtration, and reconstituting the remaining blood to the original volume with fresh plasma or 5% albumin. In treating acute rejection, plasmapheresis has been effective in removing antibodies (antibody-mediated rejection) as well as soluble mediators potentially released during acute rejection, including IL-1, IL-6, TNF-α, and the anaphylatoxin C3a. Some of these mediators, such as TNF-α and IL-1, have a direct depressant effect on myocyte contractility, and improved ejection fraction following plasmapheresis has been observed frequently in the setting of hemodynamically compromising rejection.

The technique of plasmapheresis requires a large-bore indwelling catheter inserted into the internal jugular, subclavian, or femoral vein. Although complement-mediated reactions occasionally occur during plasmapheresis, side effects are generally mild. The potential for bleeding complications appears to be low as long as the fibrinogen level is maintained above 100 mg · dL−1.

When used clinically to treat rejection with hemodynamic compromise, plasmapheresis is generally performed for 3 successive days as long as the fibrinogen level remains above 100 mg · dL−1.

When antidonor antibodies are identified in the recipient, plasmapheresis is also used following cardiac transplantation, usually at weekly intervals until these antibodies are no longer detectable.

**Immunoabsorption**
Whereas plasmapheresis is a passive process in which immunoglobulins pass through the filtration membranes with the
Photopheresis

Photopheresis is an immunomodulatory therapy based on leukapheresis. It involves drawing blood, separating the whole blood by centrifugation, and returning the red cells and plasma to the patient. Leukocytes are treated with 8-methoxypsoralen, a photosensitizing agent, and exposed to ultraviolet light in the photoactivation chamber. These treated leukocytes are then returned to the patient (Fig. 21-11).

The mechanism of action of photopheresis has not been clearly delineated, but available evidence suggests that photopheresis induces apoptosis of leukocytes that, when reinjected into the patient, are phagocytized by dendritic cells in the circulation and in lymphoid tissue. The photoactivation process induces cross-linking of DNA, which is known to induce apoptosis of lymphocytes, monocytes, macrophages, and B cells. Recent data suggest that virtually all cells become apoptotic following extracorporeal photopheresis, even terminally differentiated and slowly proliferating or non-proliferating cells such as antigen-presenting cells. Studies of extracorporeal photopheresis in a mouse heart transplant study by George and colleagues suggest that photopheresis alters the composition of recipient T lymphocytes toward a greater preponderance of T-regulatory cells, which promote down-regulation of graft-infiltrating T cells. In the mouse model, the majority of photopheresis-treated cells are phagocytized in the spleen and liver within 24 hours. Extracorporeal photopheresis reduces the infiltration of graft-specific T cells without affecting the frequency of graft-reactive T cells in the peripheral lymph nodes. Thus, based on these studies, extracorporeal photopheresis appears to alter the composition of recipient T cells toward a greater preponderance of T-regulatory cells, down-regulating a greater proportion of graft-infiltrating T cells.

A clinical study of photopheresis indicated that among patients at high risk for rejection, risk of hemodynamically compromising (HC) rejections or rejection-related death per 100 patients-year \(^3\). The upper curve (“Pre-photo risk”) represents the hazard function for this event among high-risk patients for rejection prior to photopheresis. The next lower curve (“Post-photo risk”) represents the hazard function for this group of patients following photopheresis. The lowest curve represents risk of HC rejection or rejection death among patients at low risk for rejection. (From Kirklin and colleagues.)

removed plasma, immunoabsorption involves removing specific antibodies using columns containing immunoabsorbents that specifically bind to immunoglobulins. Some centers use immunoabsorption techniques in the presence of recipient anti-HLA class I antibodies against the donor heart. Improved ejection fraction and decrease in PRA following acute vascular rejection have been reported with this therapy.
against the allograft. The result is an increase in the proportion of natural regulatory T cells in the cardiac allograft.

**Total Lymphoid Irradiation**

Total lymphoid irradiation (TLI) is low-dose radiotherapy that targets lymphoid tissues, including the cervical, axillary, mediastinal, periaortic, and iliofemoral lymph nodes, thymus, and spleen. Nonlymphoid tissue is shielded during treatment. The exact mechanisms by which TLI induces the immune response remain unclear, but it is known that radiation induces cell death from alterations in configuration of DNA, producing chromosomal breakage, translocations, and damage to purine and pyrimidine base pairs. Both T cells and B cells are susceptible to radiation injury.

TLI therapy, usually in combination with other immunosuppressive modalities, induces an initial depression in lymphocyte count that recovers after 3 to 4 months. However, the distribution of T-cell subpopulations and their expression of surface antigens show long-term changes. Some have hypothesized that TLI induces a population of natural suppressor cells that have similarities to NK cells.

TLI dosage includes three separate fields that provide radiation to all major lymphoid-bearing areas. These areas are treated with a total target dose of 800 cGy using twice-weekly doses of 80 cGy each. Azathioprine or other myelosuppressive agents are discontinued just prior to initiation of TLI to reduce radiation-induced bone marrow suppression. The treatment schedule is adjusted according to white blood cell and platelet counts.

TLI has been used extensively for refractory or severe rejection in both cardiac and renal transplantation. Donor-specific unresponsiveness to donor antigens has been demonstrated 18 to 30 months following renal transplantation with pretransplant TLI and ATG. TLI therapy has been effective in decreasing rejection frequency in adults and children following cardiac transplantation.

The most common toxicity includes leukopenia and thrombocytopenia, which are usually reversible with temporary cessation of therapy. An unknown long-term risk of malignancy may exist. A specific risk of fatal acute megakaryocytic leukemia was noted in one large series of patients treated with TLI after cardiac transplantation, with actuarial prevalence of 9% at 5 years.

**RESULTS**

**Rejection**

**Mechanisms**

Cardiac allograft rejection represents the histologic and clinical result of the immunologic response (see “Immunologic Basis of Heart Transplantation” earlier in this section) to cardiac transplantation. Potential target cells within the heart include, among others, myocytes and endothelial cells of the coronary vasculature. Donor peptide antigens provide the stimulus for the recipient alloimmune response through their presentation by donor antigen-presenting cells (donor vascular endothelial cells and so-called passenger leukocytes) and recipient antigen-presenting cells. Multiple redundant immunologic pathways exist for activation of the immune response and subsequent attack on the donor organ. The presentation of donor antigens (by antigen-presenting cells) to the appropriate recipient T cells leads to T-cell activation and clonal proliferation in the presence of appropriate co-stimulatory molecules. The vascular endothelium participates directly in the rejection process by recruiting immune cells to the allograft. Up-regulation (increased concentration on the cell surface) of endothelial molecules induces circulating activated lymphocytes to stick to the endothelial surface and migrate into the interstitial spaces of the allograft. Activated T cells generate and release cytokines, which together with up-regulation of T-cell surface receptors induces proliferation of immune cells and recruitment of macrophages. If unabated by immunosuppressive agents, these events result in release of powerful biological effectors of myocyte injury and necrosis, recognizable by histologic examination.

Success of cardiac transplantation (and organ transplantation in general) is based on the premise that immunosuppressive modalities can effectively suppress those aspects of the immune system that, when stimulated by donor HLA antigens, ultimately lead to destruction of the donor heart. The process of controlling and potentially preventing otherwise fatal allograft rejection to promote long-term survival and function of the transplanted heart involves initial immunosuppression, chronic maintenance immunosuppression, and augmentation or adjustment of immunosuppression during episodes of identified acute rejection. Because immunosuppressive agents have considerable toxicity, long-term patient survival requires a combination of immunosuppressive agents that act in concert or even synergistically against those aspects of the immune system that threaten the allograft, while minimizing their toxic effects on the overall immune system (which would set the stage for infections and malignancies) in other organ systems.

The difficulty of this task is confounded by considerable variability among patients with respect to the intensity of their immune response against the allograft and their susceptibility to immunosuppression-related morbidity.

Despite the current profound understanding of the immune response to transplantation and the myriad drugs available for targeted immunosuppression, many details of the precise inciting factors for acute rejection remain enigmatic. Patients can experience long periods (sometimes years) of apparent immunounresponsive (clinical and histologic absence of rejection criteria), only to suddenly experience a vigorous and potentially fatal immunologic attack, with no known precipitating event. The tendency for patients to display overt evidence of rejection only episodically is incompletely understood, but extensive clinical experience supported by surveillance endomyocardial biopsies indicates that the rejection process occurs in “waves” of heightened immunologic activity within the allograft. Although infectious agents (particularly viral) and possibly stress have been implicated at times, an inciting stimulus is usually never identified.

**Pathology of Allograft Rejection**

The technique of endomyocardial biopsy, based on techniques first described by Caves histologic examination of myocardial tissue, has provided the gold standard for diagnosing rejection since 1972. The histologic grading system for rejection initially developed by Billinghan at Stanford was further refined in 1990 by the International Society of Heart and Lung Transplantation (ISHLT), most recently in 2005 (Table 21-7). Rejection grades are based mainly on amount of inflammatory infiltrate and presence of myocyte damage (see Table 21-7). The major histologic...
categories of acute rejection are cellular, humoral, and hyperacute rejection.

**Acute Cellular Rejection** Histologically, acute cellular rejection is a mononuclear inflammatory response, predominantly lymphocytic, directed against the cardiac allograft. Usually both ventricles are equally involved, and thus sampling of the right ventricular septum is usually representative of histologic changes occurring elsewhere in the heart. The key identifying histologic feature of cellular rejection of sufficient severity (moderate) to warrant augmentation of immunosuppression is the presence of myocyte damage.

**Humoral (Microvascular) Rejection** In heart transplantation, humoral rejection refers to rejection resulting from immunoglobin (antibody) directed against donor antigens located on the endothelial surface of the allograft coronary microvasculature. Immunoglobin and complement are localized in the microvasculature of the transplanted heart—arterioles, capillaries, and venules. The resulting inflammatory process with neutrophils and macrophages involves the vessel wall. These inflammatory changes can be seen on endomyocardial biopsy. The hallmarks of microvascular rejection are endothelial cell activation, increased vascular permeability, and in severe forms, microvascular thrombosis and myocardial cell degeneration. Immunofluorescence studies are currently the primary modality for identifying fibrinogen, IgG, IgM, and complement components in the endomyocardial biopsy, which indicates humoral rejection. Histologic and immunofluorescence criteria for identifying humoral rejection are summarized in Table 21-8. However, it should be noted that the reproducibility of these studies is considerably less than the standard histologic methodology for identifying acute cellular rejection.

**Hyperacute Rejection** Hyperacute rejection (currently rarely observed) consists of a violent lethal immunologic attack on the allograft triggered by preformed antibodies against HLA epitopes in the donor heart or antibodies against the ABO system (in the event of inadvertent transplantation across a major blood group incompatibility). Rarely, hyperacute rejection may result from antienothelial antibodies. Activation of the complement cascade produces severe endothelial cell damage, platelet activation, initiation of the clotting cascade, and widespread microvascular thrombosis, all of which leads uniformly to graft loss. The process begins within minutes of graft reperfusion in the operating room. With current techniques of identifying preformed anti-HLA antibodies and crossmatching, hyperacute rejection is rarely observed.

**Other Diagnostic Modalities**
Although electrocardiographic analysis, cytoimmunologic monitoring, and a variety of radionuclide techniques have been investigated, echocardiography is the primary modality (other than endomyocardial biopsy) routinely used for rejection surveillance.

The most important application of echocardiography is identifying systolic dysfunction. Even though left ventricular rejection remains within normal limits during 95% of histologic rejection episodes, acute rejection is overwhelmingly the major cause of acute reduction in systolic function of the transplanted heart after initial recovery from transplantation. Other causes include advanced allograft vasculopathy, nonspecific unexplained graft failure without rejection or vasculopathy, and rarely infection. When acute depression of systolic function (ejection fraction < 50%) is observed without another clearly identified cause, acute cellular or humoral rejection should be assumed to be present and appropriately treated, with or without confirmation from endomyocardial biopsy.

**Temporal Pattern and Risk Factors for Rejection**
Although allograft rejection is the major biological phenomenon that limits long-term survival after cardiac...

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### Table 21-7 ISHLT Standardized Cardiac Biopsy Grading: Acute Cellular Rejection

<table>
<thead>
<tr>
<th>2004</th>
<th>1990</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0 R</td>
<td>No Rejection</td>
</tr>
<tr>
<td>Grade 1 R, mild</td>
<td>Intestinal and/or perivascular infiltration of myocyte damage</td>
</tr>
<tr>
<td>Grade 1, mild</td>
<td>A-Focal</td>
</tr>
<tr>
<td>Grade 2, moderate</td>
<td>Two or more foci of infiltration with associated myocyte damage</td>
</tr>
<tr>
<td>Grade 2, moderate (focal)</td>
<td>A-Focal</td>
</tr>
<tr>
<td>Grade 3, severe</td>
<td>Diffuse infiltrate with multifocal myocyte damage ± edema ± hemorrhage ± vasculitis</td>
</tr>
<tr>
<td>Grade 4, severe</td>
<td>Different infiltrate with extensive myocyte damage ± edema, ± hemorrhage ± vasculitis</td>
</tr>
</tbody>
</table>

*Data from Stewart and colleagues.*

1. Presence or absence of acute antibody-mediated rejection (AMR) may be recorded as AMR 0 or AMR 1, as required.
2. Where R denotes revised grade to avoid confusion with 1990 scheme.

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### Table 21-8 ISHLT Recommendations for Acute Antibody-Mediated Rejection

<table>
<thead>
<tr>
<th>AMR 0</th>
<th>AMR 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative for acute antibody-mediated rejection</td>
<td>Positive for AMR</td>
</tr>
<tr>
<td>No histologic or immunopathologic features of AMR</td>
<td>Histologic features of AMR</td>
</tr>
<tr>
<td>Positive immunofluorescence or immunoperoxidase staining for AMR (positive CD68, C4d)</td>
<td></td>
</tr>
</tbody>
</table>

*Data from Stewart and colleagues.*

Key: *AMR, Antibody-mediated rejection; ISHLT, International Society for Heart and Lung Transplantation.*
transplantation, an understanding of the temporal pattern and risk factors for rejection is handicapped by the time of onset and resolution as well as the actual presence of rejection. Although endomyocardial biopsy is the gold standard for identifying rejection, it only allows intermittent sampling rather than continuous surveillance. The potential for sampling error, the reality of rejection episodes that spontaneously resolve and are never identified histologically, and the general practice of decreasing the frequency of endomyocardial biopsies after the first year complicate our understanding of this event. For practical purposes, most clinicians and investigators define a rejection episode as a clinical event that is usually, but not always, accompanied by an abnormal myocardial biopsy and results in acute and temporary augmentation of a patient’s immunosuppression.

The frequency of rejection episodes tends to decrease with increasing time from transplantation, related in part to the acquired state of partial unresponsiveness achieved with current maintenance immunosuppression. Approximately two thirds of patients have one or more identified rejection episodes within the first year (Fig. 21-13). The hazard function (instantaneous risk) for initial rejection peaks at 1 to 2 months, then rapidly decreases thereafter, merging with a low constant risk of rejection after about 1 year.

Of greater concern are those patients who suffer recurring rejection, with the need for repeated augmentation of immunosuppression, possibility of hemodynamic compromise secondary to graft dysfunction, increased risk of infection, and potential contribution to allograft vasculopathy. Risk factors for earlier initial rejection and for increased cumulative rejection during the first year are listed in Tables 21-9 and 21-10. Risk factors for recurrent rejection during the first posttransplant year are listed in Table 21-11.

High-Risk Forms of Rejection

The highest-risk form of rejection is hyperacute rejection, discussed in the preceding text. Certain other forms of acute rejection are associated with risk of graft loss and death. These forms may be primarily cellular or humoral, with considerable overlap because they are categorized by the method of identifying rejection (Box 21-19).

When vasculitis (transmural anterior wall infiltration of lymphocytes and monocytes with or without neutrophils) is identified on endomyocardial biopsy, or when there is evidence of humoral rejection by immunofluorescence studies, an increase in subsequent mortality has been identified, with 1-year mortality exceeding 30% in some studies. Similarly, when aggressive histologic grades of cellular rejection (Grade 3B or 4) are identified on endomyocardial biopsy, the likelihood for progression to hemodynamic compromise and graft loss is high without prompt aggressive immunosuppressive intervention.

<table>
<thead>
<tr>
<th>Table 21-9</th>
<th>Incremental Risk Factors for Earlier Initial Rejection after Transplantation (CTRD 1990-1992, n = 1719)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk Factor</strong></td>
<td><strong>P</strong></td>
</tr>
<tr>
<td><strong>Early Phase</strong></td>
<td></td>
</tr>
<tr>
<td>Younger age (among adult recipients)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Female gender (donor and recipient)</td>
<td>.0006</td>
</tr>
<tr>
<td>If white recipient, higher number of HLA mismatches</td>
<td>.01</td>
</tr>
<tr>
<td><strong>Constant Phase</strong></td>
<td></td>
</tr>
<tr>
<td>Black recipient</td>
<td>.04</td>
</tr>
</tbody>
</table>

Modified from Jarcho and colleagues. Key: CTRD, Cardiac Transplant Research Database.

<table>
<thead>
<tr>
<th>Table 21-10</th>
<th>Incremental Risk Factors for Increased Cumulative Rejection Episodes during First Year after Transplantation (CTRD 1990-1992, n = 1719)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk Factor</strong></td>
<td><strong>P</strong></td>
</tr>
<tr>
<td><strong>Demographic (Recipient)</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>.01</td>
</tr>
<tr>
<td>Black</td>
<td>.0009</td>
</tr>
<tr>
<td><strong>Induction Therapy</strong></td>
<td></td>
</tr>
<tr>
<td>Use of OKT3</td>
<td>.003</td>
</tr>
<tr>
<td><strong>Events during First Year</strong></td>
<td></td>
</tr>
<tr>
<td>Greater number of rejections</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Prior cytomegalovirus infections</td>
<td>.003</td>
</tr>
</tbody>
</table>

Modified from Kubo and colleagues. Key: CTRD, Cardiac Transplant Research Database.

<table>
<thead>
<tr>
<th>Table 21-11</th>
<th>Incremental Risk Factors for Recurrent Rejection during First Year after Transplantation (CTRD 1990-1993, n = 1251)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Risk Factor</strong></td>
<td><strong>P</strong></td>
</tr>
<tr>
<td><strong>Demographic (Recipient)</strong></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>.01</td>
</tr>
<tr>
<td>Black</td>
<td>.0009</td>
</tr>
<tr>
<td><strong>Induction Therapy</strong></td>
<td></td>
</tr>
<tr>
<td>Use of OKT3</td>
<td>.003</td>
</tr>
<tr>
<td><strong>Events during First Year</strong></td>
<td></td>
</tr>
<tr>
<td>Greater number of rejections</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Prior cytomegalovirus infections</td>
<td>.003</td>
</tr>
</tbody>
</table>

Modified from Kubo and colleagues. Key: CTRD, Cardiac Transplant Research Database.
Mortality after rejection with hemodynamic compromise

Box 21-19 High-Risk Form of Rejection

Grade 3B or 4 rejection on biopsy
Vasculitis and evidence of humoral rejection on biopsy
Rejection with hemodynamic compromise
Acute rejection in the presence of circulating antidonor antibodies

Figure 21-14 Mortality after rejection with hemodynamic compromise. Upper curves represent actuarial survival after rejection associated with severe hemodynamic compromise, stratified according to biopsy score at beginning of rejection. “Low score” includes biopsy scores of 2 or less and “High score” biopsy scores of 3A or higher. Lower two curves represent hazard function for death after onset of rejection, stratified by biopsy score. Dashed lines enclose 70% confidence limits. Key: CTRD, Cardiac Transplant Research Database. (From Mills and colleagues.11)

Approximately 5% of rejection episodes are accompanied by hemodynamic compromise, as evidenced by clinical signs of low cardiac output, decreased ejection fraction on echocardiography, or decreased cardiac output. When inotropic agents are required to support the circulation, this serious form of rejection can be rapidly fatal if not promptly reversed. Although the mechanism of depressed systolic function is unclear, experimental studies indicate that IL-1, IL-2, and TNF may contribute.11,12,13,31 When hemodynamic compromise is associated with acute cellular rejection histology, mortality from rejection within the subsequent 2 years is about 20%. Prognosis is particularly ominous when clinical rejection with hemodynamic compromise is associated with absence of cellular rejection on biopsy, because it indicates a higher likelihood of humoral rejection. Such patients have a risk of death exceeding 50% within 2 years (Fig. 21-14).11,12,13,31

In the presence of circulating antidonor HLA antibodies, the probability increases that acute rejection will involve humoral components,11 which increases risk of subsequent rejection-related death or graft loss.11

Identifying a Rejection Episode

A major part of care after cardiac transplantation is directed toward identifying rejection. Endomyocardial biopsy remains the most important method of identification and, along with echocardiographic evaluation, is generally performed every 7 days for the first 4 to 6 postoperative weeks. Thereafter, biopsy frequency is gradually reduced to every 3 to 4 months. However, physicians caring for these patients must be aware that subtle symptoms may be the only clue to the beginning of a rejection episode. These include unexplained fever, joint pain, personality change, and any symptom that can result from cardiac failure. These are an indication for emergency endomyocardial biopsy and immediate institution of therapy if results are positive.

Treatment of Acute Rejection

When a rejection episode is identified during the first postoperative month, particularly when accompanied by any hemodynamic deterioration, treatment includes hospitalization. Otherwise, treatment can be accomplished on an outpatient basis with close surveillance.11 Decision about an inpatient or outpatient setting for treatment and the details of the treatment itself need to be made by experienced transplant physicians.

Augmenting steroid therapy is the mainstay of treating an acute rejection episode (see “Immunosuppressive Therapy” in text that follows). When the patient is treated as an outpatient, the daily prednisone dosage is increased to 100 mg in adults for 5 days. Generally, the dose is then reduced by 10 mg · day−1 until the previous maintenance dose is reached.

When treatment is given in the hospital, methylprednisolone is administered IV (usually into a peripheral vein) for 3 days in a dose of 1000 mg · day−1 (or 15 mg · kg−1 if the patient weighs < 50 kg). This is followed by prednisone 100 mg by mouth (PO) for 2 days, which is reduced thereafter by 10 mg daily until the prior maintenance dose is reached.

If the rejection episode is unresponsive, recurrent early after transplantation, or associated with high-risk features, ATG for 5 to 7 days may be added. Other measures that may be used for an unremitting episode include changing from azathioprine to mycophenolate mofetil, changing from cyclosporine to tacrolimus, treating with pulse steroids without a taper, methotrexate, plasmapheresis, photopheresis, and even total lymphoid irradiation. Decisions regarding treatment modality depend on histologic grade of biopsy, left ventricular dysfunction, time since transplantation, and prior modalities used.

When the rejection episode is believed to have been resolved, another endomyocardial biopsy is obtained. If only mild rejection is present, the episode is considered to have resolved, but this is confirmed by frequent biopsies over the next 3 months.

When the hemodynamic state becomes unstable and the rejection episode is severe and unremitting, maximal treatment must be directed toward the immunosuppressive modalities described earlier while simultaneously supporting the circulation with inotropic agents. A general therapeutic strategy for rejection with hemodynamic compromise is outlined in Box 21-20. When treating recurrent or severe rejection with augmented immunosuppression, the increased risk of infection and of tumor formation, particularly lymphomas, must be appreciated and surveillance methods heightened.

Infection

The Immunocompromised Host

The requirement for long-term immunosuppressive therapy and the resultant immunocompromised host predispose
Box 21-20 Therapeutic Strategy for Rejection with Hemodynamic Compromise

- Always consider this a life-threatening event.
- Methylprednisolone 1 g IV and daily for 3 days.
- Prompt inotropic support (preferably with dopamine, milrinone, or dobutamine, depending on blood pressure and heart rate) to maintain effective cardiac output.
- If cardiac output is clinically depressed and/or there is more than mild decrease in ejection fraction (<35%), place Swan-Ganz catheter for hemodynamic monitoring.
- Prompt plasmapheresis (patients > 15 kg) and daily for 3 days.
- Cytolytic therapy with thymoglobulin or OKT3.
- Heparinize.
- Continue maintenance immunosuppression.
- Schedule photopheresis.

From Kirklin and colleagues.

Risk Factors, Prevalence, and Evaluation

Approximately 40% of recipients suffer one or more infections requiring IV antibiotics, hospitalization, or both during the first year after transplantation. In the current era, most infections are successfully treated, with an overall mortality from infection of less than 5% during the first year. Risk factors for developing posttransplant infection are listed in Table 21-12. 

Table 21-12 Incremental Risk Factors for First Posttransplant Infection (CTRD 1/1/1990-6/30/1993, n = 2210)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Early Phase</th>
<th>Constant Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (older)</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Clinical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventilator at transplantation</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>VAD at transplantation</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Induction therapy: OKT3</td>
<td>&lt;.0001</td>
<td></td>
</tr>
<tr>
<td>Donor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cytomegalovirus (positive)</td>
<td>.0007</td>
<td></td>
</tr>
<tr>
<td>Black race</td>
<td>—</td>
<td>.0007</td>
</tr>
</tbody>
</table>

Data from Smart and colleagues. Key: CTRD, Cardiac Transplant Research Database; VAD, ventricular assist device.

Figure 21-15 Hazard function (instantaneous risk over time) for first infection of each major category of infectious agent. Key: TCRD, Transplant Cardiologists Research Database. (From Miller and colleagues.)

Heart transplant recipients to unusual organisms that may induce aggressive and sometimes fatal infections. A broad range of organisms may be involved, including the usual pathogens, organisms that are not usually a cause of infection except in immunocompromised hosts, and endogenous and donor-transmitted organisms. A proactive policy to detect infection is necessary because of the frequent blunting of usual infection signs and symptoms secondary to blunting of the normal inflammatory response by immunosuppressive medications. Infectious complications are closely linked to other posttransplant adverse events, such as malignancy (Epstein-Barr virus), allograft vasculopathy (cytomegalovirus), and acute rejection.

Risk Factors, Prevalence, and Evaluation

Approximately 40% of recipients suffer one or more infections requiring IV antibiotics, hospitalization, or both during the first year after transplantation. In the current era, most infections are successfully treated, with an overall mortality from infection of less than 5% during the first year. Risk factors for developing posttransplant infection are listed in Table 21-12. In the current era, most infections are successfully treated, with an overall mortality from infection of less than 5% during the first year. Risk factors for developing posttransplant infection are listed in Table 21-12. The time course differs for various categories of infectious agents, with bacterial infections predominating during the first month and viral infections predominating thereafter (Fig. 21-15). Bacterial and viral infection each account for about 40% of infections during the first year, whereas about only 5% are fungal or protozoal. The periods of greatest risk for bacterial, viral, protozoal, and fungal infections have particular relevance in terms of diagnostic procedures and expectant therapy. Because of the tendency for febrile responses to be attenuated in the early phase of infectious diseases by corticosteroids (frequently part of maintenance immunosuppression), even low-grade fevers should precipitate thorough investigation for infectious etiologies.

Lung and urinary tract are the most common sites of infection during the first year, accounting for about 35% and 25% of infections, respectively. Despite the prevalence of certain disease types or locations, unusual organisms, locations, and modes of presentation must always be considered in the immunocompromised patient. Initial investigation should include a careful and thorough history and physical examination, chest radiogram, complete blood cell count, and bacterial, viral, and fungal blood cultures. Other cultures should be directed by the initial evaluation. Any new or worsening pulmonary infiltrate should prompt early bronchoscopy with bronchoalveolar lavage and transbronchial biopsy. Pneumocystis carinii and cytomegalovirus are the most common nonbacterial pathogens detected on bronchoalveolar lavage. If biopsy and lavage do not produce a likely etiologic organism, open lung biopsy should be considered. Fever during the first posttransplant month should also prompt thorough evaluation of the sternotomy wound, including computed tomographic scanning. The risk of sternal infection is increased with use of a ventricular assist device as bridge-to-transplant therapy.
Bacterial Infections

The most common bacterial infections in the early postoperative period are pneumonias, indwelling IV line infections, and (less commonly) wound infections. Patients requiring ventilator support immediately before transplantation are at high risk for posttransplant pneumonia. Central venous catheters should be removed within the first 5 days posttransplantation when feasible, because bacteremia is common with prolonged indwelling central catheters. Sternal wound infections account for about 5% of serious early infections, and the risk of mortality associated with mediastinal infection approaches 20%. Early, aggressive sternal debridement and pectoralis muscle coverage play a critical role in controlling infection, enabling early mobility and reducing mortality.

Viral Infections

Cytomegalovirus (CMV) is the predominant viral pathogen causing disease in the first 3 months after cardiac transplantation. Prevalence of a positive CMV serology ranges from 40% to 80% in transplant recipients prior to transplantation. Risk factors for development of posttransplant CMV infection include use of a heart from a donor positive for CMV serology when transplanted into a CMV-negative recipient, and use of induction therapy with monoclonal antibodies or ATG. Risk of CMV transmission is reduced by using leukocyte filters when transfusing blood and by using prophylactic valganciclovir for the first several months after transplantation.

CMV infection can affect multiple organs, resulting in many clinical presentations, including a symptomatic rise in antibody titer, a systemic febrile illness with malaise and lethargy, identification of CMV antigenemia in an asymptomatic patient, or localized disease in a specific organ. The most common site for localized disease is the lung (usually with pulmonary infiltrate, shortness of breath, and hypoxemia), followed by the gastrointestinal tract (fever, diarrhea, ulceration, and occasionally major gastrointestinal bleeding). Hepatic involvement is manifest as hepatitis. Ophthalmic involvement may result in chorioretinitis with possible subsequent blindness. CMV infection is associated with accelerated rates of allograft vasculopathy and rejection. Any CMV infection should be considered life threatening and requires specific aggressive therapy. The therapy of choice for preserving renal function and reducing bone marrow suppression is valganciclovir.

Epstein-Barr virus (EBV) is discussed later in this section under “Malignancy.”

Parvovirus infection requires special mention because of its association with bone marrow depression and development of pancytopenia in children. Parvovirus may result in fifth disease, with a typical blotchy maculopapular rash and mild systemic symptoms. The diagnosis may be confirmed by use of polymerase chain reaction studies of the parvovirus gene in circulating lymphocytes or bone marrow tissue. Treatment with hyperimmune globulin is usually effective.

Fungal Infections

Opportunistic fungal infections account for a small percentage of infections, but invasive fungal infection carries a mortality of 30% or more. Although there is an early posttransplant peak of risk (see Fig. 21-15), invasive fungal infection can occur at any time following transplantation. Its development usually results from breakdown of specific and nonspecific host defenses, such as breaching of skin and mucosal barriers, immunosuppression with impairment of nonspecific defenses (phagocytic cells), disruption of humoral and cellular immunity, and fungal overgrowth in the presence of prolonged broad-spectrum antibiotic administration. The most frequently occurring fungal infections are due to Candida, Aspergillus, Pneumocystis jirovecii (carinii), and Cryptococcus neoformans. Candida is more commonly involved in sternal wound or bloodstream infections from breakdown of mucosal barriers. Aspergillus infections are primarily pulmonary, and cryptococcal infections involve the CNS (but can be disseminated). P. jirovecii is an organism of low virulence in non-immunocompromised patients, found in the lungs of humans and a variety of animals. The taxonomy of P. jirovecii has been controversial, but it is currently grouped with fungi rather than protozoa. It remains unclear whether patients with pneumocystic pneumonia represent primary or reactivation infections, because no reliable skin test or serology assay is available. Therefore, continuous prophylaxis may be indicated for patients with prior pneumocystic infection. Patients typically present with worsening diffuse pulmonary infiltrates, progressive hypoxemia, and marked dyspnea. Silver stains of pathologic specimens from bronchoalveolar lavage are diagnostic. The preferred therapy is high-dose trimethoprim/sulfamethoxazole for 4 to 6 weeks. Pulmonary support with mechanical ventilation may be required, and renal function must be closely observed during treatment. A CMV infection commonly occurs with Pneumocystis pneumonia, and therefore empirical therapy is warranted while results of CMV stains of pathologic specimens and CMV cultures are pending.

Protozoal Infections

Although protozoal infections can occur in any immunocompromised patient, toxoplasmosis is of specific importance in heart transplantation, because it most often occurs as a donor-transmitted disease when a seronegative recipient receives an infected organ. Disease onset occurs 4 to 8 weeks after transplantation and may be manifested as myocarditis, fever, pneumonitis, or (rarely) encephalitis. Therapy of choice includes pyrimethamine and sulfadiazine. Untreated symptomatic toxoplasmosis in cardiac transplant recipients is usually fatal.

Infection Prophylaxis

Antimicrobial prophylaxis after heart transplantation is an integral part of infection prevention, and the benefit has clearly outweighed the disadvantages (toxicity and antimicrobial resistance). A recommended antimicrobial prophylaxis for heart and heart lung transplantation is outlined in Table 21-13.

Prevention of infection by active immunization is recommended for specific conditions, using killed vaccine only.

Malignancy

Neoplastic disorders after cardiac transplantation arise from three major causes: preexisting malignancies, transmission of malignancy from donor to recipient, and de novo malignancy arising after transplantation. As noted in Box 21-6, preexisting malignancy is a relative contraindication to cardiac transplantation unless there is a prolonged malignancy-free interval and strong clinical evidence of cure.
However, incomplete information is available to clearly predict the likelihood of recurrence of a preexisting malignancy based on malignancy-free interval and type of malignancy. In a compilation of nearly 150 heart and heart-lung transplant recipients with preexisting malignancies treated an average of 7 years prior to transplantation, persistence or recurrence of the malignancy occurred in nearly 20%. The incidence of de novo recipient malignancy is approximately 100 times that of the non–age-controlled general population.

The prevalence and risk (hazard function) for various malignancies related to the interval following transplantation is depicted in Fig. 21-16. Less than 5% of patients develop malignancy during the first year after cardiac transplantation, with the vast majority being either lymphomas (one third) or skin neoplasms (one third). However, in the setting of chronic immunosuppression, risk of fatal malignancy gradually increases over subsequent years (Fig. 21-17).

Posttransplant lymphoproliferative disorder (PTLD) requires separate discussion because of its unique relationship to organ transplantation. PTLD is believed to originate from EBV infection of the recipient’s B lymphocytes, through blood transfusions or community contacts, or through replication of latent EBV in a recipient in the presence of chronic immunosuppression. The abnormal EBV-specific susceptibility induced by immunosuppression allows the increased burden of EBV to infect recipient B cells and induce their transformation into expanding B-cell clones, which can become neoplastic.

A number of risk factors have been identified for development of PTLD (Box 21-21). Among heart transplant recipients, risk of a pretransplant EBV-seronegative patient developing PTLD is 25 to 30 times greater than in patients who are seropositive prior to transplantation. Of particular importance is the increased risk of PTLD that has been documented with prolonged use of cytolytic therapy such as OKT3 and (likely) antithymocyte globulin. Although unproven, it has been hypothesized that OKT3 results in generation of inflammatory cytokines such as TNF, which may promote EBV transcription and reactivation from a latent state.

Various histologic classifications of lesions in PTLD have been published and include a disease spectrum ranging from plasmacytic hypoplasia (preservation of lymph node architecture and usually a benign course) at one end to monoclonal non-Hodgkin lymphoma, with clearly malignant

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Table 21-13  Infection Prophylaxis after Heart and Heart-Lung Transplantation (UAB)

<table>
<thead>
<tr>
<th>Infectious Complication</th>
<th>Prophylaxis (Adult Dosages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perioperative wound and line sepsis</td>
<td>Vancomycin 15 mg·kg⁻¹ preoperatively, then 10 mg·kg⁻¹ every 8 hours × 4 days</td>
</tr>
<tr>
<td></td>
<td>Ceftazidime 15 mg·kg⁻¹ preoperatively, then 1 g every 8 hours × 4 days</td>
</tr>
<tr>
<td>Pneumocystis carinii</td>
<td>Trimethoprim/sulfamethoxazole 1 daily (1 year); for patients allergic to sulfonamides, dapsone 50 mg daily (1 year) or pentamidine 300 mg via nebulizer every month (1 year)</td>
</tr>
<tr>
<td>Mucocutaneous candidiasis</td>
<td>Topical, nonabsorbable antifungal (nystatin) 500,000 units three times daily (6 months)</td>
</tr>
<tr>
<td>Toxoplasmosis:</td>
<td>Pyrimethamine 25 mg daily and leucovorin 10 mg daily (6 months); serology is checked at 3 months, 6 months, and 1 year</td>
</tr>
<tr>
<td>Recipient negative, donor positive</td>
<td>Valganciclovir 900 mg daily PO × 3 months, then acyclovir 200 mg 3 times daily PO × 1 year</td>
</tr>
<tr>
<td>Cyto-megalovirus:</td>
<td>Other option in addition to above: CytoGam 150 mg·kg⁻¹ IV within 72 hours after transplant, then every 2 weeks × 4 doses, then 100 mg·kg⁻¹ IV every 4 weeks × 2 doses (round dose to nearest 2500)</td>
</tr>
<tr>
<td>Recipient negative, donor positive</td>
<td>Acyclovir 200 mg PO 3 times daily × 1 year</td>
</tr>
<tr>
<td>Recipient negative, donor negative</td>
<td>Valganciclovir 900 mg PO × 6 weeks</td>
</tr>
<tr>
<td>Epstein-Barr virus (EBV):</td>
<td>EBV IgM IgG serologies are checked at 6 weeks, 3 months, and every 3 months for the first year and then every 6 months until seroconversion; at seroconversion, patient is treated with IV ganciclovir (6 weeks), then ganciclovir 1 g 3 times daily PO for 6 months, then acyclovir 200 mg PO 3 times daily for 6 months</td>
</tr>
<tr>
<td>Recipient negative, donor positive</td>
<td>Acyclovir 200 mg PO 3 times daily (6 months)</td>
</tr>
</tbody>
</table>

---

### Figure 21-16  Malignancy after heart transplantation for various malignancies. Upper curves represent parametric estimates of freedom from malignancies; lower curves are corresponding hazard functions. Key: CTRD, Cardiac Transplant Research Database; PTLD, posttransplant lymphoproliferative disorder. (From DeSalvo and colleagues.)
implications, at the other. Diagnosis of PTLD requires tissue biopsy, with sufficient tissue to allow assessment of cell type, clonality, biological studies, and architectural background. Clinical presentation of PTLD is widely variable, ranging from an infectious mononucleosis–like illness to specific symptoms related to the organ system involved. Symptomatic lymphadenopathy is a common presentation. PTLD involving the gastrointestinal tract may result in necrosis, bleeding, proliferation, and obstruction. CNS involvement can be either a localized disease or a result of dissemination of systemic PTLD. Pulmonary involvement frequently manifests as multiple nodules.

Optimal treatment of PTLD remains controversial because of absence of consensus in defining the pathology, a clear relationship between morphologic features and clinical course, large treatment trials, and relatively small numbers at any one institution. The basic options for treatment include (1) reduction of immunosuppression, (2) surgical extirpation, (3) chemotherapy, (4) antivirals, (5) anti–B-cell antibodies, and (6) cell-based therapies. The cornerstone of primary therapy involves reducing immunosuppression, with close subsequent monitoring of allograft function and frequent surveillance endomyocardial biopsy for rejection. Isolated disease amenable to surgery should be treated with extirpation. Disseminated disease usually requires additional chemotherapy or anti–B-cell monoclonal antibody administration.

Expected survival after diagnosis of PTLD is highly variable, depending on interval after transplantation, morphologic features, and anatomic location(s). It ranges from approximately 45% to 80% at 2 years. Multivisceral disease, late PTLD, and CNS involvement are associated with worse outcome.

### Survival

Survival at 1 year has gradually improved over the past several decades and currently approaches 85% (Fig. 21-18). Risk of death is greatest during the first 3 months after operation. After 1 year, there is a constant mortality of about 4% per year. Survival at 5 years is approximately 70%, at 10 years 50%, and at 15 years 30%. Median survival is 10 years. For patients alive at 1 year, median survival is 13 years. Survival after retransplantation is discussed under “Cardiac Retransplantation” later in this section.

The most dramatic improvement in survival after heart transplantation over the past 25 years has been during the first 3 to 6 months (see Fig. 21-18). Despite the obvious importance of long-term survival to patients and their families, survival at 1 year has been a benchmark for comparison of institutions as well as eras.

### Modes of Death

Mode of death during the first year and thereafter differ considerably and therefore merit separate discussion. During the first 12 months after transplant, early graft failure, rejection, and infection account for more than 60% of deaths. This is reflected in the hazard functions for specific modes of death during the first 3 months (Fig. 21-19) and cumulative mode-specific mortality during the same period (Fig. 21-20). After the first year, infection and rejection account for less than 25% of primary causes of death, and allograft coronary disease and malignancy for nearly 50% (Figs. 21-21 and 21-22).

### Risk Factors for Death

#### General Risk Factors

Among adult transplant recipients, multiple conditions or factors have been identified that are associated with increased risk of mortality during the first posttransplant year (Table 21-14). Temporary circulatory support is a major risk factor, producing a threefold increase in early mortality. In contrast, the incremental risk associated with long-term pulsatile left ventricular assist device use was
a clear overall risk factor for premature death after cardiac transplantation. Survival after cardiac transplantation is highest among patients with a negative flow cytometry cross-match to both HLA class I (T- and B-cell) antigens and HLA class II (B-cell) antigens (Fig. 21-23). Risk of death appears to be less when the blood type of the recipient and donor is identical, but the effect is a weak one. There is evidence that donor and recipient gender do not affect outcomes, but when there is donor-recipient size mismatch (e.g., smaller female donor into larger male recipient), 1-year survival may be adversely affected. Improvement in survival that occurred when triple-drug immunosuppression began (=1983) supports the idea that the immunologic response is a dominant determinant of outcomes.

In reviewing this list of risk factors, it is important to note that some powerful risk factors not identified in large multivariable analyses are apparent in other studies. Further details about additional risk factors are included in text that follows.

Histocompatibility and Other Patient-Donor Interactions Basic immunologic incompatibility between humans is statistically significant, but clinically of small importance. When survival was adjusted for covariables, an analysis of patients undergoing transplantation from 2002 through 2006 predicted only a 1.3-fold increase in 1-year mortality with pretransplant support using a long-term durable device. Cardiac retransplantation is a major risk factor (see later text in this section), but few such operations are performed.

Figure 21-19 Hazard functions for specific modes of death during first 3 months after primary cardiac transplantation in the Cardiac Transplant Research Database (CTRD), 1990 to 1999 (n = 7283). (From Bourge and colleagues.)

Figure 21-20 Competing outcomes analysis of specific modes of death during first year after transplantation in the Cardiac Transplant Research Database (CTRD). (From Young and colleagues.)

Figure 21-21 Hazard functions for specific modes of death after first year following primary cardiac transplantation in the Cardiac Transplant Research Database (CTRD), 1990 to 1999 (n = 7283). (From Bourge and colleagues.)

Figure 21-22 Competing outcomes analysis of specific modes of death during the first 10 years after transplantation in the Cardiac Transplant Research Database (CTRD), 1990 to 1999 (n = 7283). (From Costanzo and colleagues.)
Recipient Age  Patient age has been a risk factor for death after cardiac transplantation, particularly at very young age and advanced age. An age of 1 to 60 years is a weak determinant of survival.

High Pulmonary Vascular Resistance  High Rp has also been a risk factor for death, usually early after transplantation. The nature of the relationship between elevated Rp (or increasing transpulmonary gradient) and mortality risk is a continuous one, with progressive increase in risk as Rp rises. Preoperative response of Rp to vasodilator therapy has additional predictive value (For details of Rp, see “Evaluation of Comorbid Conditions” earlier in this section.)

Preoperative Status of the Patient  Patients whose cardiac output is importantly depressed before operation are at increased risk of death after transplantation. When organ dysfunction is substantial and does not recover from the effects of the low cardiac output state sufficiently rapidly after transplantation, mortality is markedly increased. The kidney is particularly vulnerable to even brief periods of low cardiac output.

The lung also appears to recover slowly from preoperative damage. Being on a ventilator up to the time of transplantation is a risk factor for death after transplantation.

When inotropes or mechanical circulatory assistance before transplantation bring the patient to operation in a reasonably good hemodynamic state, survival is similar to that of other cardiac transplant recipients. Nevertheless, having a left ventricular assist device implanted before cardiac transplantation raises the risk of death during the first year by about 25% (P = .02).

Global Myocardial Ischemic Time (Donor Heart)  With current techniques of donor heart preservation, global myocardial ischemic time does not become an important risk factor until it exceeds about 240 minutes. Risk of death is increased considerably with ischemic times of 5 to 6 hours. Speculatively, the explanation for the much longer safe ischemic time in the setting of cardiac transplantation than in reoperative cardiac surgery may be the uniformly cold temperature of the globally ischemic donor heart and possibly its complete lack of collateral circulation.

Current information suggests that the safe global myocardial ischemic time for donor hearts is considerably prolonged by preparing and storing the heart in UW solution, which has an ionic concentration similar to intracellular fluid and contains antioxidants and high-molecular-weight molecules. Use of this solution for both cardioplegia and cold storage appears to result in maintenance of high levels of high-energy phosphates and decreased lactate production. Strategies for the initial phase of reperfusion may further increase safe ischemic time of donor hearts (see “Cold Cardioplegia, Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3.)

Era  The risk of cardiac transplantation decreased during the 1980s following introduction of cyclosporine and adoption of protocols that included triple-drug therapy. Further improvement in early and late survival after cardiac transplantation and has been attributed to more precise immunosuppression agents and regimens, less severe graft coronary disease, statin drugs, and better understanding of infection complications, with greater choice of antibiotic and antiviral agents.
Coronary artery disease begins to develop early after the recipient receives the transplanted heart; virtually all patients who survive more than 1 year have some histopathologic evidence of coronary artery disease. The first step in the process appears to be concentric intimal thickening from myofibroblast proliferation and fibrosis. Within 1 to 2 years, aggregates of lipid-filled cells accumulate within the intima, and well-formed lipid cores consisting of cholesterol clefts and free-lying lipid debris (atherosclerotic plaques) can be seen. These atherosclerotic lesions are indistinguishable from those of spontaneous arteriosclerosis. Coronary vasodilator reserve is well preserved as long as the diffuse coronary artery disease has no areas of narrowing greater than about 30%. This may explain occasional occurrence of sudden death in cardiac transplant patients who have had good exercise capacity until the fatal event. However, during rejection episodes, coronary vasodilator reserve is severely impaired. Speculatively, the resulting myocardial ischemia may play a major role in producing myocardial changes and symptoms during rejection episodes. The reduction appears to be reversible in most instances.

Pathogenesis of these important lesions is uncertain, but the etiologic factors likely include a major immunologic component as well as nonimmunologic factors. The frequency with which lymphocytes are seen within the intima and adventitia of the coronary arteries of transplanted hearts supports an immunologic component. Also, patients who produce anti-HLA antibodies after cardiac transplantation have reduced survival and a greater prevalence of coronary artery disease than those who do not. A strong tendency to arteriosclerosis in the patient, as evidenced by important coronary artery disease in the native heart, may be a risk factor for this problem, as may hyperlipidemia and hypertension. Vascular endothelial damage in the cardiac allograft, perhaps beginning as early as the time of donor brain death, may set up an inflammatory response that primes the endothelium for cumulative injury during the subsequent stages of ischemic cold storage.

### Table 21-15 Posttransplant Incremental Risk Factors for All-Cause Mortality after 1 Year (CTRD 1990-1999, n = 5357)

<table>
<thead>
<tr>
<th>Medical History in First Posttransplant Year</th>
<th>Relative Risk</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild CAD</td>
<td>1.29</td>
<td>.02</td>
</tr>
<tr>
<td>Moderate and severe CAD</td>
<td>2.99</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>4.37</td>
<td>.0004</td>
</tr>
<tr>
<td>Other nonskin malignancy</td>
<td>4.74</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Lower LV ejection fractiona</td>
<td>2.05</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Rejection</td>
<td>1.36b</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Less time since last rejectionc</td>
<td>1.99</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Rejection with hemodynamic compromise</td>
<td>1.77</td>
<td>.0004</td>
</tr>
<tr>
<td>Infection</td>
<td>1.11d</td>
<td>.006</td>
</tr>
<tr>
<td>Less time since last infectionf</td>
<td>1.95</td>
<td>.002</td>
</tr>
<tr>
<td>Greater number of infectionsg</td>
<td>1.55</td>
<td>.007</td>
</tr>
<tr>
<td>Higher serum cholesterol h</td>
<td>2.14</td>
<td>.003</td>
</tr>
</tbody>
</table>

Modified from Bourge and colleagues. Relative risk compares time since last rejection of 0-30 days. Relative risk compares serum cholesterol of 200-300.

### Table 21-16 Incremental Risk Factors for Allograft CAD Death after 1 Year (CTRD 1990-1999, n = 5337)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Relative Risk</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Younger age</td>
<td>1.44</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Black</td>
<td>2.07</td>
<td>.0002</td>
</tr>
<tr>
<td>Ischemic etiology</td>
<td>1.84</td>
<td>.0003</td>
</tr>
<tr>
<td>Smoking within 6 months of listing</td>
<td>1.72</td>
<td>.008</td>
</tr>
<tr>
<td>Earlier date of transplant</td>
<td>2.5</td>
<td>.0004</td>
</tr>
<tr>
<td>Donor</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older donor age</td>
<td>1.25</td>
<td>.02</td>
</tr>
</tbody>
</table>

### Allograft Coronary Artery Disease

Accelerated coronary artery disease is the third most common cause of death after cardiac transplantation, following only infection and acute rejection. Furthermore, about 60% of retransplantation procedures are performed because of advanced coronary artery disease. Most patients with this disease fail to experience typical angina, which may be related to the likelihood that the cardiac allograft remains denervated permanently (see “Cardiac Function” later in this section). Life-threatening ventricular arrhythmias, heart failure from myocardial ischemia, silent myocardial infarction, and sudden death are usually the first signs of progression to advanced coronary artery disease in a transplanted heart.
reperfusion, and allorecognition in the recipient. Methods developed to protect cardiomyocyte function may be deleterious to vascular endothelium. Hyperkalemic (>30 mEq·L\(^{-1}\)) cardioplegic solutions exert a variable degree of injury to endothelium depending on the cation concentration and time of exposure. No preservation solution has proven to be superior (including UW), calling attention to the need for improved endothelium-protective agents. A summary of clinical risk factors are summarized in Table 21-17. Potential nonimmunologic risk factors are summarized in Box 21-22.

Two different types of lesions develop, both of which can be recognized cineangiographically. Type A lesions are discrete stenoses of the proximal and middle thirds of epicardial arteries, usually the result of arteriosclerotic plaques; about one third are complicated by luminal thrombi. Type B lesions are predominantly in the distal one third of the course of coronary arteries, forming long tubular constrictions. They appear to be the result of concentric fibrous intimal thickening and infrequently are associated with thrombi. It is this aspect of accelerated coronary artery disease that is most prevalent and most insidious. Small vessels of the coronary tree, 100 µm or less, are usually not involved. By angiographic assessment, the incidence of allograft coronary artery disease has been estimated at 10% to 15% per year, with a prevalence of about 50% by 5 years after transplantation. Freedom from mild, moderate, and severe coronary artery disease over 5 years in a large cohort of patients in the 1990s is depicted in Fig. 21-25. From Kirklin and colleagues.

Coronary artery disease in the transplanted heart has decreased over time, even though more than 70% of patients remain on adrenocorticosteroids 4 years after transplantation. This is attributed in part to a decrease in incidence of rejection and death resulting from rejection. Graft coronary artery disease appears to be reduced by better immunosuppression regimens. It has also been suggested

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### Table 21-17 Risk Factors for Any Allograft Vasculopathy by Angiography (CTRD 1990-1995, \(n = 2134\))

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recipient</strong></td>
<td></td>
</tr>
<tr>
<td>Older age</td>
<td>.02</td>
</tr>
<tr>
<td>Black</td>
<td>.008</td>
</tr>
<tr>
<td><strong>Donor</strong></td>
<td></td>
</tr>
<tr>
<td>Older age</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Male</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

**Rejections during First 6 Months**

<table>
<thead>
<tr>
<th>Number of episodes</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>.001</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Ventura. Key: CTRD, Cardiac Transplant Research Database.

---

**Box 21-22 Potential Nonimmunologic Risk Factors for Allograft Arteriopathy**

- Donor arteriosclerosis risk factors
- Presence of passenger arteriosclerosis
- Younger recipient age
- Recipient cardiac diagnosis
- Cytomegalovirus infection
- Lipid abnormalities
- Hypertension
- Diabetes mellitus
- Obesity
- Smoking
- Markers for impaired fibrinolysis
- Elevated homocysteine levels
- Immunosuppressive drugs
- Longer ischemic time
- Reperfusion injury

From Kirklin and colleagues.
that coronary artery disease may have been stabilized or retarded by use of diltiazem, other medications to control hypertension (which occurs in 67% by 1 year), and lipiddowering agents for control of hyperlipidemia (which occurs in 39% by 1 year and 41% by 4 years).33

Percutaneous coronary intervention (PCI) is often used as a palliative intervention, with midterm results similar to those of the nontransplant population for more proximal and discrete lesions. Multiple PCI procedures are often necessary as the disease progresses, and atherectomy and intracoronary stents are increasingly applied to allograft vasculopathy.18,54

Coronary artery bypass grafting has a limited role, except with left main or isolated proximal left anterior descending artery stenosis. With diffuse and severe coronary involvement, retransplantation is the best option to prolong survival (see “Retransplantation” later in this section).

Other Complications

Renal Dysfunction

Renal dysfunction following cardiac transplantation has two distinct manifestations: acute posttransplant renal failure and chronic renal dysfunction. Acute renal failure generally occurs in the setting of reduced renal reserves before transplant (generally associated with a glomerular filtration rate < 50 mL·min⁻¹ in the adult) with superimposed early graft dysfunction or introduction of posttransplant calcineurin inhibition with either cyclosporine or tacrolimus. Initial administration of cyclosporine or tacrolimus can induce a rapid and intense vasoconstriction of preglomerular afferent arterioles, which is likely mediated by an increase in sympathetic tone, activation of the renin-angiotensin system, decreased production of vasodilator molecules, and increased production of vasoconstrictor molecules.1,36

Initial vasoconstriction results in a decrease of renal blood flow and glomerular filtration rate, both of which are dose related and reversible. Specific vasoconstrictors linked to cyclosporine administration include endothelin and thromboxane.

Chronic renal dysfunction following cardiac transplantation is primarily related to chronic administration of either cyclosporine or tacrolimus. Data from the ISHLT Heart and Lung Registry indicate that approximately 20% of patients have renal dysfunction at 1 year, and 25% of patients exhibit important renal dysfunction by 4 years.11 At 4 years, about 7% of patients have a serum creatinine level greater than 2.5 mg·dL⁻¹, and about 2% are on chronic dialysis.22 Proximal tubular cells appear susceptible to injury from calcineurin inhibitors, induced by either sustained ischemia secondary to drug-related vasoconstriction or direct toxic effects of cyclosporine on tubular cells.22 These effects promote the influx of inflammatory cells into the interstitium, with resultant fibroblast proliferation and chronic scar formation. The afferent arteriolar lesions associated with cyclosporine or tacrolimus affect not only the glomeruli, but also tubules and interstitium.2,3,11

Treatment of persisting renal dysfunction (serum creatinine > 2 mg·dL⁻¹) should include reducing levels of cyclosporine and tacrolimus to the lowest levels consistent with freedom from rejection. Patients with important renal dysfunction who have a history of minimal allograft rejection should be considered for conversion to a sirolimus-based immunosuppressive regimen, which may have a renal-sparing effect if initiated before renal dysfunction is progressive. However, conversion from cyclosporine or tacrolimus late in the progression of renal dysfunction rarely reverses renal damage. When chronic dialysis is required, consideration for renal transplantation is advisable if allograft function is good and other nonrenal subsystems are intact.

Glucose Intolerance

Hyperglycemia is the direct result of adrenocorticosteroid use for immunosuppression. Reducing or eliminating corticosteroids is the most helpful intervention. Glucose intolerance is also a common complication of tacrolimus therapy. It may be necessary to use oral hypoglycemic medications and occasionally begin insulin therapy in some patients.

Hypertension

Hypertension occurs in 70% to 90% of patients on cyclosporine immunosuppression. Occurrence of hypertension is somewhat less (30%-50%) when tacrolimus is used. Its relationship to renal insufficiency and graft arteriosclerosis is not known. Blood pressure consistently measured in excess of 140/90 mmHg should be treated. Angiotensin-converting enzyme (ACE) inhibitors or calcium channel blockers are employed in conventional doses. Use of ACE inhibitors may have an additive effect with cyclosporine or tacrolimus to cause hyperkalemia. Calcium channel blockers decrease metabolism of cyclosporine and must be used judiciously and with monitoring of cyclosporine levels and appropriate dose adjustment. Diuretics may also be used in addition to primary antihypertensives. Other medications may be required in combination for patients not controlled by ACE inhibitors and calcium channel blockers.

Hyperlipidemia

Hyperlipidemia is common after cardiac transplantation and requires treatment in about 50% of patients.66 An abnormal lipid profile has been associated with increased risk of coronary events.15 Diet and exercise pattern modification are first-line treatments of abnormal lipid metabolism. Reduction of prednisone dose is helpful. Total cholesterol level greater than 220 mg·dL⁻¹ or low-density lipoprotein cholesterol greater than 120 mg·dL⁻¹ should be treated using a statin drug such as lovastatin; 10 mg daily is the usual starting dose, recognizing that in combination with cyclosporine, there is increased risk of rhabdomyolysis.

Osteoporosis

Osteoporosis begins before operation in patients having cardiac transplantation and may be due to their prolonged inactivity or prolonged use of heparin.67 Corticosteroid administration in the form of high-dose prednisone accelerates the problem after transplantation. Bone loss is greatest in the lumbar vertebrae and is rapid during the first 6 months. Vertebral compression fractures may result from this bone loss. Aseptic necrosis of the femoral head has also been noted. Patients at high risk should be treated before transplantation. High-risk factors for osteoporosis include female gender, older age, white or Asian race, thin or small body frame, prolonged immobility, early menopause (<40 years), postmenopause, glucocorticoid use, family history, low calcium intake or deficiency, excessive alcohol or caffeine intake, tobacco use, scoliosis, and use of a variety of drugs commonly taken by patients waiting for cardiac transplantation, including furosemide, warfarin, and heparin.
Postmenopausal women are given estrogen replacement. Calcium salts (calcium carbonate 1000 to 2000 mg·day⁻¹) and calcitrol beginning at 0.25 µg every other day and increasing to 0.5 µg·day⁻¹ are given before transplant and thereafter. Calcitrol (10 mg daily) may also increase bone density.⁵¹²

**Biliary Disease**

Biliary disease can affect as many as 8% of patients after cardiac transplantation, a prevalence 17 times higher than in the general population.⁶³ Increased risk of cholelithiasis is explained by reduced gallbladder emptying related to vagotomy and use of cyclosporine, which is both cholestatic and cholelithogenic. Laparoscopic cholecystectomy solves this problem and is well tolerated.

**Cardiac Retransplantation**

There is general agreement that survival after retransplantation is inferior to that following primary transplantation.⁵⁵ Risk factors for death include early retransplantation (within 6 months of primary transplant) and retransplantation for acute rejection or early allograft failure. The incidence of infection and rejection are similar following primary transplant and retransplantation.

**Cardiac Function and Quality of Life**

**Cardiac Function**

Successful cardiac transplantation allows dramatic functional improvement in most patients with advanced heart failure. The cardiac allograft affords profound circulatory rehabilitation that is often immediately apparent. Yet cardiac allografts do not function normally, even though more than 90% of surviving recipients have no activity limitation.⁶¹⁴ In the absence of recurring rejection, important allograft vasculopathy, or poorly controlled hypertension, the transplanted heart performs at rest in a similar (although not identical) manner as a healthy age- and sex-matched normal heart, but major physiologic abnormalities manifest during exercise.

Multiple factors contribute to reduced exercise reserves. Normal heart cardiectomy for transplantation severs both afferent and efferent nervous system connections. Afferent denervation affects sensory receptors in the cardiopulmonary region that exert a tonic restraining influence on sympathetic outflow to the heart and peripheral circulation.⁶⁴ Absence of these afferent fibers in the transplanted heart produces a reduced augmentation of peripheral vascular resistance and blunted plasma norepinephrine response to an abrupt decrease in central venous pressure (circulating blood volume).⁶¹₃,⁶₅ Afferent nervous pathway interruption also impairs renin-angiotensin-aldosterone regulation, which normally acts to decrease renin antidiuretic hormone secretion when blood volume is increased.⁶⁶,⁶⁸ Interruption of these afferent neural fibers results in a loss of this feedback mechanism, which normally counterbalances sympathetic renal stimulation. Chronically increased stimulation of the rennin-angiotensin-aldosterone axis creates a chronic volume-expanded state. The general decrease in vagal inhibitor effect on sympathetic output may also aggravate the hypertensive tendency after transplantation.⁵⁵

**Quality of Life**

Cardiac transplantation produces prompt and sustained improvement in the health status and perception of general well-being among most patients with advanced heart failure. The effect of cardiac transplantation on quality of life during the first 5 years has been examined in all four of its major domains (Table 21·18).

**INDICATIONS FOR ADULT CARDIAC TRANSPLANTATION**

In the final analysis, cardiac transplantation is advisable if the expected survival, quality of life, and functional outcomes are superior to other therapeutic options for advanced heart failure. The generally accepted indications for adult cardiac transplantation are listed in Box 21·24.

Heart transplantation is recommended for selected patients with advanced heart failure whose life expectancy with medical or other surgical therapies is less than 50% at 2 years. Rarely, cardiac transplantation is recommended for patients with longer expected survival but whose quality of life related to the heart failure syndrome is particularly poor despite optimal medical or surgical therapies.
Cardiac Transplantation should be reserved for those patients most likely to benefit in terms of both life expectancy and quality of life. When allocating a scarce resource such as a donor heart, a balance must be achieved between appropriate use of the resource to maximize graft survival and maximizing patient survival in those with the poorest expected outcome with other available therapies.

The stated goals of organ allocation embrace two basic concepts: fairness and utility. The concept of fairness is complex, but basically states that all patients with end-stage heart disease of equivalent severity have an equal chance of obtaining a heart transplant. Unfortunately, quantifying the probability of death for various patient subsets is currently not possible, and specific criteria for listing are not uniform among institutions.

The concept of utility must also be considered in judging any allocation algorithm. This concept embodies the notion that a precious resource like transplant organs should be used to maximally extend life. Inherent is the notion that transplantation should only be offered to patients for whom transplantation would substantially and importantly improve survival over other therapeutic options. Thus, if likely duration of survival is importantly reduced by the presence of major noncardiac organ dysfunction or comorbidities (which would either be unaffected or worsened by therapies required following transplantation), then the utility of transplantation would be unfavorable.

Based on these concepts, national organ procurement agencies establish algorithms for selecting recipients when an organ donor is identified. In the United States, this agency is the United Network for Organ Sharing (UNOS), which includes committees of transplant experts who work together to establish the rules for organ allocation.

The current allocation system in the United States gives strong priority to those patients whose heart failure is severe enough to require continuous inotropic therapy or mechanical circulatory support. Because of poor survival in higher-risk subsets and paucity of available organs, current indications for cardiac retransplantation are generally limited to (1) chronic severe cardiac allograft vasculopathy with symptoms of ischemia or heart failure or asymptomatic moderate or severe left ventricular dysfunction, and (2) chronic graft dysfunction with symptoms of progressive heart failure in the absence of active rejection.\(^{35}\)

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### Box 21-24 Indications for Adult Cardiac Transplantation

1. Cardiogenic shock or low cardiac output state requiring mechanical assistance (respirator, IABP, VAD, TAH) with reversible organ-system damage
2. Heart failure (refractory low cardiac output state) requiring continuous inotropic support
3. NYHA class III-IV with marked, progressive functional limitation despite optimal medical therapy and poor 12-month prognosis (\(VO_2 < 14 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}\) or serial decrease, clinically unstable)
4. Recurrent or rapidly progressive heart failure unresponsive to optimal medical therapy
5. Severe hypertrophic or restrictive cardiomyopathy, NYHA class IV symptoms
6. Refractory angina pectoris despite optimal medical therapy (beta-blocker, calcium blocker, nitrates) not amenable to coronary revascularization or transmyocardial cardiac laser revascularization because of diffuse distal disease, or severe LV dysfunction. Objective documentation of myocardial ischemia within the first two stages of a standard Bruce exercise protocol
7. Recurrent life-threatening ventricular arrhythmia refractory to medical treatment or insertion of ICD (frequent firings or prolonged electromechanical dissociation after cardioversion)
8. Cardiac tumors, unresectable with low probability of metastasis

Modified from Renlund.\(^{86}\)

Key: IABP, Intraaortic balloon pump; ICD, implantable cardioverter-defibrillator; LV, left ventricle; NYHA, New York Heart Association; TAH, total artificial heart; VAD, ventricular assist device; \(VO_2\), maximal oxygen consumption.

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### SPECIAL SITUATIONS AND CONTROVERSIES

#### Cardiac Transplantation for Cardiac Neoplasm

Complete excision of cardiac sarcoma or other cardiac neoplasm may be difficult to achieve because of anatomic location. Resection of the entire heart and orthotopic cardiac transplantation have been described for treating an otherwise unresectable cardiac tumor. Cardiac explantation, extracorporeal resection of the tumor with cardiac reconstruction, and cardiac autotransplantation are described in Chapter 18.

Another approach to consider for these patients is cardiectomy and replacement with total artificial heart, either as a permanent implant or as a bridge to transplantation after several months, to determine freedom from metastatic disease (see Chapter 22).
Cardiac Xenotransplantation

The continuing shortage of cardiac allografts has focused attention and research on using a species other than human as a source of hearts for transplantation. Adams and colleagues reviewed past clinical experience with cardiac xenotransplantation, including the highly publicized Baby Fae transplant performed by Bailey in 1984 (baboon to human) and the xenotransplant reported by Czaplicki in 1992 (pig to man after cross-circulation removal of preformed antibodies). They concluded that improved understanding of the immunologic barriers to cross-species transplantation has narrowed the gap between laboratory research and clinical application.

Hearts from nonprimates are destroyed within minutes after transplantation into humans because of hyperacute rejection by expression of α-galactose disaccharide (Gal) carbohydrate on vascular endothelium. Humans have circulating natural antibodies against this antigen. Once anti-Gal antibodies bind to the xenograft, the complement cascade is activated, triggering endothelial cell dysfunction, platelet aggregation, and vascular thrombosis, referred to as acute vascular rejection. In addition, there is absence of complement regulatory proteins and mechanisms to control complement activation in xenografts. Donor organs from primates do not express Gal on the endothelium and thus do not undergo hyperacute rejection in human recipients. Rejection, however, occurs within days to weeks after transplantation. Research in developing transgenic pigs has been directed toward genetically altered animals that express human complement regulatory proteins (CRP) and down-regulation of Gal expression on the porcine endothelium. Recipient strategy research has been focused on reduction of anti-Gal circulating antibody levels using extracorporeal immunoadsorption, IV injection of Gal carbohydrates to bind and neutralize circulating natural antibodies, and total lymphoid irradiation or porcine bone marrow transplantation to induce tolerance.

A number of scientific and ethical obstacles remain. Even though primate transplantation is not accompanied by hyperacute rejection, these grafts ultimately fail by acute vascular rejection, a process that is poorly understood. There are no effective therapies to control acute xenograft vascular rejection, but the complex immunologic responses are being elucidated and may allow development of specific therapeutic strategies to prevent xenograft rejection. Animal rights issues have moved xenograft transplant away from primate donors toward transgenic pig donors, which seems to cause less public disfavor, presumably because pigs have been domesticated for dietary consumption, can be grown to appropriate size, and have been used for other medical purposes. Xenosis, the possible transmission of infectious diseases from animal to human, could in turn expose the general population to disease previously unknown to humans. This threat is not easily dismissed. Porcine endogenous retroviruses are particularly important because these viruses have been shown to infect human cells in vitro. No human disease, however, has yet to be associated with these viruses.

Cardiac xenotransplantation remains a dream, but the goal may eventually be achieved. It is anticipated that initial clinical experiments will be as bridge to allotransplantation and probably will be applied as a heterotopic placement of the graft.

Section II  Cardiac Transplantation for Congenital Heart Disease and Pediatric Patients

HISTORICAL NOTE

On December 6, 1967, 3 days after Christiaan Barnard performed the first human-to-human heart transplant, Adrian Kantrowitz performed the second, in Brooklyn, New York, for an 18-day-old neonate with Ebstein anomaly, refractory heart failure, and previous aortopulmonary shunt for severe cyanosis. The donor was an anencephalic infant. The recipient died 5 hours after the transplant of heart failure and refractory acidosis. Bailey and colleagues at Loma Linda transplanted a baboon heart into a newborn infant, “Baby Fae,” with hypoplastic left heart syndrome on October 26, 1984. The baby survived 20 days. This single experience renewed intense scientific interest in the possibility of xenotransplantation, while at the same time arousing intense public debate over the issue of primate donors for human transplantation. Ironically, the Baby Fae experience did not lead to another cardiac xenotransplant procedure in the coming decade, but it did signal the emergence of neonatal heart transplantation as an option for end-stage neonatal heart disease. Over the following decade, the Loma Linda group generated a landmark experience with superb survival after infant cardiac transplantation.

CLINICAL FEATURES

Many clinical features noted for adult cardiac transplantation (see Section I) pertain to young patients with some exceptions.

Infant ABO-Incompatible Heart Transplants

Infants in the first few months of life manifest a deficiency in certain types of B-cell responses. Although such responses to protein antigen stimulation are generally competent early in life, antibody production to T-independent carbohydrate antigens is notably deficient. This finding is particularly relevant to development of natural antibodies directed against nonself A or B blood group antigens. Available evidence suggests that these natural ABO antibodies develop as a cross-reaction to similar carbohydrate epitopes on intestinal Escherichia coli in normal gut flora. This deficiency in the ability to produce antibodies against carbohydrate antigens is manifest during early infancy by the absence of natural anti-A or anti-B blood group antibodies until approximately age 4 to 6 months.

The paucity of available donors for neonates and small infants requiring cardiac transplantation and this relative neonatal immune deficiency stimulated West and colleagues in Toronto to consider the possibility of ABO-incompatible cardiac transplantation to expand the donor pool for neonatal transplantation. In 2001, they reported successful application of this strategy in 6 infants who received ABO-incompatible hearts. Most underwent transplantation before onset of isohemagglutinin anti-A or anti-B antibody production. Standard immunosuppressive strategies were
However, at the pericardial reflection the aorta usually assumes a position anterior and to the right of the pulmonary trunk. These malpositions are most easily addressed by harvesting from the donor an extended length of the aorta including the arch and pulmonary artery, including the bifurcation, and extensively separating and mobilizing the ascending aorta from the recipient’s pulmonary trunk. This allows a gentle arch of donor ascending aorta to overlie the pulmonary trunk reconstruction, with an anastomosis near the native brachiocephalic artery. The native pulmonary trunk can be partially or completely oversewn and an incision extended into the left pulmonary artery to create an anatomic position suitable for connection with the donor pulmonary trunk.

Anomalies of Systemic Venous Return

**Left Superior Vena Cava Draining to Coronary Sinus**

When the left SVC drains to the coronary sinus, the simplest approach is to leave it attached to the atrium and preserve the course and connection of the coronary sinus to the right atrium at cardiectomy (Fig. 21-26). If a biatrial transplant is selected, care must be taken to avoid narrowing the coronary sinus by the left atrial anastomosis. In the presence of a diminutive or absent right-sided SVC, this method of reconstruction may prevent endomyocardial biopsy via the left SVC because of the sharp angulation required for the bioprobe to access the right ventricular septum.

In general, mean systemic perfusion pressure should be maintained at 40 mmHg or greater during rewarming after heart transplantation with a perfusion flow rate of 2.5 to 3.0 L·min$^{-1}$·m$^{-2}$ in pediatric patients.

**Venous Cannulation**

In the presence of multiple previous operations and difficult venous cannulation, some surgeons prefer to use initial cannulation of the right atrium and subsequent direct venous cannulation while cooling, particularly if a left SVC is present. Individual caval cannulation eliminates the need for prolonged periods of circulatory arrest during transplantation. In patients with separate hepatic drainage, these veins are allowed to drain directly into the pericardium for collection by a cardiotomy sucker. Care must be taken to avoid obstructing hepatic venous drainage by a snare around the inferior vena cava (IVC). In patients with heterotaxy syndrome and azygos continuation of the IVC, the right and left hepatic veins often drain separately, and it is important to leave a cuff of atrium around the entrance of the hepatic veins to facilitate connection of the right atrium to the donor graft.

**Arterial Cannulation**

In neonates with hypoplastic left heart syndrome the pulmonary trunk and ductus are commonly cannulated, but an attractive alternative is to use a 3.5-mm polytetrafluoroethylene (PTFE) graft sewn onto the brachiocephalic artery. This permits regional cerebral circulation while implanting the donor aorta, avoiding periods of circulatory arrest. A flexible wire-reinforced cannula is desirable for arterial cannulation whenever arch reconstruction is required, because the cannula can be positioned away from the operative field (see “Arterial Cannulation” in Chapter 2).

**Malpositions of the Aorta**

In patients with a malposed ascending aorta or transposed great arteries, the ascending aorta may be distinctly leftward and relatively short compared with a normal dextroposed aorta. The pulmonary trunk is often posterior and rightward.

Figure 21-26  Appearance of left superior vena cava draining into coronary sinus following cardiectomy for cardiac transplantation. (Courtesy Pedro J. del Nido, MD, Boston, Mass.)
donor SVC and brachiocephalic vein should be harvested. An extracardiac reconstruction can be accomplished by anastomosing the donor brachiocephalic vein to the cut end of the recipient left SVC, followed by a direct right SVC anastomosis to donor right SVC (Fig. 21-27).

Alternatively, an intracardiac pathway can be constructed using the recipient’s left atrial appendage or PTFE to redirect drainage from the left SVC to the right atrium. The biatrial implantation technique is then employed, in which the left atrial and right atrial septal anastomoses deviate slightly leftward at the opening of the left SVC tunnel into the new right atrium. This technique may be less prone to kinking and thrombosis than the extracardiac reconstruction (Fig. 21-28).

Anomalies of Inferior Vena Caval Drainage

Anomalies of systemic venous drainage are common. Separate drainage of the hepatic veins to the left atrium requires creating a baffle within the left atrium to divert left hepatic drainage back to the right atrium (Fig. 21-29). The baffle must be positioned in a manner that avoids pulmonary venous obstruction. PTFE or pericardium is convenient for constructing this tunnel. A bicaval or biatrial implantation technique can then be used (see Section 1).

Anomalies of Pulmonary Veins and Atrial Septum

In the presence of uncorrected partial or total anomalous pulmonary venous connection, standard transplant procedures must be modified (see Section 1). In the presence of anomalous connections of the right upper pulmonary veins to the SVC, a recommended option is to use a modification of the Warden procedure, in which the SVC is divided and oversewn just cephalad to the pulmonary veins, and the septum is excised along with the explanted heart. The left atrial incision is fashioned to include the right atrial wall at its junction with the SVC. The entrance of the anomalous pulmonary vein is then incorporated with the left atrial anastomosis. The donor SVC is then anastomosed end to end to the recipient’s SVC.

In the presence of previous Mustard or Senning procedures (see Chapter 52) the entire interior baffle is removed and the interatrial septum reconstructed with PTFE in preparation for a biatrial connection. Alternatively, the venae cavae can be divided at their connection to the native heart and a bicaval implantation performed.
Complex Combinations of Anomalous Systemic and Pulmonary Venous Drainage

In the setting of multiple previous operations and unexpected anomalies of pulmonary or systemic venous return, little or no native tissue may be available for reconstruction. Any anomalous locations of entry into the atrial mass can be managed expeditiously by cutting the ventricular mass off the underlying atria, leaving all available atrial tissue in place while the surgeon assesses reconstructive options. Any interatrial septum is excised, leaving a “common atrium.” Any systemic venous opening to the left of the midportion of the open atria can be moved to the midline and repartitioned or tunneled with PTFE patch material so as to drain to the right side. Any pulmonary veins entering to the right of a midatrial (interatrial) septum can be repartitioned with a patch of PTFE that replaces part or all of the septum, such that there is a cut edge of PTFE partition (septum) near the midportion of the atria. The pulmonary veins drain under this partition to the left side of the atria. Then, a standard orthotopic implantation method can be used in which a newly created edge of atrial “septum” is available for the left and right atrial “septal” suture lines, such that all pulmonary venous blood drains to the left side, and all systemic venous blood drains to the right side.

Dextrocardia

In patients with isolated dextrocardia, in which the apex of the ventricles is rightward with atrial situs solitus, orthotopic cardiac transplantation can usually be performed in standard fashion. There may be rotation of the great vessels, but extensive mobilization of the aorta and pulmonary trunk allows rather standard anastomoses for the transplanted heart. Occasionally, secondary to limited space available on the left side of the pericardium, the left pleural space can be widely opened and the diaphragmatic pericardial attachments taken down partially on the left side to accommodate the apex of the transplanted heart.

Situs Inversus

Situs inversus is a unique surgical challenge because of the need to reroute systemic and pulmonary pathways and reposition the great vessels. Management of the great vessels is accomplished as discussed under “Malpositions of the Aorta” earlier in this section. Reconstruction of the systemic venous and pulmonary venous pathways can be accomplished using either the biatrial or bicaval technique.

The simplest method uses a bicaval technique in which the pulmonary vein orifices and the posterior aspect of the left atrium are isolated as a single unit with a circumferential cuff of left atrium, just as in a standard bicaval technique. Incisions in the left-sided right atrium are planned such that autologous right atrial tissue can be used to construct a partial tube from the left-sided opening of the IVC rightward along the diaphragm to provide a connection with the donor IVC opening within the right atrium.

In the presence of a normal brachiocephalic vein, a long segment of donor SVC and brachiocephalic vein is harvested to allow a right-sided anastomosis from donor SVC to the underside of the recipient brachiocephalic vein. Alternatively, the donor SVC and brachiocephalic vein can be anastomosed directly to the mobilized recipient left SVC (Fig. 21-30).

Figure 21-30 Final appearance of implantation of a situs solitus donor heart into a situs inversus recipient. Ascending aortic anastomosis is shortened, allowing superior venous drainage system to be draped over the great arteries. Key: BV, Brachiocephalic vein; LIVC, left inferior vena cava; L SVC, left superior vena cava; SVC, superior vena cava. (Courtesy Leonard L. Bailey, MD, Loma Linda, Calif.)

The general sequence of operation is transection of the SVC, including a small rim of right atrium, followed by incision of all available right atrial tissue anteriorly to the tricuspid valve and posteriorly to the interatrial septum, which is left intact and in continuity with the IVC orifice. The great vessels are divided proximally, and the left atrium is incised and the cardiac mass excised, leaving a cuff of left atrium around all the pulmonary venous orifices. The great vessels are mobilized as described above. Native atrial tissue is used to construct a partial tube (using a Hegar dilator if needed) for the IVC that reaches beyond the lower right corner of the left atrial remnant. If insufficient pericardial space is available for the donor ventricular apex, the pericardial attachments to the diaphragm on the left side are partially taken down, avoiding injury to, or cautery close to, the phrenic nerve.

Implantation involves a standard left atrial anastomosis followed by the IVC anastomosis between the constructed tube and the donor IVC orifice. The donor and recipient aorta are then trimmed appropriately to provide a tension-free anastomosis, after which de-airing and de-clamping are carried out as usual. The SVC reconstruction and pulmonary artery anastomosis (with an incision extended onto the left pulmonary artery as needed) are performed while rewarming.

Alternatively, a biatrial technique can be used by removing all interatrial septum and reconstructing the septum as described earlier in this section under “Complex Combinations of Anomalous Systemic and Pulmonary Venous Drainage.” Autologous tissues can also be used to create internal baffles to achieve the same result (Fig. 21-31).
new graft during reperfusion. In addition, excessive pulmonary blood flow may initiate pulmonary dysfunction, pulmonary hypertension, and right ventricular dysfunction. For these reasons, coiling these vessels in the catheterization laboratory immediately prior to transplantation is preferable whenever possible. Alternatively, ligation of collaterals at transplantation may be accomplished by dividing the posterior pericardium following cardiectomy (see “Managing Sources of Pulmonary Blood Flow on Cardiopulmonary Bypass” in Chapter 38).

When the pulmonary trunk requires replacement, it is advisable to perform this reconstruction before the aortic or SVC anastomosis (Fig. 21-32). After the left atrial connection is completed, the donor pulmonary arteries are connected to the recipient’s pulmonary arteries, after which the aortic and cavocaval or right atrial anastomoses are completed.

**Anomalies of Aortic Arch**

Residual or congenital defects of the aorta are often encountered, along with arch hypoplasia, interruption, or hypoplastic
Chapter 21 Cardiac Transplantation

Common to all, however, is hypoplasia of the left ventricle and ascending aorta (Fig. 21-33). The aortic arch is also small in most cases, and there may be associated coarctation of the aorta. The right ventricle and pulmonary trunk are usually large, and the ductus arteriosus continues to the descending aorta. It must be identified relative to the left pulmonary artery. The right atrium may be enlarged from high pressure and flow through a patent foramen ovale. The SVC and IVC usually connect normally.

Although a major portion of the transplant operation for this condition has traditionally been performed during circulatory arrest, alternative strategies are available to minimize or eliminate circulatory arrest to reduce the potential for neurologic damage. Prior to CPB, a 3.5-mm PTFE graft is anastomosed to the brachiocephalic artery and clamped. The patient is heparinized, and CPB is initially established with the arterial cannula inserted into the PTFE tube and secured with silk ties (this is a standard technique used by some surgeons for first-stage palliation of hypoplastic left heart syndrome; see Technique of Operation in Chapter 49). A second arterial cannula is inserted into the distal pulmonary trunk and passed well into the ductus arteriosus for distal aortic perfusion. Upon initiating CPB, a snare is secured.

Hypoplastic Left Heart Syndrome

Patients presenting with hypoplastic left heart physiology without prior palliation may have a spectrum of anomalies. Common to all, however, is hypoplasia of the left ventricle and ascending aorta (Fig. 21-33). The aortic arch is also small in most cases, and there may be associated coarctation of the aorta. The right ventricle and pulmonary trunk are usually large, and the ductus arteriosus continues to the descending aorta. It must be identified relative to the left pulmonary artery. The right atrium may be enlarged from high pressure and flow through a patent foramen ovale. The SVC and IVC usually connect normally.

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around the ductus to exclude the pulmonary arteries from arterial perfusate inflow.

Bicaval venous cannulation is employed as for the standard biatrial implantation technique, although initial cannulation of the right atrium may be employed if there is hemodynamic instability prior to initiating CPB. The perfusate is cooled to bring the nasopharyngeal temperature to 14° to 16°C and bladder temperature to 18°C. During the cooling phase, the hypoplastic ascending aorta is clamped and the heart excised as for biatrial implantation. Once the target body temperatures are achieved, the perfusate temperature is set at 16° to 18°C and low-flow perfusion is established at 1.0 to 1.5 L·min⁻¹·m⁻² for the remainder of the implantation.

The donor heart has been procured to include the entire aortic arch and some of the descending thoracic aorta. The aortic arch of the donor is tailored by excising approximately one fourth of the superior aspect of the aortic circumference, beginning distal to the take-off of the donor brachiocephalic artery. The length of donor aortic arch is then tailored to fit the aortic arch of the recipient.

The left atrial anastomosis is constructed with continuous 4-0 or 5-0 polypropylene suture as in the standard biatrial implantation. The perfusate flow is then reduced to about 0.5 L·min⁻¹·m⁻² and the recipient brachiocephalic artery clamped proximal to the PTFE graft to allow continuation of regional cerebral perfusion during arch implantation. The arterial cannula through the ductus is clamped and removed, and the ductus is ligated proximally and divided. Inferior traction on this ligature facilitates the arch reconstruction. The native aorta is divided near the brachiocephalic artery and the proximal ascending aorta remnant removed. The aortic arch is opened through its inferior aspect, extending the incision past the ductus into the upper portion of the descending thoracic aorta to encompass any coarcted segment. All ductal tissue in the upper descending thoracic aorta is removed.

The donor aortic arch is anastomosed to the recipient aortic arch with continuous 6-0 polypropylene suture. The most difficult portion of the repair is the anastomosis of the distal aortic arch of the donor to the apex of the aortotomy in the upper portion of the descending thoracic aorta of the recipient. Accuracy and complete hemostasis in this area are critical for two reasons. First, inclusion of residual ductal tissue or failure to extend the incision far enough distally could result in stenosis and recurrent coarctation; second, bleeding from this area can be difficult to control later. Exposure of this area is facilitated by placing a C-clamp on the distal aorta to prevent back bleeding, which can obscure the surgical field. Upon completion of the aortic reconstruction, CPB can be continued through the native brachiocephalic artery cannulation, or a cannula can be placed through the stump of the donor brachiocephalic artery for the remainder of the procedure. After de-airing the arch and heart, the suture lines are secured, and the aortic clamp is removed while suction is placed on the needle vent. During rewarming, the right atrial anastomosis and pulmonary trunk end-to-end anastomoses are constructed using 5-0 polypropylene suture.

Transplant after Fontan Operation
These patients are often very ill, with ascites, malnutrition, and marked venous hypertension. Multiple prior sternotomies are the norm, and specific plans are essential for establishing CPB rapidly in the event of cardiac bleeding during sternotomy. Exposure of a femoral artery and vein is advisable if the patient is large enough for femoral cannulation. If percutaneous femoral cannulae are planned in the event of an emergency, the groin should be inspected for scars of previous cutdowns or multiple catheterization procedures. If scarring is present, surgical exposure of the femoral artery and vein are advisable, because passage of dilators over a guidewire in a previously operated groin can be difficult.

The bicaval technique is employed with direct caval venous cannulation. The SVC is detached from the pulmonary artery (prior bidirectional Glenn), and the right atrial or IVC connection to the pulmonary trunk or underside of the right pulmonary artery is disconnected. Defects in the pulmonary artery are preferably reconstructed with donor pulmonary artery tissue or thin bovine pericardium.

The reconstructive requirements are often such that maximal length of SVC and brachiocephalic vein (if a left SVC is present) should be harvested from the donor, along with sufficient length of pulmonary artery branches to meet the reconstructive needs of the recipient pulmonary arteries.

SPECIAL FEATURES OF POSTOPERATIVE CARE
See Section I and Chapter 5.

Immunosuppression
Although cyclosporine remains the most commonly used anticalcineurin agent in adult heart transplantation, tacrolimus is the more common agent among pediatric patients (Box 21-25).

Surveillance for Rejection
In neonates and infants undergoing cardiac transplantation, repeated surveillance of cardiac biopsies may not be feasible because of limitations of vascular access. In this age group, echocardiographic variables have been identified that are generally predictive of acute rejection.²²³,²²⁴,²²⁵,²²⁶

Infection Prophylaxis
Prevention of infection by active immunization is recommended for specific conditions, using killed vaccine only.²²¹ Recommended childhood immunizations are given in Table 21-19.

RESULTS
Among pediatric patients, survival has progressively improved through the early part of the last decade (2000-2010), with less discernible survival improvement since then (Fig. 21-34).²²⁷ Among patients who survive the first posttransplant year, late survival is clearly superior in those transplanted during the first year of life (Fig. 21-35). Survival is the same as in adult transplant recipients once the patient reaches about 11 years of age. Patients with congenital heart disease have approximately twice the risk of early mortality compared with cardiomyopathy patients.²²⁷ The single greatest risk factor for early pediatric mortality is pretransplant support with extracorporeal membrane oxygenation, which increases
**Corticosteroids**
For neonates and small infants (<7 kg), generally 100 mg methylprednisolone IV daily for 3 days. For older infants and children, methylprednisolone 15 mg·kg\(^{-1}\)·day\(^{-1}\) IV daily × 3 or prednisolone 2-4 mg·kg\(^{-1}\)·day\(^{-1}\) PO × 3 with or without a subsequent taper.

**Cyclosporine**
Initial oral dose of about 0.3 mg·kg\(^{-1}\)·day\(^{-1}\)·day\(^{-1}\) twice daily. If renal function stable, gradually increase to oral dose of about 1 mg·kg\(^{-1}\)·day\(^{-1}\) in 3 divided doses. If renal function remains normal, rapidly increase over 3–4 days to achieve target trough levels.

**Tacrolimus**
0.05-0.15 mg·kg\(^{-1}\)·day\(^{-1}\) PO or sublingual in two divided doses. Once stable renal function is verified after initial 1-2 days of therapy, dosage can be rapidly increased to attain target level (with continued surveillance of renal function).

**Azathioprine**
2 to 2.5 mg·kg\(^{-1}\)·day\(^{-1}\). Dose reduced as necessary to maintain the white blood cell count of 3000 per mL or greater.

**Mycophenolate Mofetil**
Begin at 5 mg·kg\(^{-1}\) IV or twice daily PO and progressively increase to a target dose of 20-23 mg·kg\(^{-1}\) twice daily if tolerated (gastrointestinal symptoms). When administered IV, dose is equivalent to the oral dose.

**Cyclophosphamide**
1-1.5 mg·kg\(^{-1}\)·day\(^{-1}\). Dose reduced as necessary to maintain the white blood cell count of 3000 per mL or greater.

**Methotrexate**
5-10 mg·m\(^{-2}\)·week\(^{-1}\) in 3 every-12-hour doses.

**Sirolimus**
Loading dose: 3 mg·m\(^{-2}\) followed by Maintenance dose: 1 mg·m\(^{-2}\)·day\(^{-1}\).

**Antithymocyte Globulin**
Specifics regarding dosage, premedications, and hypersensitivity testing vary according to specific antithymocyte preparation.

**OKT3**
0.1-0.2 mg·kg\(^{-1}\) with dose adjustment by T-cell markers.

**Anti-CD25 Monoclonal Antibodies**
Basiliximab: Administer 12-mg doses using the same schedule as in adults
Daclizumab: 2 mg/kg

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**Table 21-19  Immunizations for Heart and Heart-Lung Transplant Recipients**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Before</th>
<th>After</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetanus/diphtheria</td>
<td>++</td>
<td>++</td>
<td>Revaccination every 10 years after primary series and booster</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>++</td>
<td>+/−</td>
<td>Immunogenicity of HBV vaccine only 5% to 15% in organ transplant recipients</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>++</td>
<td>+/−</td>
<td>Especially indicated for liver transplants and international travelers</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em> type B</td>
<td>++</td>
<td>+</td>
<td>Especially indicated for children younger than 6 years</td>
</tr>
<tr>
<td><em>Pneumococcus</em> (multivalent)</td>
<td>++</td>
<td>+</td>
<td>Indication after transplant is not established</td>
</tr>
<tr>
<td>Influenza A and B</td>
<td>+/-</td>
<td>++</td>
<td>Seasonal vaccination</td>
</tr>
<tr>
<td>Varicella zoster virus (attenuated live)</td>
<td>++</td>
<td>−</td>
<td>Only for seronegative patients; posttransplant use not approved</td>
</tr>
<tr>
<td>Measles-mumps-rubella (live attenuated)</td>
<td>++</td>
<td>Contraindicated</td>
<td>Primary pediatric series</td>
</tr>
<tr>
<td>Oral polio vaccine</td>
<td>++</td>
<td>Contraindicated</td>
<td>Primary pediatric series</td>
</tr>
<tr>
<td>Inactivated polio vaccine</td>
<td>−</td>
<td>Contraindicated</td>
<td>Indicated for unvaccinated posttransplant patients</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues.\(^{314}\)

the risk nearly fivefold. Risk of early death appears to increase considerably and progressively with age less than about 1 year. However, among neonates who survive the first year, long-term survival is particularly favorable,\(^{32}\) likely related to relative immaturity of their immune system at the time of transplant.

General survival and risk factors are similar for adult and pediatric heart retransplantation.

**INDICATIONS FOR PEDIATRIC CARDIAC TRANSPLANTATION**

More than 80% of cardiac conditions leading to cardiac transplantation in the pediatric population are either cardiomyopathies or congenital heart disease, with congenital heart disease not amenable to correction or palliation now comprising approximately 40% of all pediatric listings for transplantation.\(^{32}\)

The congenital cardiac malformations considered for cardiac transplantation range from unrepaird complex disease in the newborn to repaired or palliated congenital heart disease with ventricular dysfunction in the adult.\(^{32,22,24,9,15,2}\) Cardiac transplantation is currently not recommended as routine primary therapy for any cardiac malformation, but severe coronary anomalies, cardiac valve regurgitation, or ventricular dysfunction can favor primary transplantation or referral after initial palliation in selected infants with complex congenital heart disease.
Survival after pediatric transplants performed between January 1982 and June 2006, stratified by era. (From Kirk and colleagues.)

Among infants, hypoplastic left heart syndrome is currently treated at most institutions with staged operations in the Fontan pathway. In general, patients with this condition are referred for cardiac transplantation when right ventricular dysfunction or tricuspid regurgitation, or both, are severe either prior to or following initial surgical palliation. In older children and adolescents, failure of staged single-ventricle palliation is the most common form of congenital heart disease referred for cardiac transplantation (Table 21-20).

The relatively small number of pediatric patients who are referred for cardiac transplantation, and the variety of conditions that can progress to cardiac failure, have limited the ability to generate specific guidelines for transplant referrals (Box 21-26). Recent consensus guidelines from the American Heart Association suggest the following recommendations for patients with cardiomyopathies or previously repaired congenital heart disease:

- A need for ongoing IV inotropic or mechanical circulatory support for poor ventricular function and low cardiac output
- Progressive deterioration of ventricular function or functional status despite optimal medical care with digitalis, diuretics, ACE inhibitors, and β-blockade
- Malignant arrhythmias or survival after arrhythmia-induced cardiac arrest unresponsive to medical treatment, catheter ablation, or an implantable cardioverter-defibrillator

Certain situations specific to pediatric patients contraindicate cardiac transplantation, as recommended by the American Heart Association Council on Cardiovascular Disease in the Young:

- Restrictive cardiomyopathy associated with reactive pulmonary hypertension
- Progressive pulmonary hypertension secondary to systemic ventricular failure that could preclude cardiac transplantation at a later date
- Growth failure secondary to severe heart failure unresponsive to conventional medical treatment
- Unacceptably poor quality of life secondary to heart failure
- Progressive deterioration in functional status or presence of certain high-risk conditions following the Fontan procedure

Heart transplantation for pediatric heart disease is not efficacious when heart disease is associated with severe irreversible disease in other organ systems, or when it is part of a severe irreversible multisystemic disease process. Multiorgan transplantation may be considered.

Orthotopic heart transplantation for pediatric heart disease is not efficacious when heart disease is associated...
with severe irreversible fixed elevation of pulmonary vascular resistance.

- Heart transplantation is not feasible in the presence of severe hypoplasia of the central pulmonary arteries or pulmonary veins.
- The limited supply of pediatric donors, especially infant donors, makes heart transplantation not a feasible standard therapy for any specific congenital heart lesion.

**Section III  Heart-Lung Transplantation**

**HISTORICAL NOTE**

The first combined heart-lung transplant procedure was performed by Denton Cooley in Texas on September 15, 1969. The patient was a 2-month-old infant who survived only 14 hours. C. Walton Lillehei performed the same procedure in an adult patient in New York 3 months later, and that patient survived 8 days. After a sustained experimental investigation of heart-lung transplantation, Bruce Reitz and colleagues at Stanford performed the first successful combined procedure in 1981. Long-term survival became possible with the availability of cyclosporine, and the first successful series of patients undergoing heart-lung transplantation was published by Reitz and colleagues the following year.  

**CLINICAL FEATURES**

Recipient Evaluation and Selection

All the standard recipient selection criteria for isolated heart transplantation apply to patients considered for heart-lung transplantation. However, certain issues unique to this therapy require special mention. Because a heart-lung block is used that could otherwise potentially benefit three individuals with advanced heart or lung failure, there is an added responsibility to select heart-lung transplant recipients with sufficient overall reserves to both benefit from the procedure and have a good probability for midterm survival. In addition, the magnitude of heart-lung transplantation and the associated overall stress on other subsystems are, in most instances, greater than those for isolated heart or lung transplantation.

**Age**

A clear relationship between death after heart-lung transplantation and older age has not been formally demonstrated, but recipients older than age 60 are rarely selected.

**Previous Thoracic Surgery**

Major bleeding from adhesions in a previously operated thoracic space is a strong risk factor for morbidity and mortality after heart-lung transplantation. This in part relates to major transfusion requirements, potentially destabilizing effects of ongoing bleeding on cardiac function immediately after transplantation, and difficulties in identifying and preserving the phrenic nerves in the presence of dense adhesions. As a result, some centers decline patients for heart-lung transplantation if they have undergone prior thoracotomy, particularly if bilateral. With experience, patients with prior thoracotomy and sternotomy can safely undergo heart-lung transplantation (see **Technique of Operation**), but they should have well-preserved noncardiac organ function and be younger, generally less than age 50 years.

**TECHNIQUE OF OPERATION**

Preoperative and Intraoperation Preparation

Preoperative preparation for heart-lung transplantation is the same as for orthotopic heart transplantation. In the setting of no prior cardiothoracic operation, the procedure is performed through a median sternotomy. However, when one or both pleural spaces have been previously entered, a bilateral anterior thoracotomy is preferred as in the technique of bilateral lung transplantation. This allows safer dissection and control of bleeding from adhesions in both pleural spaces. A pericardial flap is developed by incising the pericardium laterally and inferiorly, leaving about 5 cm of pericardium over the superior vena cava as the base for an autologous pericardial flap to be placed around the tracheal anastomosis. Cautery must be avoided in the vicinity of either phrenic nerve, because heat-transmitted injury would catastrophically impair postoperative pulmonary function.

**Removal of Native Heart and Lungs**

CPB is established, the aorta clamped, and a standard cardiectomy performed as for bicaval orthotopic cardiac transplantation (see **“Orthotopic Cardiac Transplantation”** under Technique of Operation in Section 1). If pulmonary venous return is excessive, appropriate reduction of perfusate temperature to profound hyperthermic levels is instituted to allow intermittent low-flow perfusion to facilitate dissection and avoid excessive blood loss (see Section IV of Chapter 2). Otherwise, perfusate temperature is generally 28°C.

Beginning on the left side, an incision is made in the pericardium just anterior to the pulmonary veins as far below the phrenic nerve as possible. In the absence of dense adhesions, a pedicle of pericardium containing the phrenic nerve is developed inferiorly almost to the diaphragm and superiorly just to the level of the left pulmonary artery to avoid damaging the phrenic nerve. The left atrium is divided posteriorly in its midportion, and a cuff of left atrium along with the left pulmonary veins is dissected free and passed under the pericardial pedicle (Fig. 21-36, A). The left pulmonary artery is dissected circumferentially proximal to its branches and divided. The lower lobe of the left lung is reflected superiorly, and the inferior pulmonary ligament is divided with cautery. The posterior pulmonary attachments are divided, and the lung is mobilized away from the vagus nerve. The left mainstem bronchus is isolated by dividing lymphatic tissue with cautery and hemoclips, and the bronchus is stapled and divided. The left lung is passed off the surgical field.

Similarly, the pericardium on the right side is dissected immediately above the pulmonary vein, and the pericardial pedicle is mobilized. The inferior pulmonary ligament is mobilized, right pulmonary artery dissected circumferentially and divided, and posterior pulmonary attachments divided. The lung is gently freed from the area of the vagus nerve without cautery, and the right mainstem bronchus is isolated,
stapled, and divided. After removing both lungs, stumps of right and left pulmonary arteries are mobilized and the pulmonary trunk excised, leaving a generous cuff around the area of ligamentum arteriosum and left recurrent laryngeal nerve. The bronchial stumps are mobilized to the level of the carina with careful hemostasis of bronchial arteries (Fig. 21-36, B). Complete hemostasis is critical to achieve throughout the pleural space and mediastinum before implanting the heart-lung block.

Implantation of the Heart-Lung Block

The heart-lung block is prepared on a back table by dividing the donor trachea approximately 2 cm above the carina. It is important to leave the membranous portion slightly longer than the cartilaginous portion, because it tends to retract slightly after division. The anatomic position of each lung is beneath the pericardial pedicle on each side, but in the presence of dense adhesions from prior operation, both lungs can safely be placed anterior to the phrenic nerves, which avoids additional dissection. In that instance, the pulmonary veins are divided outside the pericardium leaving the intrapericardial pulmonary veins and posterior left atrial wall intact. This may, however, require additional mobilization of tissue anterior to the phrenic nerves to allow the lungs to sit nicely in each pleural space.

The tracheal anastomosis is facilitated by placing silk stay sutures on the donor trachea after dividing it just above the carina. It is important to avoid any additional dissection superior to the point of division in order to preserve all possible blood supply to the tracheal anastomosis. The anastomosis is constructed with continuous 3-0 polypropylene sutures in adults and 4-0 polypropylene sutures in children (Fig. 21-36, C). An air-tight anastomosis must be achieved.
without necrosis of the membranous portion and without turning excessive amounts of tissue into the tracheal lumen. The pericardium is wrapped around the trachea and sutured to the thick lymphatic tissue anterior to the suture line. Gentle inflation of the lung while immersing the tracheal anastomosis in saline allows validation of an air-tight suture line. During implantation of the heart-lung block, the organs are covered with ice slush to maintain topical hypothermia.

The inferior and superior vena caval and aortic anastomoses are constructed, as in the bicaval orthotopic heart transplant technique (see “Orthotopic Cardiac Transplantation” under Technique of Operation in Section I). During rewarming, after suture lines are completed, the lungs are gently ventilated, and CPB is discontinued as usual. Nitric oxide is used in the presence of any reperfusion-induced pulmonary hypertension.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Posttransplant management is similar to that for heart transplantation, except for additional protocols to enhance pulmonary graft function. Fiberoptic bronchoscopy is routinely performed in the operating room at the end of the procedure to clear any secretions and examine the tracheal anastomosis. It should be performed again just prior to extubation and as indicated thereafter.

Because of potential ischemia-reperfusion injury and lymphatic disruption, a reimplantation response—evidenced by pulmonary perihilar haziness on chest radiograph and increased oxygen requirement—is common 2 to 5 days following heart-lung transplantation. Diuresis and fluid restriction is the primary therapy. When this process persists 1 week or more, acute rejection should be considered, with transbronchial biopsy assessment of suspected rejection.

Current immunosuppression protocols for heart-lung transplantation are similar to those for isolated heart transplantation with the exception of the steroid protocol (see Box 21-7). Although unproven, higher-dose prednisone is considered deleterious to tracheal healing, and oral prednisone is initiated at a dose of about 0.4 mg·kg⁻¹·day⁻¹ with a rapid taper.

Surveillance for and management of lung rejection includes the same protocols that have been established for isolated single and double lung transplantation.

RESULTS

Survival

Survival is generally inferior to isolated heart transplantation, with a 1-year survival of approximately 80% and 10-year survival of 30% to 40%. Early graft failure is the most common cause of death in the first month, and infection remains the major cause of mortality thereafter, accounting for approximately one third of deaths after the first month. As in isolated lung transplantation, bronchiolitis obliterans accounts for 20% to 40% of mortality observed after the first year.

INDICATIONS FOR HEART-LUNG TRANSPLANTATION

The current general indications for heart-lung transplantation are (1) Eisenmenger syndrome with an uncorrected intracardiac defect, (2) uncorrectable congenital heart disease with atresia or diffuse severe hypoplasia of the pulmonary arteries and progressive heart failure, (3) coexistence of severe cardiopulmonary disease with advanced heart or lung failure, and (4) severe heart failure with left ventricular dysfunction and secondary pulmonary hypertension unresponsive to vasodilator therapy.

In the current era of limited donor availability combined with the success achieved in single and double lung transplantation, isolated lung transplantation is the preferred therapy for advanced lung failure associated with emphysema, usual interstitial pneumonitis, and suppurative lung disease, including cystic fibrosis. Primary pulmonary hypertension refractory to medical therapy is currently preferentially treated with bilateral lung transplantation instead of combined heart-lung transplantation.

The natural history of Eisenmenger syndrome—characterized by excessive muscularization of the pulmonary vasculature that results in marked irreversible elevation of pulmonary vascular resistance and reversal of a previously left-to-right shunt at the atrial, ventricular, or aortopulmonary level, resulting in right-to-left shunting and cyanosis—has not been characterized well enough to allow data-driven decisions regarding timing of referral for heart-lung transplantation. The time course of deterioration in this condition is slow, with 25-year survival exceeding 40%.

In general, the timing of listing for heart-lung transplantation is based on:

- Worsening cyanosis
- Right ventricular failure—particularly with marked ascites and peripheral edema—that is unresponsive to diuretic therapy
- Worsening oxygen saturation, particularly once it reaches 60% with exertion
- Progressive fatigue and dyspnea, particularly if repeated phlebotomy is required

Section IV Heterotopic Heart Transplantation

DEFINITION

The term heterotopic cardiac transplantation is used to describe placing the heart in a nonanatomic position (as opposed to the orthotopic or normal anatomic position). Although this term when used in the clinical setting has become synonymous with intrathoracic placement of the donor heart in parallel with the native heart, the terms “auxiliary” and “parallel” were used in the original publications of this technique. Heterotopic transplantation of the heart as an auxiliary pump was first described in the early 1960s. Since that time, heterotopic transplantation has found divergent roles as an experimental model and in clinical practice.

HISTORICAL NOTE

Heterotopic cardiac transplantation was first performed clinically in 1974 in South Africa, and it was used exclusively in
Cape Town for many years. A number of putative advantages of heterotopic transplantation over orthotopic transplantation were believed to justify this procedure:

- Support of a dysfunctional donor heart (due to a long ischemic time) by the native heart until donor heart recovery occurs.
- Management of elevated pulmonary vascular resistance with a heterotopic heart so that the native right ventricle can continue to support the right side of the circulation after transplantation.
- Use of a small donor heart for a larger recipient.
- Potential to function as a “built-in assist device” at the time of hemodynamically significant acute cardiac rejection.
- Support of the native heart with development of coronary vasculopathy, as protection against sudden cardiac death until retransplantation can be undertaken.
- In the rare circumstances when native cardiac failure may result from a process such as acute myocarditis, for which there is potential for recovery and subsequent removal of the heterotropic transplant.

The initial clinical experience of heterotopic cardiac transplantation in Cape Town included use of the donor heart purely for left ventricular assistance, with the donor pulmonary trunk being anastomosed to the recipient right atrium for donor coronary sinus venous return. Heterotopic transplantation was subsequently altered in favor of biventricular support. In 1983, Cooper and colleagues reported two patients who underwent heterotopic heart transplantation with donor heart ischemic times of 8 hours and nearly 13 hours, respectively, preserved with a portable hypothermic perfusion apparatus. Initial donor heart function was poor for approximately 20 hours, the circulation being supported by the recipient’s own heart until the donor heart recovered.

**TECHNIQUE OF OPERATION**

**Donor Heart Procurement**

The donor heart is procured in the standard way except that the entire ascending aorta and aortic arch are harvested. The orifices of the right pulmonary veins are oversewn with continuous 5-0 polypropylene suture. The inferior vena caval orifice is also oversewn, taking care to avoid impinging on the coronary sinus. The partition between the left superior and inferior pulmonary veins is excised and the incision extended slightly into the base of the left atrial appendage as necessary to create an opening as large as the mitral valve orifice. In addition, the entire superior vena cava and proximal brachiocephalic vein is harvested.

**Heterotopic Cardiac Transplantation**

A standard median sternotomy is made in the recipient. The right pleural space is widely opened to accommodate the donor heart. The pericardium is opened in the midline, and a pericardial flap for support of the transplanted heart is fashioned by making two perpendicular incisions on the right side that stop approximately 2 cm from the phrenic nerve. Careful hemostasis of this flap is important because it is not accessible after the heart is implanted. Great care must be taken to avoid any coagulation near the phrenic nerve. Small bleeding points at the extent of these pericardial incisions should be controlled with fine polypropylene sutures.

CPB is established with separate caval cannulation and moderate hypothermic (25°-28°C) perfusion. Myocardial preservation of the native heart is extremely important because most of the pulmonary ventricular function will arise from the native right ventricle, and the native left ventricle may be required to contribute to systemic support early after transplant. The aorta is clamped and multidose cardioplegic techniques used for the native heart, as in standard cardiac operations (see Chapter 3). Intermittent topical cooling with cold saline is employed. A left atriotomy is made in the interatrial groove as for standard mitral valve surgery (see Chapter 11), except that the incision does not extend under the superior or inferior vena cava. The opening in the donor left atrium is anastomosed to the corresponding opening in the native left atrium using continuous 3-0 polypropylene suture.

The donor superior vena cava is then anastomosed end to side to the anterolateral aspect of the recipient superior vena cava near the junction of the native right subclavian and brachiocephalic veins. This anastomosis is constructed with continuous 5-0 polypropylene suture, and the opening should be as large as the circumference of the donor superior vena cava (Fig. 21-37, A). This will provide access for endomyocardial biopsies of the donor right ventricle. The donor aorta is then anastomosed end to side to the anterolateral aspect of the native aorta with continuous 4-0 polypropylene suture (Fig. 21-37, B). Air is thoroughly evacuated from both hearts, and the aortic clamp removed with the same attention to details of reperfusion as in orthotopic cardiac transplantation. While rewarming, the donor pulmonary artery is lengthened with an appropriate-sized woven collagen-impregnated polyester graft, which is then anastomosed end to side to the anterior aspect of the native pulmonary trunk (Fig. 21-37, C). The remainder of the operation is completed as usual, taking care to leave atrial and ventricular pacing wires on both native and transplanted hearts for use postoperatively if necessary.

Use of the direct superior vena cava connection simplifies passing an endomyocardial biopsy forceps into the donor right ventricle. Infection of the pulmonary artery conduit is a potential risk of heterotopic transplantation using this method, and this complication, requiring removal of the conduit and replacement with an aortic allograft, has previously been described. An alternative technique involves ligation of donor superior vena cava and a direct connection between the donor pulmonary trunk and the recipient right atrium, which would receive coronary sinus return from the donor heart.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Permanent anticoagulation is required after heterotopic cardiac transplantation, because the native heart is a source of thrombus that may be ejected through the native aortic valve. Despite adequate anticoagulation, systemic emboli can still occur. Presence of a mechanical valve in the native heart increases risk of thrombosis and is regarded as a contraindication to heterotopic heart transplantation.
INDICATIONS FOR HETEROPTIC HEART TRANSPLANTATION

In the current era, there are two basic indications for heterotopic transplantation. First, this procedure should be considered when there is marked elevation of recipient pulmonary vascular resistance, with systolic pressure greater than about 60 mmHg and little or no pulmonary reactivity despite pharmacologic intervention. The situation is particularly dangerous for orthotopic transplantation if the pulmonary artery systolic pressure remains above 55 mmHg when the pulmonary capillary wedge pressure is below about 20 mmHg. Second, heterotopic transplantation may be considered when the donor heart is from a considerably smaller donor than the recipient (in body surface area). The limits of safe orthotopic cardiac transplantation from a smaller donor into a larger recipient are not well established, but the risk is known to be increased when a smaller female heart is transplanted into a considerably larger male recipient, and probably from a smaller-sized young teenage donor into a larger adult male recipient. It should be emphasized that every effort should be made to find a suitable teenage recipient for a teenage donor before resorting to this extreme procedure in an adult recipient.

REFERENCES

5. Fong SW, Qaundahy BY, Taylor W. Developmental patterns of ABO isoagglutinins in normal children correlated with the effects of age, sex, and maternal isoagglutinins. Transfusion 1974;14:581-9.


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Mechanical circulatory support (MCS) is a means of imparting energy for forward flow of blood in the body by manmade devices. Its intent is to remove some or all work of cardiac output from either or both left and right ventricles. Mechanical circulatory support devices (MCSDs) can be used to provide temporary ventricular assistance after cardiac surgery, with the assumption that ventricular function will recover rather quickly (days). Durable mechanical devices can be used for prolonged (months to years) circulatory support with the intent of bridge-to-transplant support, bridge to recovery (with the expectation of sufficient ventricular
recovery to allow device explantation), or permanent (destination) therapy.

Mechanical pumping mechanisms can be placed internally (implantable) or external to the body (paracorporeal). Their power source can be electric or pneumatic, located outside the body or completely within it, with electric power conducted transcutaneously. Their pump flow characteristic can be pulsatile or continuous flow.

This chapter does not include use of biological means for MCS nor passive (non–energy imparting) devices used primarily to address ventricular remodeling (see Chapter 20). This chapter also does not include short term temporary devices.

HISTORICAL NOTE

Early descriptions of mechanically supporting human circulation date back at least to the early 19th century in the writings of LeGallois. Carrel and Lindberg as well as Demikhov reported experimental application of mechanical support systems in animal models in the 1930s. However, major interest in mechanical support of human circulation would await the dawn of open heart surgery in the 1950s.

With successful application of cardiopulmonary bypass (CPB) for a cardiac surgical operation by Gibbon in 1953 and the subsequent first successful series of cardiac operations using CPB by Kirklin and colleagues at the Mayo Clinic, the stage was set for rapid proliferation of the technology of temporary MCS (in this case the heart-lung machine) for repair of cardiac malformations. Failure to successfully wean some patients from CPB stimulated surgeons to seek additional methods of mechanical support while awaiting myocardial recovery. Roller-pump technology was complicated by trauma to blood elements and difficulty in modulating pump speed in response to fluctuations in atrial filling pressures. The first application of a true ventricular assist device (VAD) was attributed to Michael DeBakey, who in 1966 reported the successful application of a pneumatically driven diaphragm pump for 10 days in a 37-year-old woman unable to be weaned from CPB following aortic and mitral valve replacements. Cooley subsequently reported the first successful bridge to transplantation in a 47-year-old man for 64 hours while awaiting heart transplantation with a pneumatically driven artificial heart, the Lioitta Heart, developed by the DeBakey-Baylor-Rice research team.

MCS research focused on pneumatic, electric, and even nuclear-powered designs through the 1980s. The experimental work of Kolff, Olsen, Jarvik, and others paved the way for the first permanent total artificial heart implant in Dr. Barney Clark by DeVries and his team in 1982. Five patients received permanent total artificial hearts under a U.S. Food and Drug Administration (FDA) protocol, with a maximum reported survival of 620 days. The close scrutiny of this initial trial of the Jarvik-7 total artificial heart stimulated intense and sometimes acrimonious debate among ethicists, economists, and healthcare experts about the application of expensive and human-intensive technologies in end-of-life situations.

Just as open heart surgery using CPB paved the way for early application of MCS, cardiac transplantation provided the stimulus for proliferation of ventricular assist systems as a bridging therapy to transplantation. With nearly 30% of patients dying while awaiting cardiac transplantation in the early 1980s, a clear need developed for effective and durable MCSDs that could safely support patients until suitable donor hearts could be identified. The improving outcomes following cardiac transplantation and the scarcity of available organs provided the impetus for a major collaborative effort among the heart transplantation community, the National Institutes of Health (NIH), and scientists and clinicians dedicated to the development of durable MCS systems. In 1984, Oyer, Portner, and colleagues reported the first successful cardiac transplant following bridging with a Novacor (WorldHeart Corp., Oakland, Calif.) left ventricular assist device (LVAD). Hill and colleagues subsequently published successful transplantation following support with a Pierce-Donachy pneumatic LVAD. About the same time (1985), Copeland and colleagues performed the first planned total artificial heart implant as a bridge to transplantation. Continuing advancements in mechanical support over the ensuing decade led to the first FDA-approved implantable device as a bridge to transplantation in 1994.

Despite the early focus on MCS as a bridging therapy to transplantation, the clear intent of the scientific and engineering community was the development of devices capable of long-term safe circulatory support. The landmark feasibility study of long-term mechanical support was the Randomized Evaluation of Mechanical Assistance for Treatment of Congestive Heart Failure (REMATCH) trial. As reported by Rose and colleagues in 2001, the HeartMate VE VAD provided significant survival benefit at 1 and 2 years compared with medical therapy for patients with very advanced heart failure who were not suitable for cardiac transplantation. This NIH-sponsored multi-institutional trial provided the impetus for FDA approval of this device for so-called destination therapy in 2002. This set the stage for multiple clinical trials in the application of long-term mechanical support.

In recent years, device technology has increasingly focused on smaller, simpler, and likely more durable continuous flow (rotary) pumps that lack the pulsatile characteristics of earlier “first-generation” pumps. Following the earlier experimental work of Saxton, Andrews, Wampler, DeBakey, and others, recent clinical applications have focused on axial flow and centrifugal pumps.

BIOLOGICAL BARRIERS

General Concepts

A biomaterial is a natural or artificial material that remains in contact with one or more internal components of the human body for the purpose of replacing organ function or treating an abnormal condition. Biocompatibility refers to the effect of a specific biomaterial on exposed host tissues, whereas hemocompatibility refers to the specific effects of a biomaterial or circulatory support system on blood components, coagulation cascade, and the tendency for thrombus formation. Successful blood pump design requires special knowledge of microlevel interactions between blood elements and the contact surface as well as macrolevel considerations that include choice of prosthetic valves (if required), inflow and outflow port design, and blood flow pathways within the pump. The ideal biocompatible surface for blood is functioning endothelium, but the creation of a functioning endothelial layer on a bioprosthetic surface remains elusive. Minimizing thrombogenicity requires avoidance of highly
thrombogenic biomaterials, specific features of pump design, and pharmacologic inhibition of the coagulation cascade. The requirement for blood-exposed pump components that minimize thrombogenicity has limited compatible materials for blood-exposed surfaces to titanium, polymers (primarily polyurethanes), silicone, graphite, and pyrolytic carbon. A fundamental concept for the understanding of blood-pump surface interaction is the process of protein adsorption to biomaterial surfaces. Following exposure of pump surfaces to circulating blood in vivo, a protein layer develops that covers the biomaterial surface. The make-up of this protein layer is determined by the protein composition of the patient’s blood, the chemical composition of the biomaterial surface (more specifically, surface charge and hydrophobicity), and surface topography (rough vs. smooth surface, porous vs. nonporous). Concentration of proteins in blood, net protein charge relative to the biomaterial surface, distribution of charges on the protein surface, and ability of the protein to undergo conformational changes all contribute to the propensity for a given protein to adsorb to the pump surface. Protein interactions with the biomaterial vary over time and are therefore dynamic. The change in composition of proteins that adsorb to the pump surface over time is termed the Vroman effect. The specific details of these protein-surface interactions contribute directly to the likelihood of pump thrombogenicity, because these proteins are biologically active and can initiate platelet adhesion and activation and trigger coagulation cascades.

Both smooth and rough surface designs have been used successfully in pump design. The textured titanium surface of the HeartMate pulsatile LVAD stimulates the formation of a thin, stable coagulum that, although counterintuitive, has proven effective in minimizing development of pump thrombus.

Application of computer simulations called computational fluid dynamics (CFD) analyses has greatly facilitated the ability to predict the effects of shear stresses in the pump flow pathway and areas of relative stasis on platelet activation and thrombus formation.

The Coagulation System

Contact between the pump surfaces and specific plasma proteins, including factor XII (Hageman factor), prekallikrein, and factor XI, can initiate the coagulation cascade via the intrinsic clotting system (also called the contact system) particularly in areas of relative blood stagnation (Fig. 22-1).

The additional critical component of thrombus formation is platelet adhesion, aggregation, and activation. Normal endothelium is antithrombogenic, in part related to active biochemical reactions involving nitric oxide and prostacyclins. In areas of low shear rates, fibronectin functions as the adhesive system for platelets, whereas von Willebrand factor (factor VIII) is the active adhesive protein for platelets at high shear rates, particularly in combination with fibrinogen. Adhesion of platelets to vascular subendothelium is facilitated by von Willebrand factor, which forms a bridge between collagen fibrils in the vessel wall and platelet receptors. Following contact activation, platelets undergo changes in shape in which they display spreading pseudopods and release the contents of their α granules (which contain fibrinogen, fibronectin, thrombospondin, von Willebrand factor, β-thromboglobulin, platelet factor IV, and platelet-derived...
growth factor), which stimulate thrombin generation. Platelet aggregation is stimulated by the release of adenosine diphosphate (ADP). Under laminar flow conditions, the released granule contents cannot accumulate, but when flow is nonlaminar, platelets are more likely to aggregate and accumulate. As newly recruited platelets release their granular contents, thrombin formation is facilitated by the generation of fibrinogen/fibrin bridges. Increasing thrombin generation accelerates the formation of thromboxane A2 and the release of ADP, which further promotes conversion of fibrinogen to fibrin and platelet activation and aggregation. Damaged red cells from shear stress–induced hemolysis also release ADP, further perpetuating platelet activation.

Preserved vascular endothelial cell function is critical for prevention of intravascular thrombus. Synthesis and release of prostacyclins inhibits platelet activation. Thrombomodulin, an endothelial cell product, neutralizes the procoagulant properties of thrombin and activates protein C, a potent anticoagulant that destroys factors Va and VIIIa. Antithrombin III binds to the endothelial cell plasma membrane and inactivates thrombin.

Specific discussion on anticoagulation therapy for pumps can be found in Special Features of Postoperative Management.

Immunologic Responses to Mechanical Circulatory Support

It remains controversial whether VADs differ in their propensity to induce an immunologic response. In vitro studies of the textured titanium surface of the HeartMate XVE indicate that T lymphocytes (probably activated helper T cells) in the neointimal surface lining express strong immunoreactivity for CD3, CD4, and CD25 (interleukin [IL]-2 receptors). Demonstrated defects in T-cell function post implant induce T-cell apoptosis and possibly decreased resistance to infection.

A major disadvantage of MCS as a bridge to transplantation is the frequency of patient sensitization against foreign HLA antigens, which increases the likelihood of developing anti-HLA antibodies against a potential donor (positive cross-match). Although the pump surface has been implicated in this process, it is more likely that transfused blood products, particularly platelets, account for sensitization. Platelets exhibit high concentrations of major histocompatibility complex (MHC) class I and class II HLA antigens (in contrast to red blood cells), and patients receiving more than 6 platelet units are more likely to develop immunoglobulin (Ig) G antibodies against MHC class I antigens.

ENGINEERING CONCEPTS IN PUMP DESIGN

General Concepts

Specific technologic barriers challenging successful MCS include development of corrosion-resistant materials with minimal toxicity and a high level of structural integrity, management of specific blood-contacting surfaces to minimize thrombogenicity and damage to blood elements, blood pump design, and methods to store energy.

Energy to generate flow from circulatory assist pumps requires conversion of either electrical or pneumatic energy (compressed gas) into kinetic energy (energy of motion). Pulsatile or volume-displacement pumps are usually driven by electric motors that either transfer power directly to a pusher plate mechanism or compress gas or liquid in order to transfer energy to the blood sack or pusher plate. Continuous flow (rotary) pumps use electric motors to transmit kinetic energy to the blood.

The principles of Starling’s law also apply to circulatory pumps, in that the pump must respond to higher inflow into the pump by increasing output. As in the natural heart, this balance is maintained in pulsatile pumps by variations in stroke volume or pump rate.

The major cause of hemolysis in blood pumps is rapid acceleration or deceleration of red cells through the pump, which can induce red cell membrane fracture. In general, pump-induced hemolysis is considered acceptable if the plasma free hemoglobin is maintained at less than 19 mg/dL. The rate of pressure increase and flow-channel velocities are maintained at levels designed to avoid high shear stress.

Proper application of fluid dynamics is critical to minimize thrombus formation. Because blood stasis—particularly flow cessation—promotes clot formation, stationary vortex flow must be avoided because the central stagnant portion of the vortex can become a nidus for thrombus formation.

Power sources and alarms must provide reliability and durability backed up by software programs designed to activate appropriate alarm systems when deviations from normal function occur. Approximately 1.6 watts of power are needed to pump 6 L/min at 120 mmHg. Power in excess of 1.6 watts is both wasted and converted to heat that must safely dissipate within the body.

Pulsatile (Volume Displacement) versus Continuous Flow (Rotary) Pumps

Major pump designs in clinical use today are either pulsatile (volume displacement) or continuous flow (rotary) pumps, which include axial flow and centrifugal pump design. The main features of these basic pump designs are summarized in Table 22-1. Pulsatile pumps cyclically change the internal volume of a pumping chamber, displacing a specific volume of blood with each ejection. Such pumps require one-way valves to generate forward flow, typically utilizing valves in the inflow and outflow portions of the pump. In hermetically sealed (not vented to the atmosphere) pulsatile pumps, cyclic displacement of blood volume within the pumping chamber must be accompanied by an equal increase of volume elsewhere within the casing. This usually occurs via a compliance sack placed outside the device but within the patient.

Continuous flow pumps consist of a rotating component that has one or more impellers (usually a disk or cylinder with vanes that propel blood forward). One or more bearings support the impeller. The assembly comprising all rotating elements is termed the pump rotor. As the impeller rotates, it imparts rotational velocity to the blood, and this rotational energy must be converted into pressure energy to achieve forward blood flow. To facilitate this process, additional stationary blades or other structures redirect the swirling blood to create pressure and forward blood flow. In axial flow pumps, the stator typically consists of stationary blades, whereas the stator of a centrifugal pump typically consists of a scroll-shaped passage or volute.
Table 22-1 Comparison Between Positive-Displacement and Rotary Pumps

<table>
<thead>
<tr>
<th>Feature</th>
<th>Positive Displacement</th>
<th>Rotary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Means of producing flow and pressure</td>
<td>Cyclically changing volume chamber (plus check valves)</td>
<td>Rotating impeller(s)</td>
</tr>
<tr>
<td>Source of energy (typical)</td>
<td>Air pressure or electricity</td>
<td>Electricity</td>
</tr>
<tr>
<td>Power requirements</td>
<td>Roughly equivalent, but rotary may be less efficient at high flow</td>
<td></td>
</tr>
<tr>
<td>Exterior size</td>
<td>Rotary typically much smaller, also requiring smaller cannula (with continuous flow)</td>
<td></td>
</tr>
<tr>
<td>Priming volume</td>
<td>Rotary typically much smaller</td>
<td></td>
</tr>
<tr>
<td>Flow range and hemocompatibility</td>
<td>Both types of pumps are plagued by risk of thrombosis at low flow and hemolysis at high flow.</td>
<td></td>
</tr>
<tr>
<td>Afterload response</td>
<td>Typically unaffected by afterload</td>
<td>Flow typically drops with increasing systemic vascular resistance (unless speed is regulated).</td>
</tr>
<tr>
<td>Preload response</td>
<td>Typically passive filling; output typically follows venous return</td>
<td>Flow will increase with venous return, but not capable of active suction (unless speed is regulated).</td>
</tr>
<tr>
<td>Failsafe (pump stoppage)</td>
<td>Provides effective valved shunt from ventricle to aorta</td>
<td>Creates effective aortic insufficiency, but nominal forward flow is still possible</td>
</tr>
<tr>
<td>Cost to manufacture</td>
<td>Differences are debatable, although rotary pumps have offered lower cost owing to (ostensibly) less complexity</td>
<td></td>
</tr>
<tr>
<td>Effect on physiology</td>
<td>Influence of pressure and flow patterns (e.g., pulsatility) on end-organ function, arterial remodeling, valvular fusion, lymphatic stasis, and so on, is still inconclusive.</td>
<td></td>
</tr>
</tbody>
</table>

Adapted from Antaki and colleagues.\textsuperscript{a2}

Figure 22-2  H-Q curve demonstrates relationship between pump speed (rpm) and pressure difference across inlet and outlet orifices of an axial flow pump. (Courtesy David Farrar, PhD; Thoratec Inc., Pleasanton, Calif. Redrawn from Antaki and colleagues.\textsuperscript{a2})

Figure 22-3  Relationship between pump flow and pressure differences across inlet and outlet orifices of HeartMate II pump during cardiac cycle. Key: \(P_{\text{aort}}\), Aortic pressure; \(P_{L}\), left ventricular pressure. (Diagram courtesy David Farrar, PhD; Thoratec Inc., Pleasanton, Calif. From Antaki and colleagues.\textsuperscript{a2})

The forward flow of blood through an axial flow pump is determined primarily by the speed of the rotor (pump speed) and the pressure difference across the inlet and outlet orifices of the pump. In the absence of obstruction to pump inflow, pressure at the outlet orifices (aorta) always exceeds inlet pressure (left ventricle). At any given pump speed, blood flow through the pump \textit{increases} as the pressure difference across the inlet and outlet orifices \textit{decreases}. At any pressure difference across inlet and outlet orifices, blood flow will increase with increasing pump speed. The relationship among flow, pressure, and pump speed is predicted by a series of flow pressure curves called \textit{HQ curves} (Figs. 22-2 and 22-3). Under physiologic conditions, inlet pressure to the axial flow pump changes in a cyclic fashion during systolic and diastolic phases of the left ventricle. In most situations, even in the presence of severe left ventricular dysfunction and absence of opening of the aortic valve, continuous flow devices contribute some degree of pulsatility to the aortic pressure waveform secondary to the changing differential pressure across the inlet and outlet orifices. Nonpulsatile blood flow occurs in situations of ventricular fibrillation, operation of the pump at too high a pump speed, or with negative inflow pressure causing left ventricular collapse around the inflow orifice.

Assessment of left ventricular volume status during axial flow pump support is facilitated by echocardiography, in which ventricular filling, presence or absence of aortic valve opening, and any tendency toward left ventricular chamber...
collapse around the inflow cannula (suction event) can be assessed. Ideally, pump speed should be adjusted to permit intermittent aortic valve opening, which minimizes the risk of a suction event and may promote more effective washout of the sinuses of Valsalva, decreasing the likelihood of thrombus formation along the aortic valve. However, optimal operating conditions for exercise reserve and promotion of reverse remodeling remain controversial.\textsuperscript{813,G5,H1}

**Bearings and Seals**

Proper design of bearings and seals within devices has provided a major challenge in the progress of MCS. Bearings are devices that provide support, guide movement, and reduce friction of motion between fixed and moving parts. A moving part may be a bladder or pusher plate in a pulsatile pump, or a rotary impeller in a rotary pump. Bearings pose a risk of wear, and therefore failure, secondary to continuous physical contact between solid components. Bearings that remain dry (without direct contact to blood) require special seals that are themselves subject to wear and failure. More recent second-generation pumps avoid seals by using blood itself as the lubricant fluid, with so-called blood-immersed bearings. The third generation of rotary pumps incorporates electromagnetic levitation; these magnetic bearings provide support through magnetic force fields.

**DURABLE CIRCULATORY SUPPORT DEVICES**

**Pulsatile Ventricular Assist Devices**

**Paracorporeal Ventricular Assist Devices**

Paracorporeal assist devices have a pump positioned outside the body cavity, with inflow and outflow cannulae that traverse the skin and subcutaneous tissues. The most commonly employed paracorporeal pump suitable for outpatient use is the Thoratec (Thoratec Corp., Pleasanton, Calif.) VAD.

The Thoratec paracorporeal ventricular assist device (PVAD) can be used for support of the left ventricle (LVAD), right ventricle (RVAD), or both ventricles (BVAD) (Fig. 22-4). The Thoratec PVAD received FDA approval for bridge-to-cardiac transplantation therapy in 1995 and has been implanted in more than 3000 patients.\textsuperscript{H3} The PVAD has a 65-mL stroke volume polyurethane chamber with two mechanical valves. The pneumatic driver applies alternating positive and negative air pressure to achieve a clinical beat rate of 40 to 110 beats/min. The PVAD is positioned on the anterior abdominal wall, with cannulas traversing the skin and mediastinum to provide connections to the heart and great vessels (Fig. 22-5). The device can be pneumatically actuated in an ambulatory setting with a portable TLC-II (Thoratec) driver. The TLC-II was approved for home discharge by the FDA in 2003.

Chronic anticoagulation with warfarin is required, with a target international normalized ratio (INR) of 2.5 to 3.5. Aspirin or other antiplatelet therapy is usually added to the anticoagulant regimen. Anticoagulation usually begins with heparin following cessation of bleeding, but some protocols recommend avoidance of heparin completely in the early anticoagulation phase.

**Intracorporeal Assist Devices**

**Thoratec Implantable Ventricular Assist Device** The Thoratec implantable ventricular assist device (IVAD) is designed to provide all the same features as the PVAD, with pump placement in the intracorporeal position (Fig. 22-6). The IVAD has the same pumping chamber, mechanical valves, and stroke volume as the PVAD. The major differences in the IVAD include a smooth, polished titanium housing for implantability, lighter weight (339 g vs. 417 g), and a narrower 9-mm percutaneous lead, compared with the 20-mm paracorporeal driveline. An optical sensor detects when the pump is full or empty. Internal implantation is appropriate for patients with a body surface area (BSA) greater than about 1.6 m\textsuperscript{2}. The same anticoagulation regimen is used as for the PVAD.

**HeartMate XVE Left Ventricular Assist Device** The largest experience with durable pulsatile VADs stems from the HeartMate XVE LVAD, a variant of which was first
Chapter 22 Mechanical Circulatory Support

introduced in 1986 with pneumatic power. More than 5000 patients have been treated with this device over the past 20 years, and it was used in the REMATCH trial, which led to its approval in the United States for permanent MCS therapy.

The HeartMate LVAD (Fig. 22-7) is a positive-displacement pump made of titanium with a polyurethane diaphragm and a pusher-plate actuator that converts electrical energy to mechanical energy. It may be powered pneumatically or electrically, but only the vented electric version (XVE) is currently used. Cannulation involves a left ventricular apical cannula and an outflow graft to the ascending aorta. Two porcine valves provide directional flow.

The vented electric system is powered by an electric motor that rotates and displaces a pusher-plate that compresses the blood sack to initiate ejection. Air displaced by the diaphragm is vented to the atmosphere by a venting apparatus incorporated into the percutaneous driveline. The vent site provides a portal for pneumatic activation in the event of electrical failure. Power is supplied by two external batteries and an external controller.

Maximum stroke volume is 83 mL, and pumping may be performed in a fixed-rate or “automatic” mode, in which the stroke volume is maintained at a level of 97% full by varying the rate in response to preload. If the rate is adjusted manually, stroke volume should be maintained between 70 and 80 mL, because slower stroke volumes increase the potential for thrombogenesis.

The most unique feature of the HeartMate XVE device is the blood pumping surface, which consists of titanium microspheres and a fibrillar texture that promotes formation of a “pseudointima” that is resistant to thrombogenesis. The neo-intimal surface that develops is composed of collagen as well as cells derived from circulating progenitors of fibroblasts, myofibroblasts, monocytes, macrophages, and endothelial cells. Anticoagulation requirements for the XVE pump are unique among current MCS systems. The textured titanium surface creates a thrombo-resistant pump that requires only aspirin for effective anticoagulation. This creates a special indication for this pump in the setting of clinical comorbidities likely to produce bleeding complications during VAD support.

Unfortunately, the major advantage of minimal anticoagulation requirements is currently outweighed by the poor long-term durability of this pump. With the current iteration of the XVE, bearing wear is a major source of device malfunction. Typically, the HeartMate XVE develops signs of bearing wear within 18 to 24 months (Box 22-1). Pump stoppage can be expected within days to weeks of the onset of signs of important bearing wear. When bearing wear is accompanied by transient pump stoppage or repetitive alarms, the patient can be switched to the pneumatic drive mode in the hospital setting while plans are made for surgical pump exchange. In the event of pump stoppage at home, emergent hand pumping can safely support the patient during transport to the hospital.

**Novacor Left Ventricular Assist Device** The Novacor LVAD (WorldHeart Corp., Oakland, Calif.; Fig. 22-8) holds a special place in the history of MCS as one of the first devices designed for permanent device support. In 1984, the Novacor was the first durable pump used as a successful bridge to transplantation. Implantation in over 1600 patients worldwide, the Novacor has demonstrated high system reliability in the outpatient setting, with a low incidence of device malfunction.

The pump drive unit incorporates a dual pusher-plate pump mechanism coupled to a pulsed solenoid energy
Converter driver. The percutaneous drive line contains the vent tube. Two porcine valves are incorporated in the inflow and outflow conduits.

Thromboembolic complications have been the major weakness of the Novacor device, despite standard anticoagulation with warfarin and antiplatelet agents. The primary source of particulate embolization was likely a friable pannus that often developed in the inflow conduit. Subsequent design modifications to include expanded polytetrafluoroethylene (PTFE) have importantly reduced embolic events. In a multi-institutional analysis, the incidence of embolic stroke was 5.3% during an average support duration of 162 days using the modified inflow conduit.

Continuous Flow Ventricular Assist Devices

Rotary (continuous flow) pumps differ from volume displacement pumps in that instead of employing a chamber that changes volume and ejects blood via unidirectional valves, rotary pumps impart forward flow by rotating impellers with no valves. (See also discussion of continuous flow technology in Engineering Concepts in Pump Design.) These pumps are electrically driven and have the distinct advantages of small size and smaller drive lines. In contrast to volume displacement pumps, rotary devices are more afterload sensitive; at constant pump speed, the flow drops with increased systemic vascular resistance (see Fig. 22-2). The absence of inflow and outflow valves in rotary pumps improves overall pump durability and simplicity but removes a key failsafe feature of one-way valves: pulsatile pumps typically have a mechanism for hand pumping in the event of an electrical failure, but no such hand pumping device is available for rotary pumps. Specifically, pump stoppage with rotary pumps induces varying degrees of “aortic insufficiency,” with nothing to prevent reversal of flow from aorta into ventricle during diastole. If not promptly corrected, this rare event is frequently fatal in the setting of advanced heart failure, which invariably accompanies pump implantation.

Although continuous flow pumps are usually not pulsatile to a degree that produces a palpable pulse (unless the native heart is rejecting), these rotary pumps typically produce some pulsatility in blood pressure (as measured with an indwelling arterial line) due to changing pump flows throughout the cardiac cycle.

Rotary pumps currently in clinical use are of two major types: axial flow and centrifugal flow. The designations axial and centrifugal refer specifically to the design of the impeller, without reference to the orientation of inlet or outlet ports. It is the rotation of the impeller that imparts rotational velocity to the blood, creating forward flow. Pure axial flow pumps act like a fan, adding energy by deflecting flow in the circumferential direction. Centrifugal pumps typically contain disk-shaped impellers, with blood entering at the center of the impeller and exiting radially at the periphery. Typically, axial pumps feature inlet and outlet ports that are opposed 180 degrees from each another, and centrifugal pumps have ports oriented perpendicular to each other. Within this spectrum of pumps lies a continuum of mixed flow pumps, incorporating aspects of axial and centrifugal design.

HeartMate II

Axial flow pumps in current use in clinical practice contain many features represented in the HeartMate II (Thoratec Corp., Pleasanton, Calif.), the only rotary pump currently approved (as of March 2011) by the FDA (Fig. 22-9). The blood pump component of the HeartMate II is composed of a straight titanium tube that houses the inlet stator, the fixed component that forms the pivotal housing for the rotor; the rotor, the rotational component that includes the impeller blades; the rotor magnet, which generates the magnetic field to induce impeller movement; and the outlet stator, which converts the radial velocity of blood flow to an axial direction (Fig. 22-10). The other major pump components include the inlet cannula, implanted into the left ventricular apex, and the outlet cannula, which returns blood from the pump outlet to the ascending aorta.

The system driver sends electric power and operating signals to the pump and receives pump information. The wearable driver is powered by either a power base unit or two 12-volt rechargeable batteries that generally provide 2 to 4 hours of power. Power transmitted to the electric motor within the hub of the rotor creates a spinning magnetic field. The pump rotor spins on two bearings located at the inlet and outlet stators. The rotor that spins within the magnetic field is the only moving component of the device. Ceramic bearings are washed by the flow of blood. Operating pump speed ranges from 6000 to 15,000 rpm and is capable of generating blood flow up to about 8 L/min. The approximate pump weight is 350 g, with a length of 7 cm and diameter of 4 cm.

Special features of the HeartMate II pump include a flexible joint between the intraventricular portion of the cannula...
and its connection to a titanium elbow that joins the pump. The flexible portion of the inlet cannula reduces the risk of malalignment of the intraventricular portion of the inlet cannula with respect to the ventricular cavity. The inlet cannula design reduces torque on the intraventricular portion of the inlet cannula. An extension in the length of the intraventricular rigid cannula improves reliability of continuous flow throughout the cardiac cycle and at various levels of left ventricular filling. The pump rotor, blood tube within the pump housing, and inlet and outlet stators are smooth titanium surfaces. The inlet and outlet elbows and the intraventricular cannula are textured with titanium microsphere coatings similar to the design of the HeartMate XVE.\(^{23,35}\)

**MicroMed-DeBakey Left Ventricular Assist Device**

The MicroMed-DeBakey LVAD (MicroMed Cardiovascular Inc., Houston, Tex.) is an axial flow pump which consists of an elbow-shaped inflow cannula that inserts into the left ventricular apex, a pump housing unit, a Dacron outflow graft which connects to the ascending aorta, and an ultrasonic flow probe that encircles the outflow grafts and provides direct measurement of pump flow (Fig. 22-11). The pump impeller is actuated by an electromagnet and is the only moving part of the pump system. Wiring from the pump and the flow probe are contained in a flexible driveline that connects to the portable controller. External components include a controller system that operates the pump and a clinical data acquisition system. A potential advantage of this pump is the presence of a flow probe that allows accurate rather than estimated pump flow. Only the pediatric version of this pump (DeBakey Child) is FDA approved, but the adult version has been extensively used in Europe.

**Jarvik 2000 Left Ventricular Assist Device**

This and the remaining continuous flow pumps discussed are not yet FDA approved in the U.S. The Jarvik 2000 (Jarvik Heart Inc., New York, N.Y.) is an electrically powered,
CorAide Left Ventricular Assist Device

The Arrow CorAide LVAD (Cleveland Clinic Lerner Research Institute, Cleveland, Ohio) is a centrifugal-flow electrically powered third-generation LVAD (Fig. 22-13). The pump can be operated in a fixed-speed mode or an automatic-control mode in which the pump speed varies according to heart rate and systemic blood pressure. The pump and electrical cable weighs about 300 g and operates at speeds between 2000 and 3000 rpm. Pump flow rates are up to 8 L/min. Blood contact surfaces are fabricated from titanium. The rotating assembly uses a combination of magnetic forces and hydrodynamic forces for suspension, in which there is no surface contact with the bearings. A unique apical cuff clamp allows positioning and fixation of the apical cannula to optimize pump flow.

axial-flow blood pump that provides continuous flow from the left ventricle to the ascending or descending thoracic aorta (Fig. 22-12). A unique feature of this device is the placement of the axial flow pump within the left ventricular cavity. The overall system consists of the blood pump, a Dacron outflow graft, percutaneous power cable, pump speed controller, and direct-current power supply. The single moving part is the impeller located in the center of the titanium housing. Electromagnetic forces rotate the impeller, which consists of an electromagnet suspended by two ceramic bearings. All blood-contacting surfaces are made of smooth titanium. The pump operates at 8000 to 12,000 rpm and can generate flows up to 8 L/min. This pump is particularly suited to “off-pump” implantation as described in Techniques of Operation.

Figure 22-11  MicroMed-DeBakey ventricular assist device.

Figure 22-12  Jarvik 2000 heart pump.

Figure 22-13  CorAide ventricular assist device.
HeartWare

The HeartWare LVAD (HeartWare Ltd., Sydney, Australia) is a miniaturized centrifugal flow pump that sits entirely within the pericardial cavity (Fig. 22-16). A unique feature is the left ventricular apical inflow cannula, which is an integral part of the pump. The device weighs only 145 g but can generate flows up to 10 L/min. An apical sewing ring attaches to the left ventricular apex and allows adjustment of the inflow cannula orientation. Impeller blades are held in place by a hybrid magnetic and hydrodynamic bearing system.

Total Artificial Heart

The major advantage of the total artificial heart (TAH) over VADs is the provision for biventricular support with an implantable device. (The only currently available implantable separate right and left VAD system is the Thoratec IVAD system [see previous section].) The major disadvantage of the TAH is the necessity of removing the native heart, which removes the option of recovery. The second major disadvantage of current iterations is the space requirement for the device, such that only patients with a BSA of about 1.7 m² or greater are suitable.

The two TAH devices currently available for clinical use are the SynCardia CardioWest C-70 TAH and the AbioCor TAH. Both pumps replace the native ventricles and all four valves in the orthotopic position.

SynCardia Total Artificial Heart

The SynCardia TAH (SynCardia Systems Inc., Tucson, Ariz.) is a pneumatic pulsatile pump in which a rigid spherical outer housing around each artificial ventricle supports a seamless blood-contacting segmented polyurethane diaphragm, two intermediate diaphragms, and an air diaphragm (Fig. 22-17). Two Medtronic 27-mm inflow valves and two Medtronic 25-mm outflow valves provide unidirectional flow. The full ejection volume of each ventricle is 70 mL per beat, and the TAH typically generates a cardiac output of 7 to 8 L/min. The atrial components are sewn to the native atrial cuffs, and the atrioventricular and ventricular outflow graft connections are via “quick snap” connectors. The external console consists of one primary and one secondary pneumatic driver, air tanks,
rapid initiation of CPB in the event of bleeding or acute cardiac decompensation during sternotomy.

A pulmonary artery catheter is routinely advised to assess the response of pulmonary artery pressure to pharmacologic interventions and device implantation. Continuous measurement of pulmonary artery and central venous (or right atrial) pressures provides critical information in determining the need for inhaled nitric oxide and/or biventricular support.

Intraoperative transesophageal echocardiography (TEE) is necessary during MCS implants for assessment of biventricular function, evaluation of aortic insufficiency and presence of a patent foramen ovale, identification of intracardiac and aortic air bubbles during implantation and subsequent de-airing maneuvers, and assessment of inflow cannula position within the left ventricle.

Prior to sternotomy, formal discussions occur with anesthesia and echocardiography colleagues regarding the pulmonary artery and central venous pressures (CVP) and interventions to optimize right ventricular function, the presence and severity of aortic insufficiency and any need to address the aortic valve surgically (see Special Issues in Mechanical Circulatory Support), the presence or absence of intraventricular thrombus, and the presence of a patent foramen ovale (which if present has to be surgically closed to prevent postimplant arterial desaturation).

Prior to initiating CPB, any pockets necessary for device implantation are developed. If an intracorporeal device that requires an intraabdominal pocket is planned, the abdominal cavity is opened and a porous PTFE membrane is implanted to isolate the pump from the intraabdominal contents and allow drainage of blood around the pump through the porous membrane into the peritoneal cavity. In creating space for the left ventricular inflow cannula, leftward dissection along the diaphragm must extend far enough to allow proper alignment of the cannula within the left ventricular cavity.
Insufficient leftward dissection (often requiring entry into the left pleural space) will result in inadequate leftward positioning of the inflow cannula (particularly with a markedly enlarged heart and leftward displacement of the apex) such that the inflow portion points against that lateral wall rather than into the central portion of the left ventricular cavity, producing chronic partial inflow obstruction.

CPB is established with ascending aorta and right atrial cannulation (unless emergent femoral cannulation is required). After initiation of CPB, the heart is maintained in a continuously beating state without cardioplegic arrest unless additional cardiac procedures are needed. Strong suction is maintained on the aortic needle vent and continuous surveillance by TEE is important for detection of any air in the ascending aorta. The left ventricular apex is displaced, and an opening is created in the left ventricle for insertion of the apical cannula. For most devices, creation of the hole is facilitated by a special coring instrument. The left ventricle is inspected for presence of any thrombus, which if present is removed.

The apical cannula for some devices is inserted directly into the left ventricular apex, and for others, an inflow collar is first sutured to the left ventricular apex and the apical cannula is inserted through the collar. Interrupted 2-0 sutures are recommended, often with an additional purse string of polypropylene for improved hemostasis.

The pump is then completely assembled, including the outflow graft, while maintaining the heart in a filled state to avoid trapping of air in the left ventricle. The apical inflow cannula is inserted and secured during continuous TEE surveillance of the ascending aorta for air. Surgical glue is often placed around the insertion site for added hemostasis. With the heart and pump filled with blood, the operating table is rotated away from the surgeon, and the pump is de-aired to allow residual air in the pump to collect in the outflow graft and be eliminated. When no further residual intercardiac air is identified by TEE, the outflow graft is measured to an appropriate length, trimmed, and clamped proximally. An end-to-side anastomosis is then constructed to the exteriorized right lateral aspect of the ascending aorta, usually with continuous 4.0 polypropylene suture. This suture line is particularly hemostatic if constructed in two layers, the first layer being a continuous horizontal mattress suture followed by a second standard layer. The drive line is brought out through a long subcutaneous tunnel, usually in the right upper quadrant. Specific care must be taken to avoid inadvertent passage of the drive line through the intraperitoneal space.

Appropriate inotropic support is initiated to optimize right ventricular function, with or without the addition of inhaled nitric oxide. The driveline and its connecting tubing is passed off the surgical field and connected to the pump console. With the outflow graft clamped (initially fully, then partially) near its connection to the aorta, standard de-airing procedures are carried out under TEE guidance, with needle vents both in the outflow graft and the ascending aorta.

Full pumping is established, and CPB is discontinued with continued surveillance by TEE for air and right ventricular function. Surveillance of right ventricular function is particularly important during the first 10 to 15 minutes after discontinuation of CPB and during protamine administration.

Prior to sternal closure, the outflow graft and apical cannulation site should be covered with bovine pericardium or PTFE patches to facilitate safe sternotomy and dissection at the time of cardiac transplantation.

**Intracorporeal Continuous Flow Left Ventricular Assist Device**

Implantation of continuous flow devices follows the same general surgical plan as for pulsatile devices, with a few notable differences. Because the pumps are smaller than most pulsatile devices, the pump pocket requires either no additional dissection or limited dissection at the level of the diaphragm on the left side to allow the pump to sit in a position that does not compromise the inflow cannula position. When the usual de-airing procedure has been completed and CPB discontinued, close surveillance of right ventricular function by TEE, right atrial pressures, and direct observation is of critical importance. Because rotary pumps of either axial or centrifugal design will continue pumping at the set speed, sudden right ventricular failure can limit blood return to the left ventricle to such a degree that air is sucked in around the inflow cannula and can potentially cause a major air embolism. This contrasts with pulsatile pumps, which either fill completely before emptying (auto mode) or can eject blood from a partially filled sac (fixed-rate mode), which greatly reduces the risk of air entrapment.

In the event of sudden, severe right ventricular failure early post bypass with a continuous flow pump, left atrial or pulmonary artery diastolic pressure should be carefully observed for rapid fall, and pump speed should then be rapidly decreased while observing for aortic air by TEE. If air is seen in the ascending aorta, the outflow graft must be clamped and CPB rapidly reestablished when heparinization is adequate.

Implantation of continuous flow pumps without CPB have been described, particularly for the Jarvik 2000 axial flow pump. The silicone polyester sewing cuff is attached to the apex of the beating left ventricle with pledgeted sutures. With the patient in Trendelenburg position to avoid air entrapment, a coring knife is used to create a suitable incision within the sewing cuff. The pump is rapidly inserted and secured with cotton tape around the cuff and pump housing. The outflow graft can be anastomosed to either the ascending or descending thoracic aorta. Frazier and colleagues have described transdiaphragmatic pump placement through a subcostal extrathoracic approach.

Replacement of failing pulsatile LVADs with continuous flow pumps requires special comment. Currently, the most common indication for pump exchange is bearing wear causing pump failure of the HeartMate XVE 18 to 24 months post implant (see “Pulsatile Ventricular Assist Devices” under Durable Circulatory Support Devices). Catheters are placed in the femoral artery and vein to allow rapid percutaneous cannulation for CPB in the event of uncontrolled bleeding. A repeat sternotomy is recommended for optimal access to both the inflow cannula and outflow graft. The apical sewing cuff and collar from the XVE is retained for simplified insertion of the apical cannula of the HeartMate II pump. The smaller HeartMate II outflow graft is connected directly to the larger residual outflow graft with a beveled anastomosis. Device de-airing is accomplished as usual. If a PTFE membrane was used in the XVE pocket, it should be removed to minimize the presence of foreign bodies around the new pump.
Paracorporeal Ventricular Assist Devices

Implantation of paracorporeal devices follows the same general procedure as for intracorporeal pumps, with the exception that the inflow and outflow cannulae are passed through subcutaneous tunnels following implantation and then connected to the pump itself. Specific protocols are followed for de-airing individual pumps via direct portals, or aspiration techniques of the pump itself following connection to the outflow graft. When biventricular support is needed, the LVAD is generally implanted first. The right ventricular device can receive inflow from either the right ventricle or right atrium. The position of skin exit for right and left ventricular inflow and outflow cannulae on the anterior abdomen must be carefully planned to allow appropriate spacing of the cannulae.

Total Artificial Heart

The technique for implantation of the SynCardia TAH has been described in detail by Copeland and colleagues. Before systemic heparinization, the arterial outflow conduits are appropriately preclotted, and drivelines are tunneled and brought out under the left costal margin. The left-sided ventricular driveline is positioned approximately 5 cm below the costal margin in the midclavicular line. The right ventricular driveline is brought through the skin about 5 cm medial to the left driveline. Both ventricles are then covered with a surgical towel and placed on the left chest until implantation.

CPB is established and the aorta cross-clamped. The recipient heart is excised on the ventricular side of the arterioventricular (AV) groove, leaving a small rim of ventricular muscle. The great vessels are divided just above the aortic and pulmonary valves (Fig. 22-19). The mitral and tricuspid valve leaflets are excised and the chordae trimmed. The coronary sinus ostium in the right atrium is oversewn to prevent backflow of blood to the AV groove.

A “neopericardium” is constructed out of three 15-× 20-cm sheets of expanded polytetrafluoroethylene (ePTFE). The first sheet of ePTFE is sutured to the pericardial reflection as posteriorly as possible at the level of the superior vena cava, inferior vena cava, and pulmonary veins on the right side (without injuring the phrenic nerve); the second sheet is sutured anterior to the left pulmonary veins on the left side; and the third sheet is placed to cover the entire diaphragmatic reflection. The three ePTFE sheets are later folded over the artificial ventricles after completion of the implantation.

The outer rims of the left and right atrial cuffs, which consist of approximately 1 cm of ventricular muscle and fat in the AV groove, are buttressed circumferentially with 1-cm-wide strips of Teflon felt to reinforce the anastomoses between the atrial cuffs and the quick connect and provide maximal hemostasis. The atrial quick connects are trimmed to 6 mm from the connectors, turned inside out, and anastomosed to the atrial cuff (first left, then right), using 3-0 polypropylene. The suture line includes the felt strip–strengthened free ventricular wall and the interventricular septum, taking care to achieve a maximally hemostatic suture line. After completion of both anastomoses, the quick connect are everted back to normal configuration, and biological glue is applied to the suture lines.

The outflow conduits from each artificial ventricle are cut to an appropriate length, determined by briefly placing the artificial ventricles in the mediastinum. The entire length of the pulmonary artery is preserved and anastomosed to the conduit with 4-0 polypropylene. The aortic anastomosis is similarly constructed. All suture lines are tested for hemostasis using a plastic tester device with saline via a three-way stopcock.

The ventricular connections to the quick connects are facilitated by grasping each side of the quick connect with a large clamp while pushing in the device. To avoid conduit angulation, the left ventricular outflow should be as close as possible to the native aorta. Orientation of the ventricle and the outflow mount is fixed by the atrial connection. Prior to completing the aortic connection, the pump and conduit are filled with saline. The right atrial inflow quick connect and the right arterial conduit are attached to the right artificial ventricle similarly. The right side is filled by partially releasing the inferior vena cava tape, completing device implantation (Fig. 22-20).

The patient is placed in steep Trendelenburg, and the aortic cross-clamp is removed with the ascending aorta vented. With the CardioWest TAH pumping at 40 beats/min, vigorous de-airing is completed under TEE guidance. The TAH pumping rate is then increased and CPB discontinued while maintaining a CVP of 12 to 15 mmHg. Cardiac output from the CardioWest TAH is usually about 7 to 8 L/min at this point. After obtaining meticulous hemostasis, the previously secured ePTFE “neopericardium” is closed over

Figure 22-19  Ventricular rim with AV valves and chordae excised. Great vessels are transected just above sinotubular junction. (Redrawn from Copeland and colleagues.)

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PART IV Other Cardiac Conditions
details and principles of implantation are similar to the SynCardia device, with the following notable features. Because the device has no external driveline, a slight caudal extension of the incision facilitates placement of the transcutaneous energy transfer coils anterior to the pectoral muscle fascia prior to heparinization. Following median sternotomy, dissection for placement of the internal battery and controller is performed in either the preperitoneal space or deep to the rectus abdominis muscle.

After initiation of CPB and aortic cross-clamping, the right and left ventricles are excised just below the AV groove to allow for anastomosis of the atrial cuffs at the level of the anuli after excision of the mitral and tricuspid valves. The left atrial appendage is ligated and the coronary sinus and any patent foramen ovale oversewn. The left, and subsequently right, atrial cuff is trimmed to an appropriate diameter and anastomosed to the native atrium at the level of the anulus, using continuous 4-0 polypropylene reinforced with felt strips. A leak-testing device is used to check each anastomosis. A cast model of the AbioCor unit is placed in the mediastinum to determine the appropriate length and orientation of the outflow grafts. The grafts are sewn end-to-end to the great vessels (4-0 polypropylene), with the aortic outflow graft placed anterior to the pulmonary artery graft (Fig. 22-22).

The pumping unit is placed in the mediastinum, and the TAH anteriorly. A rectangular piece of ePTFE is passed around the proximal aorta and secured. During chest closure, special attention is focused on device output and TEE monitoring of inferior vena caval and left pulmonary venous flows.

The technique for implantation of the AbioCor TAH has been described in detail by Dowling and colleagues. The
Antiplatelet Therapy

The mainstay of antiplatelet activity is aspirin (acetylsalicylic acid [ASA]). Aspirin irreversibly inhibits cyclooxygenase, an enzyme responsible for conversion of arachidonic acid to prostaglandin and eventually thromboxane A\textsubscript{2}, which promotes platelet aggregation. Effectiveness of aspirin therapy can be monitored by the in vitro platelet aggregation response to arachidonic acid.\textsuperscript{W3} The antithromboembolic effect of aspirin does not increase with dosages greater than about 325 mg/day, and there is probably no advantage for doses greater than 160 mg/day.\textsuperscript{W3} The ADP pathway for induction of platelet activation is not inhibited by aspirin, and ADP receptors play a central role in platelet activation secondary to shear stress.\textsuperscript{S3}

Clopidogrel irreversibly inhibits platelet activation via ADP receptors on the platelet surface. Dipyridamole inhibits platelet aggregation through a different mechanism. Specifically, dipyridamole inhibits the uptake of adenosine into platelets and endothelial cells, effectively increasing local adenosine concentration. The excess adenosine stimulates platelet adenylate cyclase, which increases platelet cyclic adenosine monophosphate (cAMP) levels, inhibiting platelet aggregation response to ADP, collagen, and platelet-activation factor.

Anticoagulation for Continuous Flow Pumps

The anticoagulation of all currently available rotary pumps includes warfarin and antiplatelet therapy (usually with aspirin). Initial anticoagulation with heparin is recommended in some protocols, though others have successfully avoided heparin without identifiable thromboembolic effects. A simplified anticoagulation protocol employs clopidogrel, aspirin 325 mg twice daily, and warfarin beginning the day after implantation. Clopidogrel is continued until the INR exceeds 2.0, after which warfarin is adjusted to maintain an INR of 2.0 to 3.0.

Anticoagulation for the Total Artificial Heart

Specific protocols have been developed for the SynCardia and AbioCor TAHs.\textsuperscript{C5, K6} Warfarin and antiplatelet agents are routinely combined with additional monitoring by thromboelastography and platelet aggregation studies.

Blood Pressure Management with Continuous Flow Pumps

Although pulsatile flow can usually be detected by direct arterial line monitoring in the early postimplant period, ambulatory blood pressure cannot be reliably measured with a standard blood pressure cuff or with automatic blood pressure devices. The normal Korotkoff sounds are typically absent with the minimal pulsation of continuous flow pumps. The most reliable estimate of mean or systolic blood pressure (depending on degree of pulsatility) is use of a Doppler device over the radial artery while gradually deflating a standard blood pressure cuff. Monitoring outpatient blood pressure with continuous flow pumps is important because of the occasional development of severe hypertension (possibly related to abnormal autonomic deregulation), which, if undetected and untreated, can result in a major intracerebral bleeding event.

**Figure 22-23** The AbioCor total artificial heart in its final position after complete de-airing and occlusion of side ports of outflow grafts. (Redrawn from Copeland and colleagues.\textsuperscript{S3})
Ventricular Suction

When pump speed in a rotary pump exceeds the ability of the left ventricle to supply a continuous inflow of blood into the inlet cannula, the resultant rapid decrease in size of the ventricular chamber can result in cavitary collapse around the inlet cannula, which impedes entrance of blood and creates a “suction event.” The result is a sudden decrease in pump flow. Ventricular suction is remedied by decreasing pump speed. The HeartMate II device detects sudden changes in pump flow by a change in pulsatility index (a measure of flow pulse through the pump described by the relationship: pulse index = [maximum flow − minimum flow] / mean flow). Sudden drops in pulsatility index and a decrease in pump flow indicates a likely suction event. The HeartMate II device incorporates a suction detection algorithm in which pump speed automatically reduces to 9000 rpm if a sudden change in pump flow pulsatility is detected, after which the pump speed slowly returns to the set speed. Observation of this phenomenon indicates the need to reduce the set pump speed.

Pump Thrombus in Continuous Flow Pumps

If thrombus develops on the pump rotor, an abnormal increase in power is required to maintain impeller speed. The increase in power consumption causes an inaccurately high estimate of pump flow and a decrease in pulsatility index caused by a reduction in cyclic power consumption (because continuously high power consumption is caused by the rotor drag induced by thrombus). In contrast, inlet obstruction (secondary to inlet cannula misalignment or thrombus on the inlet cannula orifice), or outflow obstruction (such as kinking of the outflow graft or anastomotic narrowing) produces a decrease in power consumption along with decreased pump flow and pulsatility index. The diagnosis of inflow or outflow obstruction can be aided by echocardiographic imaging, which may reveal a dilated left ventricle, which is not improved by increasing pump speed.

Pump Stoppage of Continuous Flow Pumps

In contrast to pulsatile devices (in which a hand-pumping device is usually available), continuous flow pumps carry no manual option to maintain forward pump flow in the event of pump stoppage. The physiologic sequelae of pump stoppage are discussed in “Continuous Flow Ventricular Assist Devices.”

When pump stoppage occurs, most commonly resulting from damage to the driveline, rapid decompensation and death are common secondary to a combination of severe reduction in cardiac output and a variable degree of “pump/aortic” insufficiency due to the absence of valves. If the patient is viable, emergency transport to an experienced MCS center is mandatory while cardiac output is maximized with inotropic support. Upon hospital arrival, a surgical team should be ready for emergency device exchange. An echocardiogram is necessary to evaluate for possible intracavitary left ventricular thrombus. If no thrombus is identified and soldering of damaged electrical wiring is an option, full heparinization followed by device restart (with the small possibility of thromboembolic stroke) may provide a more favorable risk/benefit ratio than emergency reoperation for pump exchange.

RESULTS

Survival

Survival and adverse events following MCSD implant are reported and analyzed in the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) supported by the National Heart, Lung and Blood Institute (NHLBI). Among isolated LVADs approved by the FDA for use in the United States, the 12- and 24-month survival are 74% and 55% (Fig. 22-24). The requirement for biventricular support confers a significantly worse prognosis (Fig. 22-25).

![Figure 22-24](https://example.com/f22_24.png)

**Figure 22-24** Actuarial and parametric survival for 1092 patients from Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database, undergoing primary left ventricular assist device (LVAD) implant. Patients are censored at transplant or device explant for recovery. Dashed lines represent 70% confidence limits. Hazard function (instantaneous risk of death) is depicted by lower curve.

![Figure 22-25](https://example.com/f22_25.png)

**Figure 22-25** Actuarial survival by device type from Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) database (n = 1420). Patients are censored at time of transplantation or device explant for recovery. Error bars represent 70% confidence intervals. Key: Bi-VAD, Biventricular assist device; LVAD, left ventricular assist device; RVAD, right ventricular assist device; TAH, total artificial heart.
Major causes of death among LVAD patients differ according to interval post implant. The most frequent cause of death during the first 30 days is cardiac failure, followed by multiorgan failure and stroke (Table 22-2). After the first month, infection is the major cause of mortality. The hazard function for death in the current era (see Fig. 22-24) has a rapidly falling early phase that merges with a gradually increasing phase at about 6 months. Risk factors for death after LVAD implant include older patient age, indicators of more advanced right heart failure, cardiogenic shock at implant, and pulsatile (vs. continuous flow) pumps (Table 22-3).

Major Adverse Events

Neurologic Events

The most devastating early complication is severe neurologic injury, usually caused by embolization of particulate matter or air. Air embolization constitutes a greater risk after device implant than during other forms of cardiac surgery. In addition to the potential for air trapping in the left atrium or left ventricle, the pump itself adds a major source of air. Even if the pump is adequately de-aired, negative pressures generated by a blood pump can suck air in through porous conduits or around cannulation sites if the left ventricle is severely underfilled. Specific maneuvers to prevent this complication include:

1. Continuous TEE monitoring of the left atrium, left ventricle, and aortic root during the terminal phases of CPB and for 10 to 15 minutes after discontinuation of bypass
2. Thorough de-airing of the pump with hand pumping (for some pulsatile devices) or short bursts of power to the pump (for some pulsatile devices and most rotary pumps)
3. Appropriate support and observation of right ventricular function after bypass to avoid sudden drops in right ventricular output to the LVAD
4. Minimizing the use of vacuum pressures until the chest is closed

The potential for thromboembolic events during and after CPB can be greatly reduced by careful examination of the left ventricular cavity by TEE prior to implant, and direct inspection of the left ventricular cavity during implantation of the inflow cannula.

Later neurologic events are generally categorized as either hemorrhagic or thromboembolic. With the exception of the HeartMate XVE (see earlier section) all other pulsatile and rotary pumps currently employed are considered inherently thrombogenic. Neutralizing this complication requires detailed analysis of thromboembolic events and a better understanding of the role of the device itself, the patient’s underlying medical condition, and the selection and management of specific anticoagulation regimens.

A relationship between clinical infections and subsequent thromboembolic strokes following MCSD implant has been observed in multiple centers, but a causal relationship and potential mechanisms such as activation of inflammatory mediators with procoagulant effect remain unproven.

Alterations in the underlying coagulation system that are not identified by the INR, partial thromboplastin time (PTT), and platelet count (see “The Coagulation System” under Biological Barriers) may contribute to development of hemorrhage or thromboembolic strokes post MCSD. The

### Table 22-2  Causes of Death after LVAD Implantation

<table>
<thead>
<tr>
<th>Primary Cause of Death</th>
<th>Early (&lt;1 mo)</th>
<th>Later (&gt;1 mo)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>% of 69</td>
<td>n</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>21</td>
<td>30.4%</td>
<td>21</td>
</tr>
<tr>
<td>Infection</td>
<td>6</td>
<td>8.7%</td>
<td>25</td>
</tr>
<tr>
<td>CNS event</td>
<td>8</td>
<td>11.6%</td>
<td>19</td>
</tr>
<tr>
<td>Multiorgan failure</td>
<td>11</td>
<td>15.9%</td>
<td>9</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>4</td>
<td>5.8%</td>
<td>6</td>
</tr>
<tr>
<td>GI bleeding</td>
<td>0</td>
<td>0.0%</td>
<td>2</td>
</tr>
<tr>
<td>Surgical bleeding</td>
<td>5</td>
<td>7.2%</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding, other</td>
<td>1</td>
<td>1.4%</td>
<td>4</td>
</tr>
<tr>
<td>Device failure</td>
<td>0</td>
<td>0.0%</td>
<td>9</td>
</tr>
<tr>
<td>Renal failure</td>
<td>3</td>
<td>4.3%</td>
<td>3</td>
</tr>
<tr>
<td>Hepatic failure</td>
<td>2</td>
<td>2.9%</td>
<td>1</td>
</tr>
<tr>
<td>Malignancy</td>
<td>0</td>
<td>0.0%</td>
<td>2</td>
</tr>
<tr>
<td>Arterial embolism</td>
<td>0</td>
<td>0.0%</td>
<td>1</td>
</tr>
<tr>
<td>Cardiac tamponade</td>
<td>0</td>
<td>1.4%</td>
<td>0</td>
</tr>
<tr>
<td>Post-explant failure to recover</td>
<td>0</td>
<td>0.0%</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>7</td>
<td>10.1%</td>
<td>18</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>69</td>
<td>100.0%</td>
<td>122</td>
</tr>
</tbody>
</table>

From Kirklin and colleagues. 


Cardiac failure includes right ventricular failure and ventricular tachyarrhythmia (VT/VF).

Key: CNS, Central nervous system; GI, gastrointestinal; LVAD, left ventricular assist device.
Chapter 22 Mechanical Circulatory Support

Other Adverse Events

The overall profile of adverse events in the current era is detailed in Table 22-4, separated by type of pump technology. Continuous flow pumps are currently associated with a major reduction in device malfunction and infection compared with pulsatile pumps during the first 6 months post implant.

K8

SPECIAL ISSUES IN MECHANICAL CIRCULATORY SUPPORT

Emergence of Continuous Flow Technology

The current preference for continuous flow technology as bridge-to-transplant therapy is reflected by data from INTERMACS, in which more than 85% of primary LVAD implants in the current era are continuous flow technology (Fig. 22-28). Survival data to date indicate a significant advantage with continuous flow technology (Fig. 22-29).

Decisions Regarding Biventricular Support

When the severity of right ventricular failure is such that isolated left ventricular support will leave the patient with excessive chronic elevation of right atrial pressure (generally

imperfection of standard coagulation monitoring has prompted greater application of more detailed analyses of the coagulation system using thromboelastography and platelet aggregation studies.

Infection

Major pump-related infections involve either the pump pocket or the driveline at the exit site. Overall freedom from major infection among 420 patients in the INTERMACS database is depicted in Fig. 22-26. In the REMATCH trial of the HeartMate XVE pulsatile LVAD, infections, including driveline and other device-related infections, were the leading cause of death. As experience with devices has evolved, the frequency of pump infections has progressively declined. Placement of larger pulsatile pumps in an intraperitoneal pocket using a porous PTFE sheet has reduced the risk of pocket infections. Smaller rotary pumps rarely develop pocket infections, particularly those that are totally intrapericardial.

Driveline infections continue to plague long-term circulatory support and will undoubtedly be an ongoing limitation until totally implantable systems are available. The most important maneuver to minimize late development of exit site infections appears to be total immobilization of the driveline at the exit site, preferably using a double stabilization technique (Fig. 22-27) to minimize transmitted driveline tension or movement at the exit site. Other advances such as novel applications of biofilm technology, instillation of biosubstances to promote tissue ingrowth around the driveline, and the potential use of muscle flaps around the driveline offer promise in reducing pump-related infections.

Gastrointestinal Bleeding

Rarely, bleeding from intestinal arteriovenous malformations (present in 10% of normal adults) is observed with continuous flow pumps (rotary devices). This complication has also been reported in patients with aortic stenosis.

Table 22-3 Risk Factors for Death after LVAD Implantation

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Early Hazard Ratio</th>
<th>P Value</th>
<th>Constant Hazard Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (older)</td>
<td>2.42</td>
<td>&lt;.0001</td>
<td>1.55</td>
<td>.0005</td>
</tr>
<tr>
<td>Bilirubin (higher)</td>
<td>1.41</td>
<td>.0002</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>RA pressure (higher)</td>
<td>2.08</td>
<td>.0009</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>1.97</td>
<td>.02</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>BTC or DT</td>
<td>—</td>
<td>—</td>
<td>1.80</td>
<td>.02</td>
</tr>
<tr>
<td>Pulsatile pump</td>
<td>—</td>
<td>—</td>
<td>2.74</td>
<td>.001</td>
</tr>
</tbody>
</table>


aHazard ratio denotes the increased risk from age 60 to 70 years.
bHazard ratio denotes the increased risk of a 2-unit (mg/dL) increase in bilirubin.
cHazard ratio denotes the increased risk of a 10-unit (mmHg) increase in RA pressure.

dKey: BTC, Bridge to candidacy; BTT, bridge to transplant; DT, destination therapy; LVAD, left ventricular assist device; RA, right atrial.

Imperfection of standard coagulation monitoring has prompted greater application of more detailed analyses of the coagulation system using thromboelastography and platelet aggregation studies.

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cHazard ratio denotes the increased risk of a 10-unit (mmHg) increase in RA pressure.

Key: BTC, Bridge to candidacy; BTT, bridge to transplant; DT, destination therapy; LVAD, left ventricular assist device; RA, right atrial.
Table 22-4  Adverse Events after LVAD Implantation*

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Pulsatile (n = 406)</th>
<th>Continuous (n = 548)</th>
<th>Pulsatile/Continuous</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Rate</td>
<td>Events</td>
<td>Rate</td>
</tr>
<tr>
<td>Device malfunction</td>
<td>45</td>
<td>2.95</td>
<td>17</td>
<td>0.82</td>
</tr>
<tr>
<td>Bleeding</td>
<td>369</td>
<td>24.22</td>
<td>360</td>
<td>17.41</td>
</tr>
<tr>
<td>Cardiac/vascular:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right heart failure</td>
<td>48</td>
<td>3.15</td>
<td>46</td>
<td>2.23</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2</td>
<td>0.13</td>
<td>2</td>
<td>0.10</td>
</tr>
<tr>
<td>Cardiac arrhythmia</td>
<td>154</td>
<td>10.11</td>
<td>218</td>
<td>10.54</td>
</tr>
<tr>
<td>Pericardial drainage</td>
<td>44</td>
<td>2.89</td>
<td>30</td>
<td>1.45</td>
</tr>
<tr>
<td>Hypertensiona</td>
<td>75</td>
<td>4.92</td>
<td>17</td>
<td>0.82</td>
</tr>
<tr>
<td>Arterial non-CNS thrombosis</td>
<td>7</td>
<td>0.46</td>
<td>6</td>
<td>0.29</td>
</tr>
<tr>
<td>Venous thrombotic event</td>
<td>38</td>
<td>2.49</td>
<td>32</td>
<td>1.55</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>11</td>
<td>0.72</td>
<td>12</td>
<td>0.58</td>
</tr>
<tr>
<td>Infection</td>
<td>431</td>
<td>28.29</td>
<td>244</td>
<td>11.80</td>
</tr>
<tr>
<td>Neurologic dysfunction</td>
<td>66</td>
<td>4.33</td>
<td>40</td>
<td>1.93</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>63</td>
<td>4.14</td>
<td>45</td>
<td>2.18</td>
</tr>
<tr>
<td>Hepatic dysfunction</td>
<td>24</td>
<td>1.58</td>
<td>14</td>
<td>0.68</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>121</td>
<td>7.94</td>
<td>89</td>
<td>4.31</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>8</td>
<td>0.53</td>
<td>9</td>
<td>0.44</td>
</tr>
<tr>
<td>Psychiatric episode</td>
<td>43</td>
<td>2.82</td>
<td>38</td>
<td>1.84</td>
</tr>
<tr>
<td>TOTAL “BURDEN”</td>
<td>1549</td>
<td>101.69</td>
<td>1219</td>
<td>58.96</td>
</tr>
</tbody>
</table>

From Kirklin and colleagues.28


bWith current reporting, identification of hypertension with continuous flow pumps is unreliable.

Figure 22-28  Bar graph depicting number of implants for each 6-month interval since the beginning of Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) prospective data collection, divided between pulsatile pumps (blue) and continuous flow pumps (red). Note that initial bar includes some additional patients implanted between June 23 and July 1, 2006, and that patients implanted between January 1 and March 31, 2009 are not included in this depiction.

Figure 22-29  Actuarial survival following primary left ventricular assist device (LVAD) implant with an initial strategy of either bridge-to-transplant (BTT) or bridge-to-candidacy (BTC) strategy, stratified by pulsatile vs. continuous flow pumps (Interagency Registry for Mechanically Assisted Circulatory Support [INTERMACS], n = 1092).
20 mmHg or higher), the likelihood is great that organ function will be importantly compromised secondary to chronic venous congestion, and/or left ventricular filling will be inadequate (secondary to inadequate right ventricular output) to provide effective LVAD flow. However, the advantages of biventricular support must be balanced against reduced success in bridging to transplantation with BVAD therapy compared with isolated LVAD support (see Fig. 22-25). A possible exception to this strategy is use of the TAH for bridging or permanent therapy.

With current implantable pulsatile or continuous flow pumps (with the exception of the TAH), the addition of right ventricular support requires a paracorporeal device. If the device cannot be successfully removed during initial hospitalization, the longer-term (outpatient) quality of life is dramatically reduced.

Although considerable variability exists in protocols at individual institutions, biventricular support should be considered if, despite appropriate doses of right ventricular inotropic support, there continues to be very poor right ventricular function (as judged by echocardiography), and signs of right ventricular failure persist (CVP in excess of 18 mmHg, ascites, and/or peripheral edema). In the operating room following implantation of an LVAD, the addition of right ventricular support should be considered if CVP persists at a level above about 19 mmHg, and cardiac output (LVAD output) is depressed despite administration of nitric oxide and suitable right ventricular inotropic support.

Given the distinctly inferior survival and postimplant quality of life when biventricular device support is required, a major therapeutic priority in advanced heart failure management should focus on referral for MCS before the advent of advanced right ventricular failure.

Aortic Insufficiency

Aortic insufficiency decreases pump efficiency by creating a loop of flow between the LVAD and the native left ventricle. Therefore, native aortic insufficiency should be recognized. In the presence of grade 3/5 or greater aortic insufficiency, specific management of the aortic valve is advisable. Mild degrees of aortic insufficiency frequently progress following LVAD implant, in part related to abnormally high radial force against the closed aortic valve secondary to high pressure (pulsatile pumps) or flow (rotary pumps) entering the ascending aorta above the valve. A variety of methods to surgically treat aortic insufficiency have been employed, but a useful technique is to fix the midpoints of the aortic leaflets together with one or more pledgeted sutures.

Myocardial Recovery

The potential for myocardial recovery days, months, or even years after MCS implant is the ideal goal of any implant that does not result in cardiac replacement. Although sufficient myocardial recovery to allow successful device explant is the desired goal, successful explant of durable long-term devices has to date been uncommon.

Extensive studies have characterized the histologic and molecular changes of chronic myocardial damage sufficient to produce terminal heart failure. Myocyte hypertrophy and interstitial fibrosis, and decreased contractile function define the phenomenon of cardiac remodeling and characterize the failing myocardium. The cellular markers of cardiac remodeling signal myocyte hypertrophy, fibrosis, and abnormal expression of specific genes that characterize the failing myocardium. These cellular and molecular abnormalities are associated with left ventricular enlargement, increase in left ventricular mass, and systolic/diastolic dysfunction. Increases in collagen content are associated with diastolic dysfunction.

In the presence of prolonged cardiac unloading with an LVAD, myocyte size and myocardial collagen content and collagen production (fibrosis) generally decline. Expression of proinflammatory cytokines—particularly tumor necrosis factor α (TNF-α), IL-6, and IL-8—is associated with cardiac enlargement and heart failure. Chronic ventricular unloading with an LVAD is associated with a reduction in expression of these cytokines. Thus, reversal of the proinflammatory state of the failing myocardium may play an important role in restoring more normal structure and function by interrupting the cycle of inflammation, necrosis, and fibrosis.

Dystrophin is a structural protein that contributes to normal contractility, likely through support of the cardiomyocyte membrane. In the failing heart, abnormal dystrophin activity can be partially normalized with chronic VAD therapy.

On an anatomic and functional level, chronic LVAD support generally results in reduction in left ventricular mass as well as left ventricular end-systolic and end-diastolic volume. Frequently there is improvement in left ventricular ejection fraction.

Available evidence suggests that in the present of chronic cardiomyopathy, prolonged unloading with an LVAD frequently induces recovery of cellular and molecular markers of cardiac remodeling, occasionally produces improvement in ejection fraction and other hemodynamic and structural parameters, yet rarely restores sufficient function to allow successful LVAD removal.

Considerable experience is accumulating with surviving patients suffering from chronic heart failure who have undergone device removal for myocardial improvement/recovery, with reported 5-year survival as high as 78%. It remains to be determined whether specific device type (pulsatile vs. continuous flow), pumping strategy (complete vs. incomplete unloading), or the addition of specific pharmacologic therapies during support (e.g., the β-agonist clenbuterol) will increase the likelihood of sufficient recovery for successful explantation.

The expectation for recovery in the setting of acute heart failure due to recent-onset nonischemic cardiomyopathy or acute myocarditis is much more favorable. Even among patients with acute myocarditis who present in cardiogenic shock and require emergent mechanical support, the natural history is usually one of progressive improvement. Such patients should be managed with the expectation that recovery and explantation will be likely, rather than proceeding with early cardiac transplantation.

Mechanical Circulatory Support as Permanent Therapy for Advanced Heart Failure

With FDA approval of the HeartMate XVE for long-term “destination therapy” (DT), widespread application of continuous and pulsatile pumps for long-term therapy in Europe,
and multiple ongoing clinical trials of continuous flow pumps as DT in the United States, the application of permanent MCS is evolving toward a larger population of advanced heart failure patients. Currently, permanent therapy is reserved for patients with refractory or recurrent class IV heart failure who are ineligible for heart transplantation.\(^{92}\)

The NHLBI-sponsored INTERMACS database has categorized subsets of class IV heart failure to better reflect current indications for device therapy. The distribution of DT patients by INTERMACS level is depicted in Table 22-5.\(^{58}\)

With the demonstration of improved survival (see Fig. 22-29) and device durability (see Table 22-4) with continuous flow pumps, greater application of MCS as long-term therapy for advanced heart failure is expected. Specific guidelines for application of device therapy for transplant-ineligible patients in INTERMACS levels 1 to 6 (subsets of NYHA class IV) await further prospective studies.

### PEDIATRIC CIRCULATORY SUPPORT

Limitations in access to cardiac transplantation for infants and children with advanced heart failure has provided a potent stimulus for development of MCS systems suitable for small patients. During the past decade, application to small children of pumps designed for adults has generated poor survival.

A multi-institutional analysis by Blume and colleagues\(^{87}\) examined the use of MCS in pediatric patients in the decade from 1993 to 2003. Although mortality during MCS support progressively decreased during the decade (8% mortality prior to transplant after 2000), the inadequacy of mechanical support systems for smaller patients is apparent by stratifying outcome according to age at implant (Fig. 22-30). Mortality during support in patients younger than 10 years of age (and especially in small children and infants) exceeded 60%. During this era, support for infants and small children was basically limited to extracorporeal membrane oxygenator (ECMO) support.

### Paracorporeal Support

Although the Thoratec paracorporeal PVAD is primarily designed for adults, it has been widely applied to the pediatric age group. Pediatric and adolescent PVAD support has been reported in over 150 patients.\(^{162}\) Approximately 50% of the patients have required biventricular support, with the vast majority of patients suffering from cardiomyopathy or acute myocarditis. The major adverse events with this device in the pediatric population are thromboembolism and hemorrhage, which were more common than among adult patients. The higher incidence of thromboembolic neurologic complications in older children and small adolescents with this device likely relates to the low pump rate (and resultant increase in stasis) when the 65-mL pump is applied to smaller patients.

Reproducible effective bridging of infants and children to transplantation requires availability of a variety of pump sizes suitable for the anticipated cardiac output. Paracorporeal volume displacement pumps are particularly prone to thrombus formation when either pump speed is low (≤50 beats per minute) or when there is consistent incomplete filling of the blood chamber.

To address the challenge of providing mechanical support in small patients, the Berlin Heart EXCOR (Berlin, Germany) was developed to include multiple pump sizes. The Berlin Heart EXCOR is a paracorporeal system with an electropneumatic drive system. Pediatric blood pumps are available in

### Table 22-5  INTERMACS Level and Device Strategy\(^a\)

<table>
<thead>
<tr>
<th>INTERMACS Level</th>
<th>BTT</th>
<th>BTC</th>
<th>DT</th>
<th>BTR</th>
<th>RT</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Pre-Implant)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Critical cardiogenic shock</td>
<td>120</td>
<td>162</td>
<td>21</td>
<td>16</td>
<td>8</td>
<td>1</td>
<td>328</td>
</tr>
<tr>
<td>2. Progressive decline</td>
<td>217</td>
<td>173</td>
<td>39</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>437</td>
</tr>
<tr>
<td>3. Stable but inotrope dependent</td>
<td>85</td>
<td>58</td>
<td>23</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>168</td>
</tr>
<tr>
<td>4. Recurrent advanced HF</td>
<td>41</td>
<td>50</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>106</td>
</tr>
<tr>
<td>5. Exertion intolerant HF</td>
<td>11</td>
<td>9</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>21</td>
</tr>
<tr>
<td>6. Exertion limited</td>
<td>5</td>
<td>5</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>7. Advanced NYHA class III</td>
<td>17</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>TOTAL</td>
<td>496</td>
<td>458</td>
<td>100</td>
<td>25</td>
<td>10</td>
<td>3</td>
<td>1092</td>
</tr>
</tbody>
</table>

From Kirklin and colleagues.\(^{58}\)

\(^a\)INTERMACS: June 2006-March 2009. Primary LVAD n = 1092.

Key: BTC, Bridge to candidacy; BTT, bridge to transplant; DT, destination therapy; HF, heart failure; INTERMACS, Interagency Registry for Mechanically Assisted Circulatory Support; LVAD, left ventricular assist device; NYHA, New York Heart Association; RT, rescue therapy.

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![Figure 22-30](image-url) **Survival after ventricular assist implantation, stratified by age. Pediatric Heart Transplant Study, 1993-2003.** (Redrawn from Kirklin.)

---

![Figure 22-30](image-url) **Survival to Transplant: Age at Listing**

---

![Figure 22-30](image-url) **Figure 22-30**
important elevation of left atrial (and potentially pulmonary arterial) pressure.

**Anticoagulation**
Following implantation of the Berlin Heart standard administration of clotting factors can be employed to achieve hemostasis, with the exception that platelet transfusion should be avoided when possible because of the associated risk of sensitization and subsequent development of anti-HLA antibodies that could affect donor matching. When bleeding and chest tube drainage are minimal, initiation of heparin infusion is recommended, although some protocols avoid heparin altogether. Warfarin therapy is guided by INR (2.5-3.5). Some centers substitute chronic heparin therapy for warfarin in small infants. ASA and dipyridamole (or clopidogrel) are initiated within the first few days. Twice-weekly monitoring with thromboelastography is recommended to assess overall anticoagulation effectiveness, and specific testing of platelet function is advisable to determine adequacy of blockade of the arachidonic acid pathway (by ASA) and the ADP pathway (by clopidogrel).

**Neurologic Events**
Intracerebral hemorrhage and thromboembolic episodes are the major causes of morbidity and mortality during pump support. Specific time-related risk of these events is not precisely documented, but the incidence of serious neurologic events during support is estimated at 7% to 8%.

**EXCOR Pediatric Experience**
The German Heart Institute reported an experience of 68 pediatric patients supported between 1992 and 2005.
Since 1999, approximately 60% of patients received isolated left ventricular support, with about 40% requiring biventricular implants. The maximum duration of support was 420 days, with 73% of patients surviving to transplantation or recovery with device explantation. Major causes of mortality were multi-organ failure, sepsis, stroke, and hemorrhage. In North America, 80 patients were supported between 2000 and 2007, with the smallest patient being 3.0 kg and 15 days of age. The longest support was 234 days, with 55% of patients undergoing cardiac transplantation, 13% weaned from the device for recovery, and 25% mortality during device support. The Berlin EXCOR is currently approved for clinical use in Europe and the United States.

**MicroMed-DeBakey VAD Child**

The MicroMed-DeBakey VAD Child is a pediatric axial flow pump of the same basic design as the adult MicroMed pump (see “Continuous Flow Ventricular Assist Devices” under Durable Circulatory Support Devices). Basic design differences include a shorter inflow apical cannula (2.5 cm), an inflow tube angle of 140 degrees, and a shorter outflow protector sleeve (2.6 inches). These design alterations allow the pump to lie at a more acute angle with less lateral space required in the child or adolescent (Fig. 22-33). Current accepted criteria for this pediatric axial flow pump include (1) bridge-to-transplant therapy, (2) patients aged 6 to 16 years, (3) refractory NYHA class IV symptoms with inotrope requirement, and (4) BSA of at least 0.7 m².
Emerging Devices

With the clear need for more effective miniaturized systems for technical circulatory support in infants and small children, the NHLBI has funded research for the development of five unique pediatric pumps: two magnetically suspended continuous flow pumps, an axial-flow apically implanted device, a pulsatile flow device, and a compact integrated pediatric cardiopulmonary assist system (Fig. 22-34). None of these devices has currently entered clinical trials.

REFERENCES

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## Section I: Chronic Constrictive Pericarditis

### Definition
Chronic constrictive pericarditis is a chronic inflammatory process that involves both fibrous and serous layers of the pericardium, leading to pericardial thickening and compression (constriction) of the ventricles. The resultant impairment in diastolic filling reduces cardiac function.

### Historical Note
It is said that Galen in AD 160 described cicatricial thickening of the pericardium in an animal and surmised that the same condition might occur in humans. The first formal account of the condition in humans was apparently that of Lower, who described both acute and chronic constrictive pericarditis in 1669. Other early descriptions were those by Bonetus in 1679 and Vieussens in 1715. Lancisi apparently understood the pathology of the condition; in 1728 he described at autopsy a patient with a small heart encased by a thick adherent pericardium in association with marked swelling of the abdomen and jugular veins.

### Modes of Death
- Incremental Risk Factors for Death
- Hemodynamic Results
- Functional Status
- Reoperation

### Indications for Operation

#### Section II: Chronic Effusive Pericarditis

### Definition

### Historical Note

### Morphology

### Clinical Features and Diagnostic Criteria

#### Pathophysiology of Cardiac Compression
- Normal
- Acute Cardiac Tamponade
- Chronic Constrictive Pericarditis
- Effusive Constrictive Pericardial Disease

#### Etiology

#### Clinical Presentation

#### Clinical Findings

#### Laboratory Investigation
- Chest Radiography
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- Two-Dimensional Echocardiography
- Computed Tomography
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- Pericardiocentesis
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- Pericardial Window via Left Anterolateral Approach
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#### Indications for Operation

#### Section III: Other Types of Pericarditis

### Purulent Pericarditis

### Tuberculous Pericarditis

### Congenital Absence of Pericardium

### Postpericardiectomy Syndrome
As a result of the observations of Morgagni in 1760 and Laennec in 1819 that pericardial adhesions were rarely associated with symptoms, little attention was paid to the possible clinical significance of chronic pericarditis for nearly a century because of ignorance of the difference between adhesive pericarditis and constrictive pericarditis. The early literature contains only four reports (Cheevers, 1842; Greisinger, 1856; Wilks, 1870; Kussmaul, 1873), largely ignored, stressing that chronic constrictive pericarditis could be clinically important.

Interest was refocused on the condition by Pick’s report in 1896 of three patients with chronic constrictive pericarditis whose clinical course had been thought in life to be due to cirrhosis of the liver. About that time, surgeons were becoming more expert and aggressive, and Weill in 1895 and Delorme in 1889 suggested that pericardectomy be used to treat this condition. Brauer in 1902 suggested removing the bony precordium as a method of relief. Apparently, the first operation directed against chronic constrictive pericarditis was carried out by Halloopeau. Both Rehn and Sauerbruck in Germany performed a successful partial pericardectomy in 1913. In 1926, Schmieden and Fischer in Germany reported a series of successful cases, as did Churchill in 1929 from Massachusetts General Hospital and Beck in 1931 from Cleveland. Surgical experience was expanded by Harrington and Barnes at the Mayo Clinic and by Heuer and Stewart at New York Hospital. By 1941, Blalock and Burwell reported surgical treatment of 28 patients.

Animal experiments began to clarify some of the perplexing problems that persisted despite the advent of surgical treatment. In 1929, Beck reproduced the syndrome by injecting Dakin solution into the pericardial cavity of dogs. He demonstrated that simple obliteration of the pericardial cavity by adhesions did not produce the syndrome; only a thick, dense scar around the heart did so, thus solving the riddle of 100 years earlier. He then demonstrated in animals that the syndrome could be relieved by pericardectomy. He also demonstrated experimentally several efficient methods of controlling the hemorrhage that could develop from the surface of the heart during the dissection required to relieve chronic constrictive pericarditis. The pathogenesis was then further elucidated by the cardiac catheterization studies of Sawyer and colleagues and by the ingenious experiments of Isaacs and colleagues. These studies led directly to development of better diagnostic and surgical methods.

MORPHOLOGY

Normally, the potential space between inner and outer layers of the visceral pericardium contains a thin layer of fluid. A demonstrable amount of fluid normally accumulates only over the atrioventricular junctions. This has provoked controversy about the pressures normally present between the fibrous pericardium and the inner layer of the visceral pericardium (epicardium).

As chronic constrictive pericarditis develops, the fibrous parietal pericardium and both layers of the visceral pericardium are involved to some extent, but details of the pathologic process vary. If the two layers of the visceral pericardium remain separate, the pericardial space contains variable amounts of fluid, often with extensive and sometimes hemorrhagic fibrinous deposits on both surfaces. This entire fibrous and fluid mass can be constricting to the heart. When the process is far advanced, the two layers of visceral pericardium thicken and fuse, and along with the fibrous pericardium, encase the heart in a thick, solid, fibrous, and often calcified envelope that is adherent to the myocardium.

In addition, cardiac muscle fiber atrophy occurs in many cases. Atrophy may appear relatively early in the course of the disease. Myocardial fibrosis also complicates late stages of chronic constrictive pericarditis.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Pathophysiology of Cardiac Compression

Cardiac compression occurs in chronic constrictive pericarditis, but is also a feature of acute cardiac tamponade and effusive constrictive pericardial disease, a condition characterized by pericardial thickening and variable amounts of fluid in the pericardial space.

Normal

Pericardial pressure is subatmospheric under normal circumstances, similar to intrapleural pressure. Both intrapericardial and intrapleural pressures become more negative during inspiration. There are small fluctuations of intrapericardial pressure related to the cardiac cycle, and the transpericardial pressure (pericardial minus pleural pressure) is highest at end-diastole, the period of largest ventricular volume. Pericardial pressure rises as ventricular volume is increased beyond normal limits by the rapid infusion of fluid. Under such circumstances the effects of pericardial restraining are predominant on the right ventricle.

Pressure-volume relationships and stress-strain characteristics of the normal pericardium are such that there is little increase in intrapericardial pressure when a small amount of fluid is placed intrapericardially. With rapid addition of more fluid, the pressure slope rises progressively. At this stage, adding small amounts of fluid causes a large increase in intrapericardial pressure, and conversely, removing small amounts causes a large decrease in intrapericardial pressure (the rationale of pericardiocentesis in acute pericardial tamponade). Furthermore, because of pericardial hysteresis, intrapericardial pressure at a given volume during fluid removal is lower than during addition of fluid.

Intrapericardial events—normal and abnormal—affect both cardiac filling and cardiac output. Such events are reflected in phasic and overall atrial and venous pressures. The effect on systemic venous pressure is of particular importance because it is easily observed in the jugular venous pressure. Normally, the inferior and superior vena cava pressures exceed atmospheric pressure by only a few millimeters of mercury (mmHg). The jugular venous (and caval) pulse consists sequentially of three positive upward waves and two downward movements. First is the a wave, generated by atrial systole. The c wave follows, caused by displacement of the tricuspid valvar apparatus toward the right atrium during isovolumic ventricular systole. A negative x descent is next, generated in part by descent of the closed tricuspid valve apparatus at the beginning of ventricular ejection and in part by decreased intrapericardial pressure resulting from reduced ventricular volume as the ventricle ejects. A positive y wave is then generated by passive filling of the right atrium from
the cavae and coronary sinus. Finally, a negative y descent occurs as blood flows rapidly from right atrium to right ventricle.

**Acute Cardiac Tamponade**

Rapid increase in intrapericardial fluid, usually blood, produces acute cardiac tamponade. Intrapericardial pressure may rise as high as 20 to 30 mmHg. Such a pressure would be incompatible with life if it were not for reflex venoconstriction, catecholamine release, and the immediate retention of sodium and water by the kidneys as part of the total body response to reduced cardiac output. As a result, venous pressure rises to the level of intrapericardial pressure, and cardiac output is maintained, although usually at a reduced level. This process has led to one definition of cardiac tamponade as a condition in which right atrial and systemic venous pressure are determined by elevated intrapericardial pressure. 

When intrapericardial pressure first rises, it tends to exceed left as well as right atrial pressure, and in patients who survive, both left and right atrial pressures rise in response to the neurohumoral compensatory mechanisms mentioned earlier. At this stage, right and left atrial pressures, right and left ventricular diastolic pressures, pulmonary artery diastolic pressure, and pulmonary artery wedge pressure are identical to intrapericardial pressure. Untreated, the patient dies when cardiac output continues to decrease despite compensatory mechanisms.

In this classic setting of acute cardiac tamponade, the heart is small and quiet, venous pressure is elevated, and systemic arterial blood pressure is depressed—a group of signs known as the *Beck triad*. Elevation of venous pressure may be mild, or it may reach 20 mmHg or more. Jugular venous wave forms are altered because the tamponade effect is least during ventricular ejection, when ventricular volume is smallest. No cardiac filling occurs during diastole, and thus there is no y descent. All filling occurs during systole, so the x descent is preserved and exaggerated.

Unless hypotension is extreme, the condition is also characterized by *pulsus paradoxus*, an inspiratory decrease in arterial systolic blood pressure exceeding 10 mmHg during quiet respiration. The mechanism underlying pulsus paradoxus in acute cardiac tamponade is complex. During inspiration, caval flow into the right atrium increases, just as in the normal situation; in fact, the percentage of increase is greater than normal. The resultant increase in right heart volume raises intrapericardial pressure still further, and pericardial transmural (intrapericardial minus intrapleural) pressure rises. Left ventricular volume is decreased as the ventricular septum is displaced leftward by the increased right ventricular volume. Left ventricular inflow is diminished because the somewhat decreased right ventricular output is easily accommodated by the expanding lung blood volume during inspiration, with less transmitial flow. These phenomena result in decreased left ventricular stroke volume and thus diminished arterial blood pressure. Another contributor to pulsus paradoxus is delay in passage of the increased caval flow of early inspiration to the left ventricle, so that by the time it has occurred, respiration has generally shifted to the expiratory phase. Also, the inspiratory decrease in intrathoracic pressure tends to decrease aortic and arterial pressure, and inspiration tends directly to decrease left ventricular contraction.

**Chronic Constrictive Pericarditis**

Basic pathophysiology of chronic constrictive pericarditis has been debated for more than half a century. By 1949, Holman and Willett concluded that constriction of the caval orifices and atria was important in its pathogenesis and for this reason adopted the median sternotomy approach for its surgical correction. In 1951, Burwell concluded from cardiac catheterization study that both right and left ventricular function were impaired and constriction of caval orifices or atria played no role. In 1952, Isaacs and colleagues showed in dogs that a change in the pressure-volume curves of the two ventricles resulted from experimentally produced constrictive pericarditis, and this was the fundamental pathophysiologic change associated with the disease (Fig. 23-1). These investigators also demonstrated during development of the constriction an increase in right and left ventricular diastolic pressure and a decrease in stroke volume. In their experimental animals, a small increase in volume resulted in a considerable increase in end-diastolic pressure. These studies indicated that lack of ventricular diastolic distensibility, and thus inability to generate an adequate preload (see “Ventricular Preload” under Cardiac Output and Its Determinants in Section I of Chapter 5), was a characteristic of hearts with chronic constrictive pericarditis. These considerations influenced Scannell and colleagues to adopt a left anterolateral thoracotomy as their surgical approach of choice by 1952.

A number of features of clinical cases of chronic constrictive pericarditis derive from these basic abnormalities of diastolic function. Ventricular filling is impaired and ventricular stroke volume reduced as a result of decreased compliance of the fused cardiac and pericardial mass. Phasic aspects of ventricular filling are also altered. For a brief period in early diastole, ventricular filling is rapid. However, the limit of
ventricular distensibility is reached rapidly, and the right ventricular pressure pulse displays an early diastolic dip and then a high diastolic plateau (square root sign). There is nearly complete diastolic ventricular filling during the first 50 milliseconds of diastole.\textsuperscript{61}

Systemic venous pressures are correspondingly abnormal; mean venous pressure is elevated. The \( x \) descent is steep and deep, corresponding to the beginning of ejection. The \( y \) descent is also steep and deep, corresponding to the early diastolic dip of right ventricular pressure. This differs from events during acute cardiac tamponade, in which the \( y \) descent is absent. The normal inspiratory increase in vena caval flow and decrease in pressure is diminished and often absent.

Pulsus paradoxus is said to be infrequent in chronic constrictive pericarditis, in contrast to the situation with acute cardiac tamponade. However, frequency of its recognition is influenced by cardiac rhythm; it is usually present when there is sinus rhythm, but impossible to detect when there is atrial fibrillation (a frequent accompaniment of chronic constrictive pericarditis).

Ventricular end-diastolic volumes are small in this disease, as are end-systolic volumes and stroke index. Rate of increase of left ventricular systolic pressure and ejection fraction are not altered.\textsuperscript{15} Thus, systolic left ventricular function under these circumstances is normal, but this does not necessarily indicate normal contractility.

**Effusive Constrictive Pericardial Disease**

Although seen in a number of settings, effusive pericardial disease is common in nephrogenic pericarditis.\textsuperscript{182} In this condition, increased volume of pericardial fluid produces the characteristic clinical picture of acute cardiac tamponade, with absence of a \( y \) descent and a preserved and prominent \( x \) descent in the jugular venous pulse. However, because of coexisting pericardial thickening, aspiration of pericardial fluid does not return the situation to normal. Rather, the thickened pericardium begins to restrain the heart, but only after the rapid filling phase of the ventricles is over. Thus, the \( y \) descent is again present and is prominent, occurring during the time the right atrium is in free communication with the right ventricle through the open tricuspid valve and simultaneously with the early diastolic dip of ventricular pressure. In effusive constrictive pericardial disease, after the fluid is removed, there is no respiratory variation in the right atrial and venous pressures, just as in constrictive pericarditis.

**Etiology**

In most patients the etiology of chronic constrictive pericarditis is not known. McCaughan and colleagues were able to identify a specific etiologic factor in only 27% of their patients, and Blake and colleagues in only 34%.\textsuperscript{87,114}

In about 10% of cases, documented acute pericarditis precedes development of chronic constrictive pericarditis. Prior to its effective treatment, tuberculosis was the etiology of chronic constrictive pericarditis in up to 17% of cases.\textsuperscript{114,27} Currently, a prominent cause is mediastinal radiation for malignant disease.\textsuperscript{510} Rheumatoid disease and sarcoidosis occasionally are causes. Trauma is another uncommon cause, with hemopericardium usually present as the precursor of pericardial thickening and constriction.\textsuperscript{66,66}

Cardiac surgery can be followed by constrictive pericarditis, but this is uncommon, probably occurring in less than 5% of patients.\textsuperscript{3,114} It may be more common after coronary artery bypass grafting than after other operations.\textsuperscript{3} The interval between the original cardiac operation and development of evidence of pericardial constriction is highly variable, ranging from 1 month to nearly 10 years.\textsuperscript{3} Mean interval is about 2 years.\textsuperscript{3}

**Clinical Presentation**

Classically, symptoms of chronic constrictive pericarditis are delayed for several years after the clinical or subclinical episode of acute pericarditis. The interval may, however, be as short as 3 to 4 weeks in those rare instances in which pericarditis develops after cardiac surgery, or 4 to 12 months after trauma or acute nonspecific pericarditis.

Initial symptoms may be only fatigue with or without modest effort breathlessness, and neck vein distention may be noticed. Insidiously, however, hepatomegaly and ascites develop, initially with or without peripheral edema. Even within the context of such evidence of appreciable fluid retention, breathlessness may occur only on exertion and not at rest; although in severe cases there may be orthopnea. Paroxysmal nocturnal dyspnea occurs infrequently.\textsuperscript{114}

**Clinical Findings**

When constriction is not severe, clinical findings may be limited to modest but persistent elevation of jugular venous pressure and slight liver enlargement with or without intermittent ankle edema. As constriction increases, there is a progressive increase in venous pressure and hepatomegaly, with eventual development of persistent peripheral edema, ascites, and pleural effusion. Venous pressure fails to decline during inspiration (Kussmaul sign), but this is not specific, in that the same findings may accompany right ventricular failure, restrictive myocardial disease, or tricuspid valve stenosis.\textsuperscript{117} By this stage, pulsus paradoxus is to be expected if sinus rhythm persists, and pulse pressure often is reduced. The apex beat is usually not palpable, but there is often systolic retraction in the left parasternal region. This retraction may be followed by a visible and palpable forward thrust extending toward the expected site of the cardiac apex. This impulse, which results from forceful ventricular filling with the onset of diastole, may be mistaken for the apex beat and used to argue against the existence of pericardial constriction. Rapid ventricular filling in early diastole is also associated with an unusually early, often loud, third heart sound that is sometimes referred to as a pericardial knock, but usually there are no murmurs.

As in other forms of heart failure, salt and water retention are present. Anand and colleagues found important increases of total body water, extracellular volume, plasma volume, and exchangeable sodium in their study of patients with proven constrictive pericarditis.\textsuperscript{114} However, renal plasma flow was only moderately decreased, and glomerular filtration rate was normal. Norepinephrine, renin activity, aldosterone, and cortisol were also increased, as was plasma atrial natriuretic hormone, although not to levels usually seen in other heart failure syndromes. The ratio of left atrial to aortic diameter measured by echocardiography was only minimally increased, indicating that in constrictive pericarditis, the atria are
Laboratory Investigation

Protein-losing enteropathy occurs in some patients with chronic constrictive pericarditis who develop ascites and hepatomegaly. They may have severe hypoproteinemia, with depression of albumin and gamma globulin, and an increased rate of leakage of plasma protein into the gastrointestinal tract. This syndrome also develops after other conditions that chronically elevate inferior or superior vena caval pressure, such as the Fontan operation and atrial switch operations with inferior vena cava obstruction (see “Protein-Losing Enteropathy” under Results in Section IV of Chapter 41, and “Superior Vena Cava Obstruction” and “Inferior Vena Cava Obstruction” under Special Situations and Controversies in Chapter 52).

Chest Radiography

The chest radiograph may be unremarkable, although about one third of patients show moderate to marked enlargement of the cardiac silhouette. Pericardial calcification is evident in about 40%, and radiologic evidence of compression in about 60%.

Electrocardiography

The electrocardiogram (ECG) is usually abnormal, with nonspecific ST-segment and T-wave changes in 90% of cases. In about 40% of patients with surgically verified chronic constrictive pericarditis, the QRS complexes have low voltage, and an atrial arrhythmia is present in 30%.

Imaging Studies

Two-Dimensional Echocardiography

Although extraordinarily useful in evaluating accumulations of pericardial fluid, two-dimensional (2D) echocardiography is less specific in diagnosing chronic constrictive pericarditis. It can, however, be helpful in studying patients with restrictive cardiac disease in general and reflects hemodynamic-respiratory interactions. Specifically, with inspiration, the right ventricle fills normally, but the left ventricle is inadequately filled because of both leftward septal movement and reservoir function of the lungs. Doppler interrogation shows diminished transmitral velocities. These are due partly to increased left ventricular afterload, negative intrathoracic pressure during inspiration, and systemic vasoconstriction associated with low cardiac output.

Computed Tomography

Computed tomography (CT) can identify thickened pericardium and distinguish this from pericardial effusion. However, anatomic findings on CT study have little diagnostic importance unless the physiologic phenomena of restriction to ventricular diastolic filling are demonstrated.

Oren and colleagues, using CT, demonstrated that the abnormally rapid early diastolic filling of the left ventricle characteristic of constrictive physiology, coupled with a measured pericardial thickness greater than or equal to 10 mm, can distinguish constrictive from normal or restrictive physiology.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) also can provide measurements of pericardial thickness and depict characteristic right atrial dilatation and right ventricular compression.

Masui and colleagues found the sensitivity, specificity, and accuracy of MRI in diagnosis of constrictive pericarditis to be 88%, 100%, and 93%, respectively.

Cardiac Catheterization

Characteristically, end-diastolic pressures are elevated and equal in the right atrium, pulmonary artery, and left atrium; this is the hallmark of chronic constrictive pericardial disease. In the report by McCaughan and colleagues, such findings were obtained in all patients coming to catheterization.

Intraventricular pressure pulse contours characteristically demonstrate an early rapid fall in diastolic pressure in the right ventricle, followed by a rapid rise to an elevated diastolic plateau (square root sign). Left ventricular pressure pulse usually has a similar contour.

Mean right atrial pressure fails to decrease normally during inspiration, or it may actually rise slightly. There is a transient increase in pulmonary blood volume and a slight reduction in right ventricular afterload, resulting in a fall in pulmonary arterial and right ventricular systolic pressure and a decline in pulmonary venous pressure and left ventricular diastolic pressure as well.

Vaitkus and Kussmaul identified the predictive accuracy of three different hemodynamic criteria for differentiating constrictive from restrictive disease (Table 23-1): (1) equalization of right and left ventricular end-diastolic pressure favors constriction; (2) constriction is associated with more modest elevation of right ventricular systolic pressure (≤50 mmHg); in restriction, it exceeds that amount; (3) in constriction, right and left ventricular end-diastolic pressure usually is greater than one third of right ventricular systolic pressure;

Table 23-1  Predictive Accuracy of Individual Hemodynamic Criteria for Constrictive Pericarditis and Restrictive Cardiomyopathy

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Constrictive Pericarditis (%)</th>
<th>Restrictive Cardiomyopathy (%)</th>
<th>Overall Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDP—RVEDP ≤5 mmHg</td>
<td>92</td>
<td>70</td>
<td>85</td>
</tr>
<tr>
<td>RV systolic pressure ≤50 mmHg</td>
<td>90</td>
<td>24</td>
<td>70</td>
</tr>
<tr>
<td>RVEDP/RV systolic pressure ≥0.33</td>
<td>95</td>
<td>32</td>
<td>76</td>
</tr>
</tbody>
</table>

(Data from Vaitkus and Kussmaul.)

Key: LV, Left ventricular; RV, right ventricular; EDP, end-diastolic pressure.
in restriction, the ratio is characteristically less than one-third.\textsuperscript{61}

When hemodynamic studies are equivocal, rapid infusion (in 6 to 8 minutes) of 1000 mL of normal saline solution produces diagnostic features of occult chronic constrictive pericardial disease.\textsuperscript{81,82} These features include not only striking elevations of filling pressures but also development of typical pressure pulse morphologic characteristics of constriction, loss or reversal of the respiratory variation of right atrial pressure, and precise diastolic equilibration of cardiac pressures.

Endomyocardial Biopsy

When diagnosis is unclear, myocardial biopsy may be useful. Normal myocardium, nonspecific changes (e.g., from irradiation), or myocarditis on biopsy must be considered nondiagnostic, because they may be present with either restrictive or constrictive disease.\textsuperscript{83} Finding amyloid disease is diagnostic of a restrictive etiology.

Minor Thoracotomy

Despite the studies mentioned previously, distinguishing between chronic constrictive pericarditis and restrictive cardiomyopathy can remain difficult, and a minor thoracotomy may be useful in a few circumstances.\textsuperscript{84} A small left anterior thoracotomy incision placed in the line of the formal anterolateral incision that would be used for pericardectomy is made, and the pericardium is exposed through the interspace and biopsied. If the pathologic diagnosis is chronic constrictive pericarditis, the incision is extended and a formal pericardectomy performed. If no pericardial pathologic condition is found, diagnosis favors restrictive cardiomyopathy, and operation is terminated as a minor procedure. If recurring pericardial effusion is found with a more or less normal pericardium, wide removal of the pericardium can be easily accomplished with slight extension of the incision.

\textbf{NATURAL HISTORY}

Knowledge of the natural history of surgically untreated patients with chronic constrictive pericarditis is incomplete. The interval between an etiologic event and onset of clinical evidence of constriction varies between a few months and many years. Factors that determine rate of progression of the disease and its symptoms are unknown. Atrial fibrillation commonly occurs at some stage and can result in sudden deterioration in circulatory status.

Somerville has estimated that once signs and symptoms of chronic constrictive pericarditis develop, a semi-invalid life can be led over an interval of 5 to 15 more years.\textsuperscript{85} When the clinical syndrome includes ascites, progression is more rapid, particularly in children.\textsuperscript{86}

\textbf{TECHNIQUE OF OPERATION}

Because patients with chronic constrictive pericarditis coming to operation are often seriously ill, an arterial catheter is inserted into the radial artery for pressure recording, in addition to usual preparations in the operating room. A central venous pressure line and often a pulmonary arterial catheter are also inserted.

Approach may be through a left anterolateral thoracotomy or a median sternotomy.

\textbf{Left Anterolateral Thoracotomy Approach}

The patient is positioned supine, with a roll beneath the left scapula. The left hand is secured beneath the left buttock, with the elbow padded and positioned on the left side of the table (Fig. 23-2, A). A curving left anterolateral skin incision is made beneath the breast anteriorly and more laterally over the fifth interspace. Incision is carried through the pectoralis major anteriorly, and the fifth interspace is opened. The interspace incision is extended well anteriorly. The internal thoracic vessels can be ligated and divided and the fifth costal cartilage disconnected from the sternum if exposure is inadequate. The rib spreader is inserted and the interspace incision extended laterally with scissors as the spreader is gradually opened.

The left phrenic nerve is identified and freed from the pericardium if possible. Occasionally the nerve is mobilized with a narrow strip of pericardium to avoid injury. The pericardium is incised through an area of minimal calcification posterolaterally if possible, over what is presumed to be left ventricle (Fig. 23-2, B). On occasion, this initial incision through the abnormal pericardium takes the dissection immediately onto the myocardium; in other cases, it enters a fluid-filled space (see “\textbf{Morphology}” earlier in this section).

When a space is entered, the initial longitudinal incision is carried anteriorly and posteriorly from its superior and inferior extremities. The anterior pericardial flap is dissected as far as the right atrioventricular groove, beneath the elevated thymus and prepericardial fat, and resected (Fig. 23-2, C). The posterior flap is dissected far posteriorly and excised. Dissection must be carried superiorly onto the pulmonary trunk, because failure to relieve pericardial bands across it can result in postoperative gradients and severe right ventricular hypertention.\textsuperscript{87} The piece of pericardium left inferiorly is dissected off the diaphragm except in the area of the central fibrous tendon, from which it often cannot be removed. Fibrous plaques adherent to the epicardium are then dissected off through the entire area of resection. If the epicardium is thin and relatively normal, it need not be disturbed. If it is thickened, it must be removed either in its entirety or in a sufficient number of areas to allow more normal diastolic filling of the ventricles. Failure to do this severely compromises results of operation.\textsuperscript{88}

If no pericardial space is found, the entire longitudinal incision and its anterior and posterior extensions are made only through the fibrous pericardium. Then the incision is deepened in an area that seems to be over myocardium rather than over the interventricular or atrioventricular groove. Slowly and carefully, the posterior flap is dissected off the left ventricular myocardium. At first, this dissection is done only in areas in which it proceeds reasonably well, leaving the epicardium on the myocardium wherever it is thin and normal. When dissection in this plane is not possible, such as in an area of calcification or dense scarring, islands of calcification and scarring may be left attached to the myocardium but separated from other areas. Dissection moves to the anterior pericardial flap whenever progress ceases posteriorly and vice versa. Particular care is necessary when dissection passes across the interventricular groove containing the coronary vessels; here, islands of calcific plaque may need to be left in place.
Dissection is carried just across the atrioventricular groove and onto the atria. It is important to be certain that all constrictions in the atrioventricular groove are removed, because they can result in gradients between atrium and ventricle. No special effort is made to free the venae cavae or cavoatrial junctions, because constriction does not occur in these areas. When dissection is complete, the pericardial flaps, as well as the diaphragmatic portion of the pericardium, are excised (Fig. 23-2, D).

If a pulmonary arterial catheter is not placed, a polyvinyl catheter can be inserted into the left atrium via the appendage or left pulmonary veins to monitor pressure and assist in postoperative care. Two pleural drainage catheters are inserted, the tip of one being placed posteriorly and inferiorly and that of the other anteriorly and superiorly. The interspace incision is closed with heavy pericostal and perichondrial absorbable sutures, and the muscle layers are closed with continuous absorbable sutures. The skin is closed with a continuous subcuticular suture.

**Median Sternotomy Approach**

The median sternotomy approach may be used with or without cardiopulmonary bypass (CPB). In either event, the sternum is divided in the usual manner (see “Incision” in Section III of Chapter 2). The pericardium is opened vertically anteriorly. Often it is necessary to use a knife for this maneuver, and particular care must be taken when the plane between the thickened (visceral) pericardium and the myocardium is reached. The pericardial flaps are then dissected laterally, superiorly and inferiorly, as described in preceding text. To the right, dissection passes across the atrioventricular groove and proceeds across the anterior and lateral walls of the right atrium, as long as the cleavage plane there is readily
C, Flaps have been dissected back, completely liberating both left and right ventricles, leaving where necessary small calcific plaques in situ. First portion of pulmonary trunk has been completely unroofed. D, Appearance at end of procedure. Thickened pericardium has been removed from diaphragm.
found. If it is not, this portion of thickened pericardium can be left in situ. In the former instance, the pericardial flap is excised about 1 to 2 cm anterior to the right phrenic nerve. To the left, dissection proceeds across the front of the ventricles and then over the lateral left ventricular wall. This pericardial flap is excised about 1 cm in front of the left phrenic nerve. Dissection continues posterior to the pericardial nerve but in the plane between myocardium and epicardium until the entire left ventricle is freed (up to the atrioventricular groove posteriorly and over the diaphragm inferiorly). It is usually possible to remove the thickened, often calcified, outer pericardial layer, because there is generally a cleavage plane between this and the overlying thickened pleura containing the pericardic nerve. The same is usually true of the thickened pericardial tissue inferiorly overlying the diaphragm. Operation is completed as described earlier.

The need for CPB is debatable. However, if CPB is anticipated, the obvious approach is median sternotomy. The improved exposure afforded by CPB must be balanced against the probability of increased blood loss. When CPB is used, it may be most convenient to use the femoral vessels for both venous and arterial cannulation (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2). Then, after CPB has been established at 34°C to 37°C, the thickened pericardium can be incised and dissection accomplished.

Choice of Surgical Approach

The main advantage of the left anterolateral approach is the excellent exposure afforded for complete liberation of the left ventricle and complete removal of the diseased pericardium over it, including its diaphragmatic surface. The main advantage of median sternotomy is the ease with which the incision is made and the improved exposure obtained for removing pericardium from the right ventricle. It is a better approach when CPB is used, although CPB can be used with the anterolateral approach by cannulating the femoral vessels (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2). Although there are proponents of near-routine use of CPB for pericardectomy, there is no clear evidence that this improves outcomes after operation. One proposed advantage, is the ability to liberate the cavoatrial junction and to remove the pericardium over the right atrium, although the benefit of this is controversial.

Complementary Techniques

A high-speed Burr or ultrasonic dissector may help to define the epicardial layer and dissect the adherent calcified pericardium away from the myocardium. Complete resection of all thickened and constrictive epicardium is as important for achieving a good result as complete removal of the parietal pericardium. However, in some patients (particularly those with postoperative or postirradiation constriction), it is impossible to develop a consistent plane of dissection. Usually that plane is apparent by encountering dark pink myocardium, the surface of which expands into the pericardial incision and contracts vigorously. In cases in which the epicardial peel is exceptionally adherent, a cross-hatching “waffle” procedure described by Heimbecker and colleagues or multiple incisions of the peel (turtle cage operation) allow myocardial expansion and restoration of adequate hemodynamics.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is given as described in Chapter 5. Low cardiac output early postoperatively occurs commonly in patients who have advanced disability, fluid retention, and ascites preoperatively. Low cardiac output may require maintaining left atrial pressure at a relatively high level (15 mmHg or more) and using catecholamine infusions for 12 to 48 hours. Intraaortic balloon pulsation is effective in these patients when cardiac output is low and unresponsive to other measures.

RESULTS

Survival

Early (Hospital) Death

Hospital mortality after pericardectomy for chronic constrictive pericarditis does not approach zero even in the current era. In an earlier era, early (hospital) mortality was 10% to 15%. More recently, it has been about 5%. Nataf and colleagues reported 2% to 3% operative mortality in 84 patients operated upon between 1979 and 1989 using a median sternotomy. Others have reported similar results.

Time-Related Survival

Patients operated on for chronic constrictive pericarditis have a time-related survival that is less than, or in favorable cases similar to, that of an age-gender-ethnicity–matched population (Fig. 23-3). Survival, including hospital deaths, at 1, 5, 10, and 20 years is about 90%, 75%, 65%, and 55%, respectively.
Chapter 23 Pericardial Disease

Factors in the early phase after operation. Preoperative NYHA functional class is also a risk factor for death late after operation (see Fig. 23-4). Correspondingly, high right ventricular end-diastolic pressure preoperatively has been a risk factor (Fig. 23-5). Moderate to severe tricuspid regurgitation is also associated with increased early mortality.

Previous radiation therapy over the chest is an important risk factor for unfavorable results and a higher time-related prevalence of death than otherwise occurs (Fig. 23-6). Mode of Death

About 75% of postoperative in-hospital deaths occur from acute or subacute cardiac failure. Postoperative hemorrhage and respiratory failure are other modes of early death.

Only about 5% of patients continue to have chronic heart failure after recovery from a satisfactory pericardectomy. Such patients have usually had long-standing symptoms (Fig. 23-4) or were older at operation.

Incremental Risk Factors for Death

Preoperative functional status is a powerful risk factor for death in the early hazard phase after operation. Thus, early risk approaches zero for patients in New York Heart Association (NYHA) functional class I or II preoperatively, 10% (CL 8%-14%) for those in NYHA class III, and 46% (CL 29%-64%) for those in NYHA class IV. Related to this is the fact that ascites and peripheral edema, usually associated with preoperative NYHA class IV, have been identified as risk factors in the early phase after operation.

Surgical approach—that is, left anterolateral thoracotomy or median sternotomy with or without CPB—has not affected outcome beyond what could be due to chance alone (Fig. 23-7).

**Figure 23-4** Survival, excluding hospital deaths, after pericardectomy according to preoperative New York Heart Association (NYHA) functional status. Database is same as in Fig. 23-3.

**Figure 23-5** Relationship of hospital mortality after pericardectomy (depicted along vertical axis) to preoperative right ventricular end-diastolic pressure. (Data from Seifert and colleagues.)

**Figure 23-6** Survival after pericardectomy according to whether pericarditis was typical chronic constrictive or postradiation ($P = .0005$). Vertical bars depict standard error of estimates. (Data from Seifert and colleagues.)

**Figure 23-7** Survival, excluding hospital deaths, after pericardectomy according to surgical approach. Database is same as in Fig. 23-3.
Section II  Chronic Effusive Pericarditis

DEFINITION

Chronic effusive pericarditis is a condition in which an inflammatory reaction of the pericardium stimulates accumulation of appreciable amounts of pericardial fluid. The fluid itself may be an indication for therapeutic intervention, or, coupled with loss of compliance of the pericardium, it may provoke the syndrome of pericardial constriction.

HISTORICAL NOTE

Chronic effusive pericarditis is more common currently than in earlier eras because of improved therapy and thus longer survival of patients with malignant disease, and because of the appreciable number of patients whose lives are prolonged by long-term dialysis for end-stage renal disease.

MORPHOLOGY

Chronic effusive pericarditis is usually of the so-called bread-and-butter type, with dense strands of fibrin bridging the space between the layers of the visceral pericardium. Both the visceral and parietal layers may be thickened and adherent to one another, and the entire area may be hemorrhagic. Pericardial fluid may occupy the entire pericardial space or may be loculated into several areas.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Pathophysiology

Rarely, acute cardiac tamponade develops in patients with chronic effusive pericarditis. More commonly, fluid accumulates sufficiently slowly that this does not occur. Instead, the patient presents with signs and symptoms of effusive constrictionary pericardial disease (see “Pathophysiology of Cardiac Compression” in Section I for the pathophysiology of this and other types of cardiac compression).

Etiology

Although precursors of chronic effusive pericarditis (e.g., advanced renal disease, dialysis, malignant disease, trauma) are recognized, precise etiologic mechanisms are not known (except in cases of frank pericardial involvement by malignant disease or collagen vascular disease). It was once believed that accumulation of pericardial fluid in patients with chronic renal failure was related to serum creatinine levels or degree of nitrogen retention, but this is not the case.

Chronic effusive pericarditis that develops during dialysis, and particularly during hemodialysis rather than peritoneal dialysis, is more refractory to medical treatment than that which develops from chronic renal disease itself. This syndrome appears more likely to develop in young women than in men. Infection was once thought to

Figure 23-8  Preoperative and late postoperative New York Heart Association (NYHA) functional class in 141 patients undergoing pericardectomy for chronic constrictive pericarditis. (Data from McCaughan and colleagues.)

Hemodynamic Results

Virtually all patients with a good result have normal resting hemodynamic characteristics after adequate surgical treatment of chronic constrictive pericarditis. During exercise, 10% to 20% may show mild elevation of pulmonary artery pressure or failure to increase cardiac output. When considerable amounts of thickened pericardium are left over the ventricles, hemodynamic improvement is less complete.

Functional Status

Most patients have a good long-term result from pericardectomy for chronic constrictive pericarditis, with nearly all in NYHA class I or II (Fig. 23-8).

Reoperation

Only a small percentage of patients (~2%) require reoperation.

INDICATIONS FOR OPERATION

Diagnosis of chronic constrictive pericarditis is, in general, an indication for operation. When physiologic effects of constriction are minimal, and particularly when other serious disease is present, operation may be delayed until more marked signs and symptoms appear.

Occasional patients are seen with fatigue, dyspnea, and chest pain, but without the characteristic clinical and laboratory features of chronic constrictive pericarditis. When diagnosis of pericardial constriction is made by rapid volume expansion in the catheterization laboratory (see “Clinical Features and Diagnostic Criteria” earlier in this section), pericardectomy is indicated, because symptomatic and long-term results are good under these circumstances.

Because of unfortunate results in patients whose chronic constrictive pericarditis is the result of previous radiation therapy, operation is advisable only when symptoms are advanced and there is near certainty that the cause of the symptoms is cardiac constriction by the pericardium.
be responsible for chronic effusive pericarditis, but this occurs rarely.45

Acute nonpurulent pericarditis often becomes a chronically recurring disease, which sometimes develops into chronic effusive pericarditis.

Symptoms
Onset of pericarditis may be heralded by chest pain—from mild to excruciating—and may be difficult or impossible to distinguish from angina. Some patients present with fever, leukocytosis, and a pericardial friction rub, but have little pain. A few patients present with evidence of acute cardiac tamponade.

Signs
The most striking abnormality on physical examination is gross elevation of jugular venous pulse. The characteristically absent y descent and preserved x descent are found in the jugular venous pulse wave. A pericardial friction rub may or may not be audible. Arterial blood pressure may be depressed, and pulsus paradoxus may be present.

Chest Radiography
An enlarged and globular cardiac silhouette on the chest radiograph supports diagnosis.

Electrocardiography
When nephrogenic or other forms of effusive pericarditis are acute, characteristically there is widespread ST-segment elevation.518,822 Later, the ECG may be normal or, if the disease becomes chronic, typical ECG features of chronic constrictive pericarditis may evolve.

Echocardiography
For patients with chronic effusive pericarditis, 2D echocardiography is a highly useful diagnostic modality. Not only can the diagnosis be made with this technique, but also aspiration of the pericardium can be made precisely and effectively by concomitant observation of the pericardial space.

NATURAL HISTORY
Development of chronic effusive pericarditis in patients with malignant disease is unpredictable unless there is malignant involvement of the pericardium. Nephrogenic pericarditis develops in about 15% of patients on chronic hemodialysis. It has a tendency to occur early in the course of dialysis.52

The natural history of this complication without intervention is unknown. Presumably, some patients with considerable effusion die with acute cardiac tamponade; in others, chronic constrictive pericarditis develops and follows its natural history.

TECHNIQUE OF OPERATION
Pericardiocentesis

The cardiologist generally performs pericardiocentesis in the cardiac catheterization laboratory, under hemodynamic and electrocardiographic control, after localizing the fluid by echocardiography. Either the subxiphoid or apical route is used, depending on location of the fluid. Previously, morbidity associated with this method was considerable. However, Callahan and colleagues have found pericardiocentesis directed by 2D echocardiography to be safe.43 Allen and colleagues compared percutaneous catheter drainage with subxiphoid pericardiotomy for treatment of pericardial effusion.43 Subxiphoid pericardiostomy had no operative deaths (0%; CL 0%-2.0%) and 1 complication (1.1%; CL 0.1%-3.6%) among 94 patients. Percutaneous catheter drainage resulted in 1 death (4%; CL 0.6%-14%) and 4 complications (17%; CL 9%-29%) among 23 patients (P < .005). The authors concluded that catheter drainage was suitable only for patients with hemodynamic instability.

Subxiphoid Pericardial Window
Either local anesthesia, conscious sedation, or general anesthesia may be used. A vertical midline incision about 4 cm in length is made over the xiphoid process and upper abdomen. The linea alba is divided, and the xiphoid is removed or retracted upwardly with the distal sternum. The diaphragm is dissected away from the undersurface of the sternum and xiphoid, fat is removed from over the pericardium, and the pericardium is opened under direct vision. All fluid is aspirated, and loculations may be broken up gently with the tip of a suction device. A large pericardial window as possible is made by excision of pericardium. Percardial tissue and fluid are sent for bacteriologic and histologic study. A drain is inserted and placed on 10- to 20-mmHg suction and the wound is loosely closed. Generally, the tube is left for several days and then removed.

Percutaneous Balloon Pericardiotomy
Percutaneous balloon pericardiotomy involves use of a percutaneous balloon–dilating catheter to create a nonsurgical pericardial window. Under local anesthesia, a needle is introduced via the subxiphoid approach, followed by a guidewire and dilator. Some fluid is removed, and radiographic contrast is injected into the pericardial space. A dilating balloon is placed so as to straddle the pericardial border. The balloon is inflated to create a window, and the remaining fluid is drained. Ziskind and colleagues reported that this procedure was successful in 46 of 50 patients (92%; CL 86%-96%) treated for tamponade or large effusion.21

Pericardial Window via Left Anterolateral Approach
A small left anterolateral incision is made, similar to the anterior portion of the incision described for treatment of chronic constrictive pericarditis. A simple pericardial window is created, usually anterior to the phrenic nerve. After evacuation of fluid, posterolateral and anterior chest tubes are brought out from the left pleural space through lower intercostal stab wounds. The incision is closed.
These operations can be performed through a standard left anterolateral incision or median sternotomy (see Technique of Operation in Section I).

RESULTS

These procedures can be curative when applied to chronic effusive pericarditis of unknown etiology. In this circumstance, however, use of a pericardial window is less effective than subtotal or complete removal of the pericardium.\(^1\),\(^5\),\(^6\),\(^7\)

When operation is done for palliation of an underlying malignant disease, long-term survival is considerably less than in patients with benign disease. However, relief of symptoms is generally excellent, although about 10% of such patients have recurrent effusions or late pericardial constriction.\(^8\)

Usually, such patients have been treated by a pericardial window; when the recurrence is symptomatic, subtotal or complete pericardectomy is indicated.\(^9\)

INDICATIONS FOR OPERATION

When symptoms are important and persist despite 7 to 10 days of intensive medical treatment, or when acute pericardial tamponade develops, operation is indicated. Under most circumstances a pericardial window is indicated, and the subxiphoid approach is chosen because of its greater simplicity and equal effectiveness compared with a window created through the transthoracic route.\(^1\) When a satisfactory result is not obtained, or when chronic effusive pericarditis recurs or constriction develops, subtotal or total pericardectomy is indicated.

Section III Other Types of Pericarditis

PURULENT PERICARDITIS

Intractable purulent pericarditis is uncommon in the current era. It is most commonly caused by *Staphylococcus aureus*, less often by *Haemophilus influenzae*. When it occurs and the pericardial abscess is not loculated, pericardiocentesis with 2D echocardiographic control is usually the initial treatment.\(^9\) Unless the process subsides rapidly after one or two aspirations, more adequate drainage is required. This can be accomplished with a tube through the subxiphoid approach (see Technique of Operation in Section II).\(^2\)

Majid and Omar reported 12 cases with 1 death (8%; CL 1%-26%).\(^1\) In children with staphylococcal pericarditis accompanied by symptoms of fever, respiratory difficulty, or tamponade, urgent pericardectomy and drainage are indicated.

TUBERCULOUS PERICARDITIS

In developed countries, tuberculosis occurs uncommonly, and tuberculous pericarditis occurs in only about 1% of patients in whom tuberculosis develops.\(^1\),\(^3\),\(^4\),\(^7\) In earlier times, mortality among patients with tuberculous pericarditis was as high as 40%.\(^8\)

When the amount of pericardial fluid is moderate and examination by 2D echocardiography shows little pericardial thickening, medical therapy alone is appropriate. When effusions are persistent after medical therapy with or without periodic aspirations under echocardiographic control, when the pericardium becomes thickened, or when signs of pericardial constriction develop, either because of the fluid or a cicatricial process in the pericardium itself, operation is indicated. Optimal procedures and their sequencing are the same as those described for chronic effusive pericarditis in Section II. If chronic constrictive pericarditis develops, then a full pericardectomy is indicated (see Technique of Operation in Section I).

CONGENITAL ABSENCE OF PERICARDIUM

Congenital absence of the pericardium may be partial or (less often) complete. In most instances the defects occur on the left side. Most patients are asymptomatic, but symptoms may develop because of herniation of cardiac tissue, either spontaneously or following a surgical procedure.\(^c\),\(^d\),\(^e\)

According to van Son and colleagues, in patients with partial left defects, chest radiography may show prominence of the left hilum or pulmonary trunk caused by herniation of the left atrial appendage through the defect.\(^2\) Echocardiography, MRI, and CT are useful in confirming the diagnosis.\(^c\),\(^d\),\(^e\),\(^f\) Complete absence of the left pericardium may be characterized by leftward displacement of the heart and aortic knob, a long prominent pulmonary artery, and a flattened left cardiac silhouette. Pericardial defects are rarely of clinical importance, although moderate-size defects may produce cardiac strangulation.\(^1\),\(^3\),\(^4\)

Most are discovered during cardiac surgery, and usually the only treatment is pericardiostomy by longitudinal extension of the existing defect to relieve tension at the defect and prevent herniation.

POSTPERICARDIOTOMY SYNDROME

Postpericardiotomy syndrome is an inflammatory pericarditis occurring in 10% to 40% of patients following cardiac surgery.\(^9\) It develops days to several months after surgery and is accompanied by pleuritic chest pain, low-grade fever, and pericardial friction rub on auscultation. Uncommonly, it progresses to chronic constrictive pericarditis. The Task Force on the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology lists colchicine as a class IIa indication for acute pericarditis. A randomized double-blind multicenter placebo-controlled Italian clinical trial has been completed to test the safety and efficiency of colchicine in preventing postpericardiotomy syndrome. Patients were randomized to 1 mg colchicine twice daily on day 1 and 0.5 mg twice daily for a month in those weighing 70 kg or more, and half that amount in those weighing less than 70 kg, versus a placebo. Postpericardiotomy syndrome within the subsequent 12 months was 8.9% vs. 21% \((P = .002\), respectively, and disease-related hospitalizations were 0.6% vs. 5.0% \((P = .02\), respectively. Gastrointestinal side effects were higher in the colchicine group \((8.9% vs. 5.0%, P = .2\). In symptomatic patients, the pain and effusions can
often be relieved by bed rest and aspirin or nonsteroidal anti-inflammatory drugs (ibuprofen, indomethacin). Although symptoms can also be resolved with corticosteroids (prednisone), their use should be avoided whenever possible because of the side effects.

REFERENCES

A

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## Acute Traumatic Aortic Disruption

### Definition

Acute Traumatic Aortic Disruption refers to the tearing or ripping of the inner layer of the aorta, which is a major blood vessel carrying blood from the heart to the rest of the body. This condition can be life-threatening if not treated promptly.

### Historical Note

The incidence of acute traumatic aortic disruption has increased due to improvements in road safety and injury management, but it remains a rare but severe condition.

### Morphology

- **Upper Descending Thoracic Aorta**
- **Ascending Aorta**
- **Other Sites**

### Clinical Features and Diagnostic Criteria

#### Pathophysiology

- **Clinical Features**
- **Diagnostic Imaging**
  - Chest Radiography
  - Computed Tomography
  - Transesophageal Echocardiography
  - Aortography
  - Magnetic Resonance Imaging

### Natural History

#### Technique of Operation

- **Preoperative Management**
- **Repair of Acute Traumatic Disruption of Upper Descending Thoracic Aorta**
- **Operative Strategies**
- **Open Repair**
- **Endovascular Stent-Grafting**
- **Repair of Acute Traumatic Disruption of Ascending Aorta**

### Special Features of Postoperative Care

#### Results

- **Survival**
  - Early (Hospital) Death
  - Open Operation
  - Endovascular Stent-Grafting
  - Time-Related Survival
  - Modes of Death
  - Risk Factors for Premature Death
  - Paraplegia

### Indications for Operation

- **Special Situations and Controversies**
  - Choice of Operative Procedure
  - Paraplegia after Aortic Clamping
  - Risk Factors
    - Duration of Aortic Clamping
    - Temperature
    - Level of Aortic Clamping
    - Variability in Blood Supply of Spinal Cord
    - Variability in Collateral Circulation to Spinal Cord
    - Intraspinal Pressure
    - Upper Body Blood Pressure
  - Methods to Minimize Spinal Cord Injury
    - Whole-Body Hypothermia during Simple Aortic Clamping
    - Perfusion of Distal Aorta during Aortic Clamping
    - Reattachment of Intercostal and Lumbar Arteries
    - Drainage of Cerebrospinal Fluid
    - Localized Cooling of Spinal Cord during Aortic Clamping
    - Monitoring Somatosensory and Motor Evoked Potentials
    - Pharmacologic Interventions
    - Methods for Perfusing the Distal Aorta during Aortic Clamping
    - Left Atrial–to–Femoral Artery Bypass
    - Aortic-Aortic Shunting
    - Partial or Total Cardiopulmonary Bypass

### Grafts for Use in Aortic Surgery

- **Type**
- **Preclotting of Synthetic Grafts**
- **Grafts Treated Before Packaging**
- **Endografts**
DEFINITION
Acute traumatic aortic disruption is rupture of all or part of the aortic wall, usually occurring as a result of blunt trauma. A theoretical sequence of injury involves initial rupture of the intimal and medial layers. After a period of unpredictable duration, rupture of the adventitial layer occurs. Patients are considered to have acute disruption when it occurs within 14 days of injury. Chronic traumatic aortic disruptions and posttraumatic aneurysms (pseudoaneurysms) are discussed in Chapter 26. Paraplegia as a complication of aortic surgery, and grafts used to replace or exclude the aorta, are also discussed in this chapter.

HISTORICAL NOTE
Although the lethal nature of acute traumatic aortic disruption had been recognized for centuries and was noted by Strassmann in 1947, data supporting lethality of traumatic disruption and temporal relationships between trauma and subsequent death were delineated by Parmley and colleagues in 1958. The first report of successful repair of traumatic disruption of the thoracic aorta apparently was by Dshanelidze in 1923 (cited by Clarke and colleagues). In 1957, Gerbode and colleagues reported successful repair of such an injury, as did Klassen and colleagues in 1958 (according to Passaro and Pace and Vasko and colleagues). In 1998, Kato and colleagues at Stanford University reported successful treatment of three patients with acute traumatic aortic disruption using endovascular stent-grafts constructed from modified Z stents covered with woven polyester or expanded polytetrafluoroethylene (PTFE) graft material and deployed through a delivery sheath from a peripheral artery.

MORPHOLOGY
Upper Descending Thoracic Aorta
Traumatic aortic disruptions occur most commonly in the upper descending thoracic aorta at or near the aortic isthmus. In the study of Parmley and colleagues, 45% of disruptions occurred at this site. In a more recent multicenter study by the American Association for the Surgery of Trauma (AAST) reported by Demetriades and colleagues, 82 (74%) of 110 acute aortic injuries occurred in this location. Occasionally, the disruption may occur at the origin of the left subclavian artery and extend proximally to involve the distal portion of the aortic arch.

A traditional view has been that with abrupt deceleration of the thorax, such as occurs in a high-speed vehicular accident in which the body is thrown against a near-stationary object, the ligamentum arteriosum and intercostal arteries anchor the upper descending thoracic aorta to the thorax, as do the thoracic exits of the brachiocephalic vessels. These structures decelerate with the thorax, but the distal end of the aortic arch and most proximal part of the descending thoracic aorta continue to move forward. Aortic disruption tends to develop at the interface between these two areas, although the sum of the forces involved and directions of their effects are complex. The force needed to produce rupture is equivalent to an intravascular pressure of 2500 mmHg.

There are other theories regarding the mechanism of blunt aortic injury (Fig. 24-1). Aortic rupture from a sudden increase in intraabdominal pressure may explain the association between blunt aortic injury and diaphragmatic rupture. A “water-hammer” effect, which involves simultaneous occlusion of the aorta and a sudden elevation in blood pressure, and the “osseous pinch” effect from entrapment of the aorta between the anterior chest wall and the vertebral column have also been postulated. Most injuries probably involve a combination of forces.

Disruption can be complete, including aortic adventitia and mediastinal pleura. If the deceleration forces are less severe, the mediastinal pleura and the adventitia are spared. With lower initial velocity or less rapid deceleration, the mediastinal pleura and adventitia remain intact, while a fracture develops in a portion of the circumference of the aorta, usually posteriorly.

If the person survives the immediate post-disruption period, the periaortic hematoma begins to liquefy about 2 weeks after the traumatic event. It is gradually absorbed or evacuated into the aorta, and a false aneurysm (pseudoaneurysm) develops. The false aneurysm may remain stable for a long period and even calcify, but it can enlarge and rupture.

Ascending Aorta
Disruption of the ascending aorta is uncommon (10% of isolated cases of disruption without other major visceral injuries reported by Parmley and colleagues and 3.6% [4 of 111 patients] reported by Demetriades and colleagues). Again, the mechanism is sudden deceleration, which is apt to be severe in unrestrained drivers who strike the steering wheel. Cammack and colleagues showed that vertical forces of deceleration tend to lead to rupture of the ascending aorta and arch, and horizontal forces to rupture of the descending aorta. Disruption occurs most commonly in the distal portion of the ascending aorta, near the origin of the brachiocephalic trunk. Less commonly, it is in the proximal portion of the ascending aorta. As in the upper descending thoracic aorta, disruption may be complete or partial.

Other Sites
Disruptions can occur in the lower thoracic aorta (often in association with spinal fractures) and in the aortic arch and abdominal aorta.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA
Pathophysiology
When complete disruption occurs that includes the investing mediastinal pleura or pericardium, hemorrhage is free and exsanguinating, and death occurs instantly or within a few minutes. When the tear involves all layers of the aortic wall but the mediastinal pleura remains intact, a large amount of blood escapes into the retropleural tissues, and signs and symptoms of hemorrhagic shock appear. Usually under such circumstances, some blood or plasma passes through the mediastinal pleura to produce a left hemotorax or pleural fluid collection. When the adventitia of the aorta remains essentially intact, a smaller extravasation of blood occurs, and the mediastinal hematoma is less extensive. The aortic
Theories of blunt aortic injury. Many blunt aortic injuries probably involve a combination of forces, including stretching, shearing, torsion, a “water-hammer effect” (which involves simultaneous occlusion of the aorta and a sudden elevation in blood pressure), and the “osseous pinch” effect from entrapment of the aorta between the anterior chest wall and vertebral column. (From Neschis and colleagues.\textsuperscript{1})

Clinical Features

Persons with acute traumatic aortic disruptions frequently have other severe injuries, including liver and spleen lacerations with intraabdominal hemorrhage, and head injuries. Such injuries have their own clinical features and diagnostic criteria that may affect management of the aortic disruption (see Indications for Operation later in this chapter).

Those who survive to reach the hospital may be in profound hemorrhagic shock if a large mediastinal extravasation has occurred or if there has been extensive intraabdominal or extremity bleeding. Some patients, however, are hemodynamically stable after initial resuscitative measures, and a few show no signs of hemodynamic instability. In such patients, upper body hypertension is common.\textsuperscript{2} Some patients in whom other trauma is not severe complain of interscapular back pain, but pain is generally not a major part of the presentation.

Evidence of impaired blood flow beyond the disruption is uncommon. However, a small number of patients with acute disruption of the descending thoracic aorta who reach the hospital alive have paraplegia or paraparesis (2.6%; CL 2.2%-3.0%, of the 1742 patients in the meta-analysis of von Oppell and colleagues\textsuperscript{3}). Rarely, patients have severe lower body and leg ischemia.

Diagnostic Imaging

Chest Radiography

The chest radiograph is usually abnormal, but with variable findings. There may be opacification of the left hemothorax and rightward shift of the mediastinum resulting from massive collection of fluid in the left pleural space. These features are not diagnostic of aortic disruption, because bleeding after trauma may come from intercostal or pulmonary vessels, cardiac and pericardial rupture, or traumatic rupture of the left hemidiaphragm with intrathoracic splenic rupture.

Commonly the radiograph shows only diffuse upper mediastinal widening (Fig. 24-2), which in the setting of a severe injury strongly suggests upper descending aortic disruption. However, rightward shift of the trachea, blurring of the normally sharp outline of the upper descending thoracic aorta, and opacification of the usually clear space between it and the pulmonary trunk may be evident; all these findings suggest aortic disruption.\textsuperscript{4}

Computed Tomography

Computed tomography (CT) has been evaluated as a screening examination to detect aortic injury in patients with blunt chest trauma.\textsuperscript{5} In the early years of its use, time required to perform the study (60-70 minutes) in patients who often were severely injured, low sensitivity and positive predictive value, and lack of demonstrated cost effectiveness limited its utility.\textsuperscript{6} It is, however, essential for managing patients with...
associated head trauma and for assessing presence of intra-abdominal and retroperitoneal injuries.

Now, helical CT of the thorax can be performed more rapidly than conventional CT, and its sensitivity for detecting blunt aortic injury equals that of aortography (discussed later). In trauma centers, it is currently the most widely used technique to diagnose traumatic aortic disruption. Findings indicative of aortic disruption include extravasation of contrast, intimal flaps, mural thrombus, paraaortic hematoma, wall thickening, pseudoaneurysm, and pseudocoarctation (Fig. 24-3). Advantages of helical CT over other imaging techniques include its wide availability, speed of performance, sensitivity, and relatively low cost.

**Figure 24-2** Chest radiograph 6 hours after a high-speed automobile accident. Upper mediastinal shadow is abnormally wide, and outlines of distal aortic arch and upper descending thoracic aorta are blurred.

**Figure 24-3** Computed tomographic axial (A) and three-dimensional (B) images of a posttraumatic pseudoaneurysm of the aortic isthmus. The aortic disruption (small arrow), periaortic hematoma (asterisk), and a large pleural effusion (large arrow) are shown. (From Botta and colleagues.)

**Transesophageal Echocardiography**

Transesophageal echocardiography (TEE) is a highly effective method for imaging the proximal ascending aorta, distal aortic arch, and descending thoracic aorta. Its characteristic finding is presence of a mural flap (Fig. 24-4). Two studies comparing TEE with aortography or with findings at operation or autopsy in 101 and 32 patients, respectively, have demonstrated a sensitivity of 91% and 100% and a specificity of 100% and 98%, respectively. A more recent prospective comparison of TEE to helical CT demonstrated a sensitivity, specificity, negative predictive value, and positive predictive value of 93%, 100%, 99%, and 100%, respectively, for TEE, compared with 73%, 100%, 95%, and 100% for helical CT. TEE can be performed with minimal risk in the emergency room, intensive care unit, or operating room and can be carried out simultaneously with other diagnostic or therapeutic procedures. It requires less than 30 minutes to complete and provides, in addition to images of the aorta, information about ventricular function and wall motion. It can detect presence of cardiac valvar lesions and pericardial fluid. A limitation is that the distal ascending aorta and brachiocephalic trunk cannot be imaged clearly because of interposition of the column of air in the distal trachea and right bronchus between the probe in the esophagus and the aorta. Thus, presence of a tear in these locations cannot be excluded. In centers with extensive experience, TEE can be used as the primary diagnostic imaging technique in patients with blunt chest trauma.

**Aortography**

Until recently, aortography has been the definitive diagnostic study for acute aortic disruption (Fig. 24-5), the imaging modality against which all subsequently developed imaging techniques have been compared. Its specificity approaches 100%, and prevalence of false positives and false negatives is low. The procedure is associated with some risk, is time consuming, and requires a skilled interventional radiology team. Up to 90% of studies performed to determine presence of aortic disruption are negative.
With increasing use of CT as the primary diagnostic imaging study, aortography is being used less frequently. In a multicenter study by the AAST, it was used to screen for traumatic aortic disruption in only 8.3% of 193 patients treated during a 26-month interval in 2005-2007, as compared with 87% of 274 patients treated during a 30-month interval in 1994 to 1996.\(^4\)

**Magnetic Resonance Imaging**

Magnetic resonance imaging (MRI) provides excellent images of vascular structures in the thoracic aorta and provides diagnostic accuracy similar to aortography.\(^3\) Its use in the acute trauma patient is limited because of the confining nature of the scanners and the time required to obtain images.

### NATURAL HISTORY

Risk of death, generally from massive intrathoracic hemorrhage, is greatest immediately after the injury. As time passes, the instantaneous risk of death (hazard function) decreases, but the patient remains at risk of death from hemorrhagic shock over the next several days (Fig. 24-6). Shock may be secondary either to initial blood loss into a large mediastinal hematoma or to renewed bleeding into the adventitia and mediastinal pleura as arterial blood pressure rises after the initial period of hypotension.\(^1\) Probability of survival for at least 4 hours after the accident is not improved with certainty by rapid transport from accident scene to hospital.\(^15\) About 40% to 50% of persons die within 48 hours of the traumatic event.\(^18\)

Instantaneous risk of death in surgically untreated patients begins to level off about 7 days after injury (see Fig. 24-6). Most patients who survive this long without treatment survive much longer. However, a low constant risk of death from hemorrhage persists because of propensity of the false aneurysm (see **Morphology** earlier in this chapter) to rupture even years later.\(^6\) It has been estimated that even after 10 years, 20% of patients with this type of traumatic false aneurysm will die of rupture within the subsequent 5 years.\(^35,69\)

### TECHNIQUE OF OPERATION

**Preoperative Management**

When a presumptive diagnosis of acute traumatic aortic disruption or other major vascular injury is made based on an abnormal chest radiograph, hemodynamic monitoring and medical therapy are instituted before diagnostic imaging (CT, TEE, or aortography) is performed. In hemodynamically...
stable patients, medical therapy should include intravenous infusion of a vasodilator (usually sodium nitroprusside) to avoid hypertension, limitation of intravenous fluid infusion once the systolic arterial blood pressure exceeds 90 to 100 mmHg, and administration of a \( \beta \)-adrenergic antagonist when heart rate exceeds 80 to 90 beats/min. This therapy should be continued while diagnostic studies and any surgical procedures, if indicated, are performed.

Repair of Acute Traumatic Aortic Disruption of Upper Descending Thoracic Aorta

Operative Strategies

Open operative repair has been the standard surgical treatment of traumatic aortic disruption of the descending thoracic aorta for more than 50 years. Development and recent widespread availability of endovascular stent-grafts have dramatically altered management. The first patients with traumatic aortic disruption of the descending thoracic aorta treated this way were reported by Kato and colleagues in 1997. The technique is now widely used in trauma centers throughout the world. A prospective multicenter study by the AAST reported by Demetriades and colleagues compared the methods of definitive repair of traumatic aortic disruption in two time intervals: 1994-1996 (274 patients, 50 participating centers) and 2005-2007 (193 patients, 18 participating centers) (Table 24-1). In the latter interval, 65% of patients were treated with stent-grafts. Although there are no randomized trials comparing endovascular stent-grafting with open repair, ease of insertion, reduced operative time, and reduction in major postoperative complications are attractive features of the technique that have led to increasing use.

Open Repair

Spinal cord ischemic injury resulting in paraplegia or paraparesis is a devastating complication of surgical repair, and the optimal technique for avoiding injury to the spinal cord during open repair remains arguable (see detailed discussion in “Paraplegia after Aortic Clamping” under Special Situations and Controversies later in this chapter). In their meta-analysis, von Oppell and colleagues noted that the mean number of patients with acute traumatic aortic disruption admitted to any unspecified center was 2.6 per year (range 0.2-10.7 patients). The centers in most of the reports (39 of 60 with data suitable for analysis) treated fewer than this mean number of patients per year. Thus, annual experience with this condition is limited in all but a few centers. With simple aortic clamping, von Oppell and colleagues found that the earliest reported case of paraplegia occurred after a clamp time of 24 minutes; if clamp time extended to 34 minutes, cumulative risk of paraplegia increased to 18%. At 60 minutes, risk approached 80%, and at 120 minutes, 100%. In contrast, when distal aortic perfusion was used, the earliest paraplegia occurred after a clamp time of 34 minutes, and risk of

<table>
<thead>
<tr>
<th>Time after Trauma</th>
<th>Probability (%) of Survival for:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>24 Hours</td>
</tr>
<tr>
<td>0 hours</td>
<td>74</td>
</tr>
<tr>
<td>12 hours</td>
<td>85</td>
</tr>
<tr>
<td>24 hours</td>
<td>89</td>
</tr>
<tr>
<td>2 days</td>
<td>92</td>
</tr>
<tr>
<td>3 days</td>
<td>94</td>
</tr>
<tr>
<td>4 days</td>
<td>95</td>
</tr>
<tr>
<td>5 days</td>
<td>96</td>
</tr>
</tbody>
</table>

(Data from Parmley and colleagues.)

Table 24-1 Methods of Definitive Repair of Blunt Thoracic Aortic Injuries (American Association for the Surgery of Trauma)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 207*</td>
<td>68 (35)</td>
<td>125 (65)</td>
</tr>
<tr>
<td>Open</td>
<td>207 (100)</td>
<td>68 (35)</td>
<td></td>
</tr>
<tr>
<td>Endovascular</td>
<td>0 (0)</td>
<td>125 (65)</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Demetriades and colleagues. Patients in extremis or managed nonoperatively excluded.

Figure 24-6 Hazard function (deaths · day\(^{-1}\)), or instantaneous risk of death across time, after acute traumatic aortic disruption. Time zero is time of trauma. Dashed lines enclose 70% CLs. There is an early phase of rapidly falling risk and a constant late phase. The two graphs differ only in the scales of the axes; in A the horizontal axis is hours after time zero, and in B it is days, and the vertical axis is expanded. The relationships are such that the following are conditional probabilities of survival without treatment:

\[
\begin{align*}
\text{Time after Trauma} & \quad \text{Probability (%) of Survival for:} \\
0 \text{ hours} & \quad 74 \quad 50 \\
12 \text{ hours} & \quad 85 \quad 61 \\
24 \text{ hours} & \quad 89 \quad 66 \\
2 \text{ days} & \quad 92 \quad 73 \\
3 \text{ days} & \quad 94 \quad 77 \\
4 \text{ days} & \quad 95 \quad 80 \\
5 \text{ days} & \quad 96 \quad 82
\end{align*}
\]
paraplegia at 120 minutes was approximately 18% \( (P < .0001) \) (Fig. 24-7).

A comparable protective effect of distal aortic perfusion was demonstrated in a subsequent meta-analysis by Jahromi and colleagues and in a single institution by Katz and colleagues. Taken together, these findings strongly suggest that distal aortic perfusion, achieved either by partial cardio-pulmonary bypass (CPB) and mild hypothermia or by left atrial–to–distal arterial bypass, should be used for most patients with acute traumatic aortic disruption undergoing open repair. Simple aortic clamping should be reserved for patients in whom anticipated clamp time is less than 20 to 25 minutes (although this is not always predictable) and for patients with life-threatening hemorrhage.

An arterial catheter is inserted in the patient’s right arm to monitor blood pressure; nasopharyngeal and bladder or rectal thermistors are placed for temperature measurement. If not already in place, a Swan-Ganz catheter is inserted for measurement of pulmonary artery pressure and cardiac output. A double-lumen endotracheal tube is inserted whenever possible. At least one large-bore needle must be securely in position in a peripheral vein. The patient is placed in a right lateral decubitus position, but with hips rolled back toward a supine position so that the left femoral vessels are accessible (Fig. 24-8, A [inset]). Facilities are organized for aspirating shed blood from the thorax in a sterile manner, washing and compacting red blood cells, and rapidly returning them to the patient.

A left posterolateral incision is made, and the thorax is entered through either the fourth intercostal space or the bed of the resected fifth rib. The rib spreader is positioned and opened in stages over several minutes, and the opening into the thorax anteriorly and posteriorly is lengthened with scissors. As soon as the rib spreader has been partially opened, unclotted blood and clots are removed from the thorax, taking great care not to exacerbate the bleeding by disturbing the mediastinal hematoma. Usually there is no active bleeding into the pleural space (persons with such bleeding usually have not survived to this point), but if it is occurring, immediate control is obtained by digital pressure.

Once the rib spreader has been positioned, the lung is covered with a moist laparotomy pad and retracted anteriorly with a malleable retractor held by an assistant. The mediastinal pleura is still undisturbed, and at this point a decision is made about the technique that will be used for spinal cord protection during aortic clamping (see previous text and "Paraplegia after Aortic Clamping" under Special Situations and Controversies later in this chapter).

A synthetic aortic tube graft is then selected (see “Grafts for Use in Aortic Surgery” under Special Situations and Controversies later in this chapter), as are clamps for aortic control. A few stay sutures are placed along the mediastinum behind the hilum of the lung and held anteriorly by clamps, which replace the malleable retractor.

The mediastinal pleura is opened adjacent to the hematoma at three points: (1) over the mid-descending thoracic aorta, (2) over the aortic arch, and (3) over the left subclavian artery (see Fig. 24-8, A-B). Dissection is carried around the aorta and subclavian artery at these three sites so that clamps can be placed. Tapes can be placed around the vessels, but they are not necessary and generally should be avoided. If accessible, the vagus nerve—identified as it descends over the aorta—is protected. When the hematoma is small and general condition of the patient is good, dissection is carried along the anterior surface of the aorta toward the hematoma from below, and down the aortic arch and the subclavian artery from above. The aortic arch is usually dissected circumferentially between the left carotid and left subclavian arteries (see Fig. 24-8, B).

When the hematoma is extensive or the hemodynamic state is unstable, dissection is not performed until the clamps are in place. When this dissection has been accomplished, clamps are placed in a preliminary manner, one across the aortic arch between the left carotid and left subclavian arteries, one across the subclavian artery, and one on the descending thoracic aorta (Fig. 24-8, C). With this maneuver, reasonable control of bleeding can be established, although there may be bleeding retrogradely into the aorta from intercostal arteries above the distal aortic clamp. After the clamps are placed, dissection is carried toward the hematoma from the distal clamp, and this clamp is expeditiously moved proximally as far as possible to allow blood from the distal aorta to perfuse as many intercostal arteries as possible. The surgeon must recognize that clamping the distal aortic arch rather than aorta beyond the left subclavian artery causes a greater increase in left ventricular afterload and also decreases collateral flow to the lower body and spinal cord from the left subclavian artery. Thus, whenever possible, the clamps on the arch and left subclavian artery should be replaced with one on the aorta just beyond the left subclavian artery (Fig. 24-8, D).

Dissection now continues toward the site of disruption, staying in the periaortic tissue plane (see Fig. 24-8, C). At some point the hematoma is entered, and blood and clot are evacuated rapidly. Usually there will be some bleeding into the field from the intercostal arteries between the disruption...
and distal clamp. This blood should be aspirated through a system that returns blood to the patient. Alternatively, the bleeding intercostal arteries can be occluded with bulldog clamps (see Fig. 24-8, D). They should not be ligated or oversewn (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies later in this chapter); the aorta can often be tailored to preserve their origins.

When disruption involves only part of the circumference of the aorta, direct repair can often be made with interrupted pledged evverting mattress sutures or a simple whip stitch of 4-0 or 5-0 polypropylene (Fig. 24-8, E). Although Fontan and colleagues report being always able to make a direct repair with partial or complete disruption, this method is considered advisable only if the tissues are of good quality. Otherwise, a segment of the tube graft already selected is anastomosed to the two ends of the aorta using a 4-0 or 5-0 polypropylene suture (Fig. 24-8, F-G). The distal clamp is released, anastomotic bleeding between the sutures is secured with fine interrupted sutures, and the proximal clamp is slowly removed. Disruptions that involve the middle or lower descending thoracic aorta are repaired in a similar fashion after obtaining proximal and distal control of the aorta.
Incisions in mediastinal pleura

Figure 24-8, cont’d  C, Dissection is continued around the aorta and left subclavian artery in these locations, and clamps are placed first on the proximal aorta between the left carotid and left subclavian artery then on the left subclavian artery, and finally on the distal aorta. Pleura over mediastinal hematoma is incised, and hematoma is removed. D, Aortic clamps are repositioned, wherever possible, to locations just above and below area of disruption to permit perfusion of subclavian artery and as many pairs of intercostal arteries as possible. Bleeding from intercostal arteries closest to the aortic tear is controlled with bulldog clamps. E, If tear is incomplete, aorta can be repaired by direct suture.

For patients in shock resulting from massive intra-thoracic hemorrhage, full cardiopulmonary bypass and hypothermic circulatory arrest permits salvage of the shed blood in the pleural space and mediastinum and eliminates the need for mediastinal dissection of placement of clamps proximal and distal to the aortic tear. Kawahito and Adachi utilized this technique in 10 patients with hemorrhagic shock and major associated injuries. Nine of the patients were discharged from the hospital without complications.

After repair is completed and any devices used for distal aortic perfusion have been removed, as much of the mediastinal pleura as possible is closed over the operative site. One intercostal drainage catheter is positioned posteriorly and inferiorly in the chest cavity, and another anteriorly and superiorly. The incision is closed after making certain the lung has been reexpanded and the catheters are attached to a suction apparatus.

Endovascular Stent-Grafting

Endovascular stent-grafting should be performed under general anesthesia in a standard cardiovascular operating
room with a C-arm fluoroscopy unit, or in a “hybrid” operating room with a fluoroscopy unit designed for endovascular surgery. The operating team must be prepared to convert to an open procedure if necessary, and a cardiopulmonary perfusion team should be available on standby.

Access to the aorta is established through a common femoral, external iliac, or common iliac artery. If the common femoral artery is large enough to admit the sheath necessary for deployment of the endovascular stent-graft (EVSG), the procedure can be performed percutaneously or through a small incision in the groin area. If the femoral artery is not of suitable size, access is obtained through a small extraperitoneal incision in a lower quadrant of the abdominal wall to expose the external or common iliac artery. An 8- or 10-mm segment of collagen- or gelatin-impregnated polyester graft is sutured end-to-side to the artery and is used as a conduit through which the graft is deployed. Only low-dose heparinization (2500-5000 units) is required.

Appropriate flexible guidewires are advanced under fluoroscopic guidance into the ascending aorta, and the sheath through which the EVSG will be inserted is passed over the guidewire and positioned in the abdominal aorta. The diameter of the aorta proximal and distal to the site of the tear is determined from a previously obtained CT angiogram (or alternatively, using TEE or intravascular ultrasound), and the appropriate-sized EVSG is selected. The diameter of the graft is 10% to 15% greater than the diameter of the aorta. In general, 2 cm of aorta proximal and distal to the site of disruption is essential for proper sealing of the graft. This may require covering the orifice of the left subclavian artery. Length of the graft should only be long enough to ensure an adequate seal, thus avoiding unnecessary coverage of adjacent intercostal arteries. Once the graft is deployed, angiography or CT imaging is performed to assess adequacy of the seal and to be certain that the left carotid artery has not been compromised (Fig. 24-9). If the left subclavian artery is

Figure 24-8, cont’d  F-G, In most cases, a woven polyester tube graft is sutured to proximal and then distal aorta.

Figure 24-9  Same patient as in Fig. 24-3. After deploying an endovascular stent-graft, the disrupted aorta is excluded (A), and flow to the left subclavian artery has been preserved (B). (From Botta and colleagues.812)
covered and there is evidence postoperatively of compromised circulation to the left arm, a left carotid–to–left subclavian artery bypass graft with simultaneous embolization of the proximal left subclavian artery, or left subclavian artery transposition to left carotid artery, should be performed.

After satisfactory deployment of the EVSG has been confirmed, the sheath and guidewires are removed, and the artery through which they were inserted is repaired with a 5-0 or 6-0 polypropylene suture. If a graft was used for access, it is excised, leaving a small remnant attached to the artery that is oversewn with a 5-0 or 6-0 polypropylene suture.

Repair of Acute Traumatic Disruption of Ascending Aorta

When the ascending aorta is disrupted, preparations are made for standard CPB as the patient is being transferred to the operating room (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2).

In the operating room, the usual peripheral and monitoring devices are placed. After the patient is anesthetized and intubated, one member of the surgical team performs a median sternotomy while another exposes a common femoral artery and vein in the groin. The pericardium is opened just enough to expose the right atrial appendage. No dissection should be performed in the region of the hematoma. If there is active bleeding, control is obtained with digital pressure.

The patient is heparinized and the femoral artery cannula is advanced. A single right atrial venous cannula is placed (see Cardiopulmonary Bypass Established by Peripheral Cannulation in Section III of Chapter 2) and CPB established. If the right atrium is not accessible, a long cannula is inserted from a common femoral vein (preferably the right) and positioned with its tip in the middle of the right atrium. Body temperature is reduced by cooling the perfusate (see “Technique in Adults” in Section IV of Chapter 2). As this is being done, the thymus gland is divided, the pericardium is opened more widely, and the pericardial reflection is carefully dissected away from the hematoma over the distal portion of the ascending aorta. If massive hemorrhage occurs, perfusion flow is reduced to 0.5 L · min⁻¹ · m⁻² until enough of the aorta can be dissected to place an aortic occlusion clamp beyond the site of disruption. If the tear does not involve the brachiocephalic trunk, this clamp is placed just proximal to its origin from the aorta, although the clamp may have to be angled so that it excludes more of the undersurface of the aortic arch. Once this clamp is positioned, full CPB flow may be resumed and perfusate temperature stabilized at 28°C to 32°C.

After this clamp has been placed, the aorta is opened and cardioplegic solution is administered directly into the ostia of the coronary arteries using perfusion cannulae (see “Perfusion of Individual Coronary Arteries” in Chapter 3). Alternatively, or as an adjunctive measure, cardioplegic solution can be infused retrogradely into the coronary sinus (see “Technique of Retrograde Infusion” in Chapter 3). A venting catheter is placed into the left ventricle, either through a purse-string suture in the right superior pulmonary vein or through the opened aorta.

The area of disruption is dissected carefully. Usually there has been sufficient damage to the aorta that a tube graft is required for reconstruction of aortic continuity (see “Grafts for Use in Aortic Surgery” under Special Situations and Controversies later in this chapter). Repair is made by the technique described for graft interposition for descending thoracic aortic disruptions (see previous text). After the anastomosis is completed, the clamp on the aorta is released. Aortic root reperfusion is begun, and the remainder of the procedure is completed (see “De-airing the Heart” in Section III of Chapter 2).

If the disruption clearly involves the brachiocephalic trunk or aortic arch, or if it is unclear whether the brachiocephalic trunk is involved, no dissection or manipulation of the aorta and hematoma is begun until the patient has been cooled by the perfusate to a nasopharyngeal temperature below 18°C. Then, with the patient in moderate Trendelenburg position, CPB is discontinued, an aortic clamp is placed across the uninvolved proximal portion of the aorta, cardioplegic solution is administered through a previously placed aortic infusion cannula, and the aorta is opened at the area of disruption without placing a clamp distally. Repair is accomplished by the technique used to repair aortic arch aneurysms (see “Replacement of Aortic Arch” under Technique of Operation in Chapter 26). When disruption involves the origin of the brachiocephalic trunk or left carotid artery, the damaged segment is resected and an appropriately sized collagen- or gelatin-impregnated woven polyester graft is sutured to the normal artery distally and to the aortic arch proximally, or to the graft that has replaced the aortic arch and ascending aorta.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is that usually given after other major cardiovascular operations (see Chapter 5). Many patients have systemic hypertension early postoperatively, and particular care is taken to control it. Associated injuries are managed appropriately.

RESULTS

Survival

Early (Hospital) Death

Many patients who would otherwise have died survive after repair of acute traumatic aortic disruption, but the proportion surviving varies according to the particular circumstances. Associated severe injuries decrease probability of survival. Paradoxically, rapid transport systems between accident site and hospital, although giving the patient a potentially better chance to survive, may actually decrease the proportion of surgical survivors, because more severely injured patients reach the hospital.

Open Operation VonOppell and colleagues performed a meta-analysis of 88 articles published in English between 1972 and 1992 related to surgical management of acute aortic disruption in which sufficient information was available to permit estimation of mortality and prevalence of paraplegia. Of 1742 patients who reached the hospital alive, 179 (10%) died before surgical intervention. An additional 61 patients (3.5%) exsanguinated despite emergency thoracotomy for profound hemodynamic deterioration. Ten patients were managed without operation. Intraoperative deaths occurred in 111 patients (6.7%), and an additional 201 patients (11.5%) died in the postoperative period. Thus,
overall mortality for patients who arrived at the hospital alive was 32% \( (\text{Table 24-2}) \). Of 1492 patients who reached the operating room in a presumably stable hemodynamic state, mortality was 21%. This mortality ranged from 0% to 54% in individual institutions.

In a more recent analysis, Demetriades and colleagues reported a 24% early mortality rate among 68 patients treated between 2005 and 2007 in 18 trauma centers. In a meta-analysis of 17 retrospective cohort studies from 2003 to 2007 involving 369 patients treated with open repair, 30-day mortality was 20% (72 patients; CL 17%-22%). It ranged from 0% to 50% in individual centers.

**Endovascular Stent-Grafting** In the study of Demetriades and colleagues noted previously, early mortality for 125 patients treated concurrently by EVSG was 7.2% (9 patients; CL 4.9%-10%). In the meta-analysis of 17 retrospective cohort studies by Xenos and colleagues, 30-day mortality for 220 patients treated concurrently by EVSG was 7.9% (18 patients; CL 6.1%-10.0%). It ranged from 0% to 25% in individual centers.

**Table 24-2** Meta-analysis of Patients Reaching Hospital Alive or Operating Room in Stable Condition after Acute Traumatic Disruption of Descending Thoracic Aorta

<table>
<thead>
<tr>
<th>Variable</th>
<th>Reaching Hospital (% of 1742 Patients)</th>
<th>Reaching Operating Room (% of 1492 Patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mortality</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>179</td>
<td>10.3</td>
</tr>
<tr>
<td>Emergency thoracotomy</td>
<td>61</td>
<td>3.5</td>
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<tr>
<td>Intraoperative</td>
<td>117</td>
<td>6.7</td>
</tr>
<tr>
<td>Postoperative</td>
<td>201</td>
<td>11</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>558</td>
<td>32 (CL 31-33)</td>
</tr>
<tr>
<td><strong>Paraplegia</strong></td>
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<td></td>
</tr>
<tr>
<td>Preoperative</td>
<td>46</td>
<td>2.6</td>
</tr>
<tr>
<td>Postoperative (new)</td>
<td>147</td>
<td>8.4</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>193</td>
<td>11 (CL 10-12)</td>
</tr>
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</table>

Table 24-3 Meta-analysis of Prevalence of New (Postoperative) Paraplegia According to Surgical Technique

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>New Paraplegia</th>
<th>Clamp Time (Minutes)</th>
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<tr>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
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<tr>
<td>Surgical intervention and outcome data available</td>
<td>1428b</td>
<td>145</td>
<td>10</td>
</tr>
<tr>
<td><strong>Technique</strong></td>
<td></td>
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<tr>
<td>Simple aortic clamping</td>
<td>443</td>
<td>85</td>
<td>19</td>
</tr>
<tr>
<td>Distal perfusion:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Passive shuntingc</td>
<td>424</td>
<td>47</td>
<td>11</td>
</tr>
<tr>
<td>Active shuntingd</td>
<td>561</td>
<td>13</td>
<td>2.3</td>
</tr>
</tbody>
</table>

*Modified from von Oppell and colleagues. Represents 96% of 1492 patients reaching operating room in stable condition.
Includes patients with shunting from the ascending aorta and left ventricle.
Includes patients with heparinless partial bypass with centrifugal pump, cardiopulmonary bypass with oxygenator, and heparinless femoral vein to femoral artery bypass without oxygenator.

**Time-Related Survival**

Long-term survival of patients discharged after open repair is excellent. Long-term results after EVSG are unknown.

**Modes of Death**

Most deaths occur in the postoperative period (see Table 24-2). Principal modes of intraoperative death are hemorrhagic shock and cardiac failure. Modes of postoperative death are central nervous system injury and organ failure (lung, kidney, liver).

**Risk Factors for Premature Death**

A higher Injury Severity Score (ISS) and older age appear to be important risk factors for increased hospital mortality. Surgical technique is not a risk factor for hospital mortality.

**Paraplegia**

The proportion of patients who develop paraplegia or paraparesis after open surgical repair is variable. In the meta-analysis of von Oppell and colleagues, new paraplegia occurred in 9.9% (CL 9.1%-10.8%) of the 1492 patients who reached the operating room (see Table 24-2). Prevalence of paraplegia varied according to the operative technique used (Table 24-3). The highest prevalence (19%) was associated with use of simple aortic clamping; lowest prevalence (2.3%) was associated with “active shunting,” defined as augmentation of distal perfusion by CPB with an oxygenator and full CPB, by a centrifugal pump and no heparin, or by femoral vein to femoral artery bypass without an oxygenator or heparin. Prevalence with “passive shunting” (no augmentation of distal perfusion) was 11% (P < .0001 compared with “active shunting”). Categorization of surgical technique employed was possible in 96% of the 1492 patients. The high prevalence of paraplegia in the simple aortic clamping group was associated with the lowest weighted average clamp time (32 minutes; range 13-62 minutes) (see Table 24-3 and “Paraplegia after Aortic Clamping” under Special Situations and Controversies later in this chapter). In the meta-analysis of Jahromi and colleagues of 618 patients from 20 reports published between 1966 and 2000, a lower prevalence of paraplegia was observed among patients in whom left heart bypass (0 of 84 [0%; CL 0%-2.3%]; odds ratio 6.4; P = .07) or partial CPB (5 of 227 [2%; CL 1.2%-3.7%]; odds ratio 3.4;
Prevalence of paraplegia after EVSG is lower than that after open repair. In the study of the AAST, paraplegia occurred in 1 (0.8%) of 125 patients treated by EVSG between 2005 and 2007. In the meta-analysis of 17 retrospective cohort studies of 215 patients treated by EVSG from 2003-2007 and with data suitable for analysis, paraplegia/paraparesis occurred in 1 patient (0.5%).

### INDICATIONS FOR OPERATION

Immediate surgical repair of acute traumatic aortic disruption is indicated for patients with massive hemothorax or signs of impending rupture. Among patients in whom the hematoma is contained within the mediastinum, immediate repair is usually indicated unless there are severe coexisting injuries that require medical or surgical management. Several studies have demonstrated that mortality from rupture among patients who reach the hospital alive and who have a contained rupture is low (approximately 5%). Thus, injuries that may be more immediately life threatening (e.g., intraabdominal or intracranial hemorrhage, severe pulmonary or myocardial contusion, extensive fractures) should be treated before repair of the aortic disruption.

When diagnosis is made more than several days after injury, operation is usually advisable, but unless the hematoma is large or there is evidence of active bleeding, operation can be performed urgently or electively rather than emergently. In the interim, arterial hypertension and tachycardia should be treated with sodium nitroprusside and β-adrenergic blockade. Frequent monitoring of the thoracic aorta with CT scanning or MRI is essential during this interval.

After about 14 days, management is similar to that for chronic thoracic aortic aneurysm (see “Special Features of Postoperative Care” in Chapter 26).

### SPECIAL SITUATIONS AND CONTROVERSIES

#### Choice of Operative Procedure

As noted, EVSG has replaced open operation as the most commonly performed intervention for acute traumatic aortic disruption. It is associated with lower early mortality and a lower occurrence of paraplegia. Other advantages over open repair include avoidance of thoracotomy, aortic clamping, and left heart bypass or CPB.

However, endovascular treatment requires expeditious imaging, personnel trained in endovascular procedures, and availability of endografts of variable sizes. Currently in the United States, treatment of acute traumatic aortic disruption with an endograft is an off-label use of the device. Because the aortas of younger individuals are smaller than those of patients with aneurysms, for which these devices were initially designed, oversizing has been associated with collapse of the stent-graft. Other complications unique to EVSG include endoleaks, component migration, stent fractures, injury to the arteries used for access, and cerebral or left upper-extremity ischemic events resulting from coverage of the left subclavian and left carotid arteries. In the study by the AAST, prevalence of device-related complications among 125 patients was 20% (CL 16%-24%).

### Long-term results of EVSG are unknown. The thoracic aorta becomes ectatic and tortuous with aging, so there is a theoretical risk of graft dislodgement over time. A study of proximal aortic diameters using CT imaging following endovascular repair of blunt thoracic aortic injury in 17 patients followed for at least one year, demonstrated a significant increase in the rate of dilatation at the level of the aortic isthmus when compared with the aorta distal to the end of the endograft (0.83 mm/yr vs. 0.47 mm/yr, P=0.025). Long-term performance and mechanical properties of currently used grafts are unknown. Frequent imaging, currently with CT, is recommended and may be necessary for the life of the patient. Cost of this imaging and the associated risk of excessive radiation are not insignificant.

All these factors must be taken into consideration when deciding on the method of operative management for individual patients. Until additional information becomes available, a selective strategy, treating young patients with limited associated injuries by open operation and older patients with comorbid conditions or those with extensive associated injuries by EVSG, may be advisable.

#### Paraplegia after Aortic Clamping

Paraplegia or paraparesis can develop as a result of ischemia of the spinal cord after operations in which the distal aortic arch, descending thoracic aorta, or thoracoabdominal aorta is temporarily clamped. It usually develops immediately, but occasionally onset is delayed for several hours or days.

### Risk Factors

#### Duration of Aortic Clamping

When the aorta is clamped just beyond the left subclavian artery under more or less normothermic conditions, probability of developing paraplegia or paraparesis is directly related to duration of clamping. In humans, this probability is essentially zero when duration is less than 15 minutes. In patients with acute traumatic aortic disruption, the probability approaches 100% when duration is 1 hour or longer. Use of moderate or profound systemic hypothermia has been associated with lower prevalence of spinal cord ischemia after operations on the descending thoracic and thoracoabdominal aorta compared with operations performed at normothermia. Use of profound systemic hypothermia (<20°C) permits extension of the duration of aortic occlusion and spinal cord ischemia to more than 100 minutes without an increase in prevalence of paraplegia or paraparesis (Fig. 24-10). Selective cooling of the spinal cord by infusion of cold (4°C) saline into the epidural space to achieve cerebrospinal fluid (CSF) temperatures of 24°C to 28°C has been associated with lower prevalence of spinal cord ischemic injury following

\[ P = .02 \text{ was used when compared with simple aortic clamping (14 of 194 [7.2%; CI 5.3%-9.7%]).} \]

Lettinga-van de Poll and colleagues of 284 patients treated in 62 centers up until January 2006, procedure-related complications occurred in 41 patients (14%; CI 12%-17%). Need for repeat intervention is also a concern.
repair of thoracoabdominal aortic aneurysm with the simple aortic clamping technique than observed without cooling in otherwise comparable patients.\textsuperscript{61}

**Level of Aortic Clamping** When a clamp is placed for 60 minutes on the abdominal aorta beyond the origin of the renal arteries (about the level of L2), paraplegia or paraparesis occurs in less than 0.1% of cases.\textsuperscript{66} When a clamp is placed at the level of the diaphragm for 60 minutes, paraplegia or paraparesis develops in about 10% of patients.\textsuperscript{514} As already discussed, when the proximal clamp is on the aorta just beyond the origin of the left subclavian artery for 60 minutes in patients with acute traumatic aortic disruption, more than 80% develop clinical evidence of spinal cord ischemic injury.

Evidence from experimental studies indicates that clamping of the left subclavian artery and the thoracic aorta just beyond the origin of the left subclavian artery further increases risk of paraplegia or paraparesis.\textsuperscript{66,91} This is because the left subclavian artery gives origin to the left vertebral artery, which joins with the right vertebral artery to form the anterior spinal artery.

When two clamps are placed across the thoracic aorta, the distance between them is related directly to probability of paraplegia, at least in experimental animals.\textsuperscript{98,91} This implies that as the distance between the clamps is increased, more of the intercostal arteries, and thus the spinal arteries, are excluded from the collateral circulation coming from the proximal and distal aorta.

**Variability in Blood Supply of Spinal Cord** The anterior spinal artery is formed at the level of the medulla by spinal artery branches from each of the vertebral arteries. As the anterior spinal artery passes down the spinal cord, it is connected to a variable number of radicular arteries (usually five to eight) that are formed from spinal branches of the intercostal and lumbar arterial branches of the descending thoracic and abdominal aorta.\textsuperscript{67,510,562} (Fig. 24-11). A particularly large radicular artery is present in most humans (the arteria radicularis magna, or artery of Adamkiewicz). It arises from the T5 (fifth thoracic vertebral level) to the T8 level in 15% of people, T9 to T12 in 75%, L1 to L2 (lumbar level) in 8%, L3 in 1.4%, and L4 to L5 in 0.2%.\textsuperscript{13,97} Its ligation in pigs usually results in paraplegia or paralysis.\textsuperscript{92} Clamping the aorta distal to the origin of this large artery probably imposes only a small risk of paraplegia or paraparesis, whereas clamping proximal to it imposes a considerable risk. In the latter situation, perfusion of the distal aorta may provide adequate protection of the lumbar spinal cord if perfusion pressures are adequate. If the segment of aorta that contains this or other large radicular arteries is resected or excluded, or if the artery is ligated, there is considerable probability of paraplegia or paraparesis.\textsuperscript{66,92} In this circumstance, reimplantation of the critical intercostal artery or arteries is advisable.

**Variability in Collateral Circulation to Spinal Cord** When collateral circulation around the part of the aorta exteriorized by a pair of aortic clamps is well developed, as in most patients undergoing operation for aortic coarctation, the aorta can probably be clamped safely at that level for a long interval. However, some patients with coarctation have incomplete collateral circulation and greater likelihood of developing paraplegia.\textsuperscript{514} (see “Collateral Circulation” under Morphology in Section I of Chapter 48).

Patients coming to operation for chronic degenerative descending thoracic or thoracoabdominal aneurysm frequently have little or no flow through some of the intercostal or lumbar arteries because of previous progressive occlusion of the origins of these arteries from the aorta. This usually

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure24-10.png}
\caption{Figure 24-10 Risk of paraplegia or paraparesis according to duration of spinal cord ischemia in 60 patients undergoing resection and graft replacement of the descending thoracic aorta using hypothermic (under 20°C) cardiopulmonary bypass and intervals of circulatory arrest. Duration of spinal cord ischemia was defined as time between onset of circulatory arrest or aortic clamping and establishment of antegrade flow to intercostal and lumbar arteries below the T6 interspace. Dashed lines enclose 70% confidence intervals. \textit{P} value relates to association between ischemic time and probability of developing paraplegia or paraparesis. (Modified from Kouchoukos and colleagues.\textsuperscript{65})}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure24-11.png}
\caption{Figure 24-11 Summary of findings of the blood supply to the spinal cord in eight human cadaver dissections. Sizes are mean sizes for these arteries when distended under pressure with blood. Level of origin of the arteries may vary in any one person; however, the diagram summarizes the most commonly identified sites of origin. Key: ARM, Arteria radicularis magna; C, cervical; L, lumbar; µ, microns; T, thoracic. (From Svensson and Crawford.\textsuperscript{93})}
\end{figure}
chronic process is infrequently associated with paraplegia because of concomitant development of collateral circulation. The collateral circulation, when well developed, may be sufficient to permit aortic occlusion without ischemic injury to the spinal cord.\textsuperscript{2,2,3} However, it can also be precarious and sensitive to even minor fluctuations in arterial pressure, cardiac output, and intraspinal pressure during and early after graft replacement of the diseased aortic segment.

**Intraspinal Pressure** An increase in intraspinal pressure, which can occur following occlusion of the descending thoracic aorta, is believed to increase spinal cord ischemia and thus the probability of paraplegia.\textsuperscript{54,58,56} Presumably, increased intraspinal pressure compresses the delicate spinal arteries sufficiently to reduce blood flow through them. In theory, increase in pressure, reflected by increase in the measured intrathecal pressure, reduces spinal cord perfusion pressure (defined as distal aortic pressure minus CSF pressure). Increased venous pressure may result following occlusion of the thoracic aorta and may also increase CSF pressure, thus reducing spinal cord perfusion pressure.\textsuperscript{59}

**Upper Body Blood Pressure** Reduction of upper body blood pressure when the thoracic aorta is clamped decreases flow (through collaterals) to the lower body and reduces spinal cord collateral flow. Thus, upper body hypotension during aortic clamping increases the probability of paraplegia.\textsuperscript{51}

**Methods to Minimize Spinal Cord Injury**
Generally, aortic operations should be performed in a manner that recognizes the risk factors for paraplegia while accomplishing an effective procedure with minimal blood loss and injury to various organs. At times, difficult situations may force compromises:

- A double-lumen endotracheal tube should be used whenever possible to permit optimal exposure in the left hemithorax.
- If the aorta is clamped without distal perfusion, upper body blood pressure should be maintained above normal values. Cardiac function should be monitored carefully.
- The proximal aortic clamp should be placed beyond the left subclavian artery whenever possible and as far distally on the aorta as possible.
- The more distal of a pair of clamps should be positioned as close to the distal extent of the disruption as possible.
- Operation should be planned and performed to minimize duration of aortic occlusion.
- Hemostasis should be accurate to avoid hypotension after removal of the clamps.

**Whole-Body Hypothermia during Simple Aortic Clamping** Hypothermia clearly prolongs the safe ischemic time for the spinal cord, just as it does for all other organs\textsuperscript{36} (see Section I of Chapter 2). This was demonstrated more than 50 years ago by Hufnagel and Gross,\textsuperscript{52} later by Beattie and colleagues,\textsuperscript{51} and reaffirmed by the elegant experimental study of Pontius and colleagues.\textsuperscript{59} The studies of these three groups indicate that the spinal cord can recover normal function after aortic occlusion for 60 minutes at a whole-body temperature of 30°C.

Hypothermia to a nasopharyngeal temperature of 30°C to 32°C can be achieved simply. In neonates and infants, operation is performed with the patient on a cooling and heating pad and with operating room temperature about 16°C (60°F) during thoracotomy. If at the time of aortic clamping, the patient’s temperature has not reached 32°C to 33°C, additional cooling is obtained by 5 to 10 minutes of ice water lavage of the left pleural space. Even in adults, such lavage is effective in reducing body temperature 2°C to 3°C within 5 to 10 minutes. In neonates and small infants, rewarming after the clamps are removed is easily accomplished with the pad (now heating rather than cooling) and by raising room temperature. The rewarming process is slower in larger patients but can be facilitated by use of a warming blanket placed over the lower abdomen and legs.

Cooling to 30°C or lower without extracorporeal support usually requires formal surface cooling, which is cumbersome and time consuming in large patients. It is generally inadvisable for operations on the descending thoracic and thoracoabdominal aorta.

**Perfusion of Distal Aorta during Aortic Clamping** When a pair of aortic clamps are applied close together to the most proximal part of the descending thoracic aorta (e.g., in operations for acute traumatic aortic disruption), perfusion of the distal aorta by any one of a number of methods minimizes spinal cord ischemia and development of paraplegia.\textsuperscript{1,2,3} This was demonstrated by Stranahan and colleagues in 1954 by use of an external shunt.\textsuperscript{57} However, distal aortic perfusion prevents paraplegia only if the short segment of aorta exteriorized by the clamps does not give origin to critical radicular arteries, which can occur following occlusion of the descending thoracic aorta.\textsuperscript{1,2,3} The experimental studies of Connolly and colleagues and Laschinger and colleagues\textsuperscript{22,1,1,3} support the concept that managing acute traumatic aortic disruption by perfusing the distal aorta while a pair of aortic clamps is on the upper descending thoracic aorta neutralizes the incremental risk of longer clamp times on probability of paraplegia (see “Variability in Blood Supply of Spinal Cord” earlier in this chapter). If the critical arteries originate from the exteriorized segment and the aortic clamps remain in position for a considerable period, perfusion of the distal aorta cannot be expected to afford complete protection to the spinal cord consistently.

The study by Katz and colleagues\textsuperscript{55} and the meta-analyses of von Oppell and colleagues\textsuperscript{59} and Jahromi and colleagues\textsuperscript{52} support the concept that managing acute traumatic aortic disruption by perfusing the distal aorta while a pair of aortic clamps is on the upper descending thoracic aorta neutralizes the incremental risk of longer clamp times on probability of paraplegia (see Fig. 24-7). Other studies also support this concept by showing that distal aortic perfusion restores spinal cord blood flow, maintains spinal cord function, and restores function temporarily lost by a brief period of inadequate perfusion of the distal aorta.\textsuperscript{22,1,1,3} The experimental studies of Connolly and colleagues and Laschinger and colleagues\textsuperscript{22,1,1,3} suggest that distal aortic perfusion needs to be about 60 to 70 mmHg or more to provide low probability of paraplegia and high probability of adequate lower-body organ function during and after an operation performed at normothermia (=37°C).\textsuperscript{51,1,3}

**Reattachment of Intercostal and Lumbar Arteries** During resection of a segment of the thoracic or upper abdominal aorta from which arteries critical to spinal cord blood flow emerge, perfusion of the intercostal and lumbar arteries seems logical, as does their reattachment to the aorta as part of the reconstruction. One way of accomplishing reconstruction of spinal cord blood flow is tailoring the resection and graft so that most of the posterior wall of the aorta, from which origins of the lower intercostal and lumbar arteries arise, is preserved (see Fig. 25-11, D in Chapter 25). The graft is cut obliquely at one end for an appropriate end-to-end anastomosis. Another method is creation of an oval
opening in the graft and anastomosis of the opening to the aortic wall around the origin of critical intercostal and lumbar arteries (see Fig. 26-18, F-G in Chapter 26).

The importance of reattaching intercostal and lumbar arteries in preventing spinal cord ischemic injury and the resulting paralysis remains controversial. Several groups have reported a low prevalence of neurologic deficits after resection and graft replacement of extensive thoracoabdominal aortic aneurysms without reattaching any intercostal or lumbar arteries.\textsuperscript{1,11,88} However, emerging consensus is that, at least for extensive thoracoabdominal aortic aneurysms that require prolonged periods of aortic occlusion—particularly those resulting from aortic dissection where large numbers of intercostal and lumbar arteries may be patent—reattachment of patent lower intercostal (below the T6 or T7 level) and upper lumbar arteries reduces the prevalence of postoperative neurologic deficits.\textsuperscript{1,11,13,89-93}

**DRAINAGE OF CEREBROSPINAL FLUID** In experimental studies, reducing intraspinal pressure by drainage of CSF is associated with reduced prevalence of paraplegia.\textsuperscript{88,94} In some clinical studies, the protective effect of CSF drainage has not been conclusively demonstrated when comparable groups of patients (randomized and nonrandomized) are evaluated.\textsuperscript{11,100}

In three clinical studies and in a randomized trial, use of CSF drainage in combination with other adjuncts such as distal aortic perfusion, intravenous infusion of naloxone, an endorphin (opiate) receptor antagonist, and epidural cooling has been associated with reduced prevalence of lower-extremity neurologic deficits compared with historical controls.\textsuperscript{1,11,14,52}

**LOCALIZED COOLING OF SPINAL CORD DURING AORTIC CLAMPING** Experimental studies by Colles and colleagues\textsuperscript{99} and Colon and colleagues\textsuperscript{97} have shown that infusing cold crystalloid solution or blood into an isolated segment of the descending aorta provides protection against paraplegia for an occlusion period of 30 to 45 minutes. Berguer and colleagues\textsuperscript{85} and Wissell and colleagues\textsuperscript{83} demonstrated the protective effect of irrigating the subarachnoid space with cold (5°C) saline solution during an occlusion interval of 45 minutes in dogs, and Marsala and colleagues\textsuperscript{44} showed similar protection with cold irrigation of the epidural space. Clinical experience with these techniques is limited. Fehrenbacher and colleagues have used infusion of 8°C to 10°C crystalloid solution containing heparin, mannitol, and methylprednisolone into isolated segments of the lower thoracic and upper abdominal aorta before implanting the intercostal and lumbar arteries contained in these segments into an aortic graft.\textsuperscript{55}

Normothermic left heart bypass and segmental clamping of the aorta were also used to minimize duration of spinal cord ischemia. Paraplegia occurred in 1 (4.3%; CL 0.2%-17%) of 23 patients with extensive thoracoabdominal aortic aneurysms. Cambria and colleagues infused 4°C normal saline solution into the epidural space of 70 patients with descending thoracic or thoracoabdominal aortic aneurysms.\textsuperscript{11} Simple aortic clamping was used in all but one patient. Two patients (2.9%; CL 0.6%-8%) developed lower-extremity neurologic deficits. In their extended experience with this technique for repairing thoracoabdominal aortic aneurysms, spinal cord ischemic injury (paraplegia or paraparesis) occurred in 11% (CL 8.2%-13%; 19 of 180 patients) in whom epidural cooling was used, and in 20% (CL 15%-25%; 18 of 91 patients) in whom it was not used ($P = .04$).\textsuperscript{87}

**MONITORING SOMatosensory and Motor Evoked Potentials** In patients undergoing resection of thoracoabdominal aortic aneurysms, Cunningham and colleagues demonstrated that after occluding the proximal descending thoracic aorta, responses monitored in the cerebral cortex after stimulation of the posterior tibial nerve demonstrated an increased latency and decreased amplitude within 3 to 4 minutes.\textsuperscript{123} Responses disappeared after 5 to 10 minutes and returned 8 to 9 minutes after unclamping the aorta. Mizrahi and Crawford demonstrated similar changes within 10 minutes after occluding the aorta in 13 patients and observed rapid reversal of these changes after restoration of flow in the aorta.\textsuperscript{99}

Although monitoring of somatosensory evoked potentials appears to be a sensitive method to detect spinal cord ischemia and impending paralysis, the technique has several limitations. Because the potentials are conducted through the posterior (sensory) column of the spinal cord and not the anterior (motor) column, ischemia and resulting paraplegia may occur despite recording normal impulses. General anesthetics, changes in temperature, drugs, hypoxia, hypotension, and ischemia of peripheral nerves that occurs following aortic occlusion may affect sensitivity of recorded impulses.\textsuperscript{122}

Direct stimulation of the spinal cord rather than a peripheral nerve appears to increase sensitivity of the technique.\textsuperscript{67,84}

Monitoring somatosensory evoked potentials in patients during operations on the descending thoracic and thoracoabdominal aorta alone or in conjunction with other adjuncts that may reduce the risk of spinal cord ischemic injury (e.g., distal perfusion, hypothermia, CSF drainage, reimplanting intercostal or lumbar arteries) has not consistently reduced the prevalence of paraplegia.\textsuperscript{11,13,22,23,67,83}

Achouh and colleagues have shown that monitoring these potentials is a poor screening tool for development of a neurologic deficit.\textsuperscript{11} Among 444 patients undergoing thoracoabdominal or descending thoracic aortic repair, they observed a sensitivity of 62% and a specificity of 81% for the technique. The negative predictive value, however, was 99%, indicating a low event probability in the absence of changes in the evoked potentials.

Monitoring motor evoked potentials may be a more accurate method to detect spinal cord ischemia intraoperatively.\textsuperscript{22,14,51,6} Clinical experience with this technique is limited.\textsuperscript{71,87,93} Monitoring these potentials appears to have a strong negative predictive value for immediate neurologic deficit, similar to that for somatosensory evoked potentials.\textsuperscript{11,87}

However, use of the technique has not been shown to substantially reduce or eliminate the occurrence of spinal cord ischemic injury in patients with extensive repairs of the thoracoabdominal aorta, and the positive predictive value is low.\textsuperscript{71,87}

**PHARMACOLOGIC INTERVENTIONS** Many pharmacologic agents have been evaluated for their neuroprotective effects in experimental studies of spinal cord ischemia (Box 24-1). Few have been extensively evaluated in humans, however. Thiopental and methylprednisolone are widely used clinically for protection of the brain and spinal cord during operations requiring circulatory arrest and clamping of the descending thoracic aorta.\textsuperscript{99} Naloxone has been used in humans in combination with CSF drainage during operations on the thoracoabdominal aorta, and a low prevalence of spinal cord ischemic injury was observed.\textsuperscript{11} Intrathecal administration of papaverine, a potent vasodilator, has also been associated with reduced prevalence of paraplegia in a small series of patients.\textsuperscript{518}

As the pathophysiology of spinal cord ischemic injury is more clearly elucidated, it is likely that pharmacologic
agents will be used more frequently as adjuncts to the other interventions described in the preceding text during thoracic aorta operations that involve interrupting blood flow to the spinal cord.\textsuperscript{62,64,65} Methods for Perfusing the Distal Aorta during Aortic Clamping

A wide variety of techniques have been used to perfuse the distal aorta during operations that involve clamping the descending thoracic aorta.

Left Atrial–to–Femoral Artery Bypass As the left thoracotomy is being made, with the patient in a right lateral decubitus position and the left leg fully extended, the left common femoral artery is exposed. After thoracotomy and before addressing the aortic patholgy, the pericardium is opened anterior to the phrenic nerve. A purse-string suture is placed around the base of the left atrial appendage. After a full dose of heparin, or after a reduced dose of 100 to 150 units \(\cdot\) kg\(^{-1}\) (1-1.5 mg \(\cdot\) kg\(^{-1}\)), or after no heparinization,\textsuperscript{61,63} a standard femoral arterial cannula (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2) is inserted into the femoral artery (or an aortic cannula can be inserted into the distal descending thoracic aorta) and a 28F, 30F, or 32F venous cannula is inserted into the left atrium through the appendage. Alternatively, a 28F cannula, which is usually sufficiently large, can be inserted into the left inferior pulmonary vein extrapericardially.\textsuperscript{12} The cannulae are connected to each other through a vortex pump (see “Temporary Ventricular Assistance” in Section I of Chapter 5) using standard or heparin-covered tubing. Bypass is then commenced at a flow of about 1.5 L \(\cdot\) min\(^{-1}\) \(\cdot\) m\(^2\) (in adults). During bypass, mean pulmonary artery pressure should be maintained above 18 to 20 mmHg to avoid pumping excessive blood from the atrium to the distal aorta, which may result in inadequate perfusion of the proximal aorta and hypotension. Blood volume must also be maintained at appropriate levels by infusing blood and fluids to avoid hypotension.

Decannulation is effected as soon as the aortic clamps are removed. If heparin was used, protamine is administered in an appropriate dose (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). Left atrial–to–femoral artery bypass has been shown to provide better postoperative lower-body organ function than passive shunts,\textsuperscript{65,66} and there is increasing evidence that when carefully implemented, it is associated with a lower prevalence of spinal cord ischemic injury and renal dysfunction than when distal perfusion is not used, particularly when aortic occlusion time exceeds 40 minutes.\textsuperscript{51,69,70,71,72,73,74,75,76} Maintaining distal perfusion with this technique also reduces need for vasodilating agents during aortic clamping and reduces prevalence of hypotension and acidosis after unclamping.\textsuperscript{31}

Aortic-Aortic Shunting Aortic-aortic shunting is a passive process (unless a pump is interposed\textsuperscript{69}) in which arterial pressure above the aortic clamp drives blood through the shunt into the distal aorta. A full or half dose of heparin may be given, or none at all. A 9-mm Gott heparin-bonded shunt may be used,\textsuperscript{69} or a simple shunt constructed from standard perfusion tubing and cannulae. Proximally, the shunt is inserted through a purse-string suture into the aortic arch or ascending aorta (which can at times be difficult), or into the apex of the left ventricle. The distal end of the shunt is similarly inserted into the descending thoracic aorta. Alternatively, the shunt may be extended and connected to a cannula placed in the femoral artery. The shunt is opened as soon as the aorta is clamped. Flow through the shunt should be monitored, either with a flow probe incorporated into the shunt or by measuring arterial pressure distal to the lower aortic clamp.\textsuperscript{69} After removing the aortic clamps, decannulation is effected in a standard manner, and protamine may be given if heparin has been administered.

Hemodynamic state during aortic clamping and lower-body organ function postoperatively are better with this method (and with left atrial to femoral artery bypass) than with simple aortic clamping.\textsuperscript{61,64,65,10} Flows between 1100 and 4900 mL \(\cdot\) min\(^{-1}\) (mean 2500 mL \(\cdot\) min\(^{-1}\)) have been measured in patients having resection of descending thoracic aorta aneurysms.\textsuperscript{69} Shunt flow is dependent on proximal aortic pressure and resistance in the arterial compartment distal to the lower aortic clamp. Reducing pressure in the proximal aorta with nitroprusside may be necessary to avoid cardiac failure. A zero prevalence of lower-extremity neurologic deficits (0%; CL 0%-0.5%) has been reported by Verdant and colleagues, who used this technique in 866 patients with aneurysms confined to the descending thoracic aorta.\textsuperscript{72}

Partial or Total Cardiopulmonary Bypass CPB in the setting of aortic surgery through a left thoracotomy or

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**Box 24-1 Pharmacologic Agents That May Reduce Frequency or Severity of Spinal Cord Ischemic Injury**

<table>
<thead>
<tr>
<th>Class</th>
<th>Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steroids</td>
<td>Methylprednisolone$^{12}$</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>Thiopental$^{62,66}$</td>
</tr>
<tr>
<td>Anesthetics</td>
<td>Lidocaine$^{66}$, Tetracaine$^{81}$</td>
</tr>
<tr>
<td>Opiate (Endorphin) Receptor Antagonists</td>
<td>Naloxone$^{61,66}$, Nalmefene$^{71}$</td>
</tr>
<tr>
<td>N-methyl-D-aspartate (NMDA) Receptor Antagonists</td>
<td>MK-801$^{71}$, Dextorphan$^{64,68}$, Magnesium$^{67}$</td>
</tr>
<tr>
<td>Protein Synthesis Inhibitors</td>
<td>Cyclohexamide$^{64}$</td>
</tr>
<tr>
<td>Calcium Antagonists</td>
<td>Flunarizine$^{64}$</td>
</tr>
<tr>
<td>Free-Radical Scavengers</td>
<td>Allopurinol$^{68}$, Superoxide dismutase$^{22,68}$, Dimethyl sulfoxide (DMSO)$^{68}$</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>Papaverine$^{51,57,58}$</td>
</tr>
<tr>
<td>Hypoglycemics</td>
<td>Insulin$^{67}$</td>
</tr>
</tbody>
</table>
When CPB is conducted at normothermia or mild hypothermia (>32°C), the heart continues to beat, so some pulmonary blood flow continues and CPB is only partial for the upper body. For the lower body, supplied by that part of the aorta distal to the lower aortic clamp, CPB is complete. A pulmonary arterial pressure monitoring catheter should be in place, and if left heart decompression is inadequate, a venting catheter can be placed in the pulmonary artery or left inferior pulmonary vein. When conducted at hypothermia, either as continuous perfusion or in preparation for hypothermic circulatory arrest, CPB is usually total because the heart becomes ineffective as lowering of body temperature proceeds.

Use of hypothermic circulatory arrest for aortic surgery using a lateral approach began in 1964 and was used only sporadically during the next 20 years. High prevalence of pulmonary complications was reported by Crawford and colleagues in 1987. With increasing experience, prevalence of pulmonary and other major complications has been reduced.

Currently available information indicates that this technique has an important place in aortic surgery, particularly when extensive operations are required and when clamping of the proximal descending thoracic aorta cannot be safely accomplished. It is of particular value in patients who require resection of the entire descending thoracic and most or all of the abdominal aorta. The combination of CPB, using femoral cannulation, hypothermic circulatory arrest, implanting patent lower intercostal and upper lumbar arteries into the graft, and early insertion of a second arterial cannula into the graft after the proximal anastomosis has been

Thoracoabdominal incision can be established effectively in most patients using the femoral artery and vein (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2). Special long catheters are required for adequate venous drainage (Fig. 24-13). The tip of such a catheter can be positioned accurately in the mid-right atrium using TEE.
completed allows perfusion of the heart and head vessels as the more distal parts of operation are being completed935,12,13 (see Fig. 26-19 in Chapter 26).

Grafts for Use in Aortic Surgery

Type
Through the years, PTFE and polyester grafts (knitted or woven and of various weaves), autologous and bovine pericardium, and allograft aorta and pulmonary trunk have been used to augment or replace a portion of the systemic or pulmonary arterial pathway. Although this discussion will focus on grafts for aortic replacement, it is relevant to pulmonary arterial replacement and to patches used in these locations and inside the ventricles and atria.

Issues related to graft type include ease of handling, compliance, durability, hemostatic properties, and thickness and adherence of the neointima that develops. Autologous pericardium, either untreated or immersed in 0.6% glutaraldehyde for 5 to 30 minutes (the advantages of which remain arguable), is easy to handle and suture. It is compliant, durable (although sometimes given to stretching or contracting), and impervious to blood. It is extremely useful as a patch graft. Tube grafts fashioned from pericardium are no longer used for aortic replacement. In neonates and young infants, allograft aorta is ideal for augmenting the aorta, as is allograft pulmonary artery; both are useful as extracardiac conduits to the pulmonary arteries. They are also used in the sinutubular portion of the ascending aorta. The wall of the aortic allograft calcifies (pulmonary allograft wall does so to a lesser degree), but it functions well for a number of years (see “Isolated Aortic Valve Replacement” and “Replacement of Aortic Valve and Ascending Aorta, En Bloc” under Technique of Operation in Chapter 12 as well as Technique of Operation in Section II of Chapter 38).

Intracardiac patches need not be impervious to blood immediately after insertion, and thus the Sauvage knitted polyester patch (see Chapter 35, footnote 4) works well.

Contoured patches are more conveniently cut from tube grafts, and double-velour woven polyester grafts (see later) are easily handled, compliant, and durable. They may be backed by pericardium (autologous or bovine) if the patch is large and must be immediately hemostatic. PTFE is entirely satisfactory for patches and small tube grafts, and is generally impervious to blood. However, it is susceptible to kinking, and bleeding through suture holes may be persistent.

When a patch or tube graft forms part of the wall of a blood vessel or the heart in a heparinized patient, demands for hemostasis are stringent. A number of solutions to this problem have become available. Knitted polyester grafts with a baseline water permeability of about 2000 mL·cm⁻²·min⁻¹ have enjoyed favor in the past because of ease of handling and development of a thinner and more adherent neointima after insertion than is the case with woven grafts.12,13 In heparinized patients, untreated knitted polyester grafts, which permit massive hemorrhage through the graft, are unsuitable for use for any external vascular surface. Newer types of woven polyester grafts are as soft and easy to handle and sew as knitted grafts and are more impervious to blood. Bovine pericardium is an excellent patch material for the aorta, major systemic arteries, and the pulmonary artery. Its handling characteristics and ready availability make it an optimal substitute. It can also be used as a tube graft in the pulmonary arterial circulation.

Preclotting of Synthetic Grafts
A number of useful methods of preclotting grafts can be used in heparinized patients. In one, preclotting is obtained by aspirating about 50 mL of the nonheparinized patient’s blood from the heart or aorta, clamping one end of the graft and stretching it and injecting the blood into the other end under as high a pressure as can be generated. As the blood exudes from the graft, it is collected in a small pan, and after the first injection is completed, the blood is reaspirated from the pan and again injected under high pressure. This process is continued until most of the blood has clotted. Before the graft is inserted, the clots are aspirated or wiped from the interior (not rinsed out with saline solution), and the device is ready for use.

A second method involves autoclaving the graft.12,12 The general technique of autoclaving as part of the preclotting process was suggested by Betha and Recemtsma, who soaked grafts in heparinized whole blood before autoclaving. Alternatively, 5% albumin, concentrated serum albumin, plasma, or platelet-rich plasma can be applied to the graft prior to autoclaving.

Various preclotting techniques affect inner-surface thrombogenicity of polyester grafts and their tendency toward thromboembolism. According to experimental studies in dogs by Gloviczki and colleagues, with low-porosity polyester woven grafts, the area of desirable thrombus-free surface was greatest when the graft was not preclotted or when it was preclotted with blood in the standard manner.13 Among autoclaved grafts, those soaked with platelet-rich plasma rather than blood had the most thrombus-free surface, and this was correlated with the lowest prevalence of thromboembolism. Albumin alone and platelet-free plasma were not tested.

Grafts Treated Before Packaging
The convenience of grafts that are ready for insertion without further treatment after removal from the package is evident.12 Woven and knitted grafts impregnated with albumin, collagen, or gelatin are now commercially available. In experimental and clinical studies, these grafts demonstrate less transinterstitial bleeding than preclotted grafts. Woven grafts appear to be preferable to knitted grafts in fully heparinized patients who require replacement of segments of the thoracic aorta.

Endografts
The initial thoracic endovascular stent-grafts used clinically were hand-made from polyester or PTFE aortic grafts covered with modified Z stents.13 Several commercially manufactured endografts approved by the U.S. Food and Drug Administration for treating descending thoracic aortic aneurysms are currently available. They have undergone numerous modifications in construction as clinical experience has increased. The currently available grafts are constructed from self-expanding nitinol or stainless steel stents that are sutured to the outer surface of thin PTFE or polyester grafts. They are available in various diameters and lengths and incorporate different systems for anchoring the grafts to the aortic wall. Long-term durability of these grafts is unknown.
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DEFINITION

Acute aortic dissection is an event of sudden onset in which blood leaves the normal aortic lumen through a usually discrete point of exit (intimal tear) and rapidly dissects inner from outer layers of the media to produce a false lumen. However, dissection of the media can occur in the absence of an intimal tear. Patients are considered to have an acute dissection when the process is less than 14 days old, and a chronic dissection thereafter (see “Chronic Aortic Dissection” under Morphology and Morphogenesis in Chapter 26).

HISTORICAL NOTE

Aortic dissection was recognized in the 16th century, but knowledge of many of its aspects was incomplete and confused. D6 Laennec introduced the term dissecting aneurysm in 1819. Shennan’s 1934 treatise was a landmark in developing knowledge of this entity, documenting among other things its seriousness. D11 Surgical treatment began in the mid-1930s. Early operations were indirect, consisting of creating a distal internal femorotomy (reentry passage) between true and false lumens or attempting to restore circulation directly to major branches sheared off by the dissection. D13, S10 With failure of these methods, surgical attention turned to the tendency of the false lumen to rupture, and efforts were directed by Paulin and James in 1948 to wrapping the area of dissection and by Johns in 1953 to suturing the rupture. D13, S26

Modern treatment of aortic dissection is a contribution of DeBakey, who in 1955 reported the successful outcome of an operation performed in 1954 in which the aeurysmal descending thoracic aorta resulting from dilatation of the false lumen was resected, entry into the false lumen distally oversewn, and end-to-end anastomosis performed. D6 Subsequently, DeBakey and colleagues devised a classification of aortic dissection that is widely used today (see “Morphology” later in this chapter). D8 The first successful repair of chronic ascending aortic dissection with aortic regurgitation was reported in 1962 by Spencer and Blake in a patient with chronic dissection, although the procedure was proposed by Bahnson and Spencer in 1960. B4, S19 Spencer and Blake carried out the operation that is currently widely used, including suspension of aortic valve commissures. The first successful repair of acute ascending aortic dissection with aortic regurgitation was reported by Morris and colleagues in Houston in 1963. M13 Moderate aortic regurgitation persisted postoperatively, and 15 years later the regurgitation was severe, with moderate heart failure. Aortography showed a persisting double lumen that extended distally to the aortic bifurcation. Aortic valve replacement was performed in 1977. L6 The patient continued to be well in 1989 (Morris GC: personal communication, 1989). Further successful surgical experiences with acute dissection of the ascending aorta were reported by DeBakey and colleagues in 1964. D7 In 1965, Wheat and colleagues demonstrated the possibility of improving management of acute aortic dissection by medical measures directed at controlling arterial hypertension while maintaining adequate organ perfusion. W4

Technological improvements in cardiopulmonary bypass (CPB) circuitry and in synthetic replacements for the involved aortic segments have contributed to improved outcomes following surgical treatment of acute aortic dissection. Use of hypothermic circulatory arrest, described initially by Barnard and Schrire and by Borst and colleagues in the early 1960s to treat aneurysms and other conditions involving the aortic arch, and applied systematically by Griep and colleagues in a series of patients described in 1975, permitted extension of operative procedures into the aortic arch. B7, B21, G10 In 1982, Livesay and colleagues described a technique for open distal anastomosis in treating both ascending aortic aneurysms and dissections, a technique that is now widely used. D1, L3 Use of gelatin-resorcinol-formaldehyde (GRF) glue to strengthen the disrupted layers of the aorta before they are approximated and sutured directly or to an aortic graft was described in 1979 by Guilmet and colleagues in France. G12 It is extensively used in Europe and in other parts of the world but is not approved for use in the United States. BioGlue, an albumin and glutaraldehyde-based adhesive, has been approved for this purpose in the United States by the U.S. Food and Drug Administration (FDA). Kato and colleagues in Tsu, Japan, and Dake and colleagues at Stanford University introduced endovascular stent-grafting initially to manage vascular ischemic complications of acute aortic dissection, then to exclude the primary tear in the descending thoracic aorta. The combined experience of these two groups was reported in The New England Journal of Medicine, which focused not only on early mortality and morbidity, but also specifically on the fate of the false lumen 5 to 28 months after stent-grafting. D2

MORPHOLOGY

Morphologic Substrates

In many patients in whom an aortic dissection develops, the aortic wall shows only changes commensurate with patient age. D3, H6, L5, S7, S22 Thus, it appears that once blood enters the aortic media, cleavage of concentric elastic lamellar plates can occur in even an essentially normal aorta; this event permits rapid and extensive dissection. Dissection usually proceeds distally but may also extend proximally.

Medial degeneration (cystic medial necrosis) of the aorta of a greater degree than is normal for age is present in about 20% of patients with acute aortic dissection and may predispose to dissection. L5, S28 Rarely, aortitis is a predisposing factor. H5

Marfan syndrome is an important morphologic substrate for acute aortic dissection, and acute dissection develops in 20% to 40% of patients with this syndrome. H5, B9, S96 In fact, aortic root dissection and rupture and chronic aortic regurgitation are the primary causes of death in these patients. N5, M14 Many patients with Marfan syndrome and aortic dissection exhibit no medial degeneration; therefore, this syndrome appears to be, per se, a risk factor for acute dissection. I5

Defective synthesis of fibrillin, a glycoprotein that is an important component of elastic tissue in the medial layer of the aorta, has been demonstrated in patients with Marfan syndrome. T10, S3 The genetic defect of Marfan syndrome and the fibrillin gene have been mapped to the same region in the long arm of chromosome 15. K1, M1 Turner, Noonan, vascular Ehlers-Danlos, and Loew-Dietz syndromes are other genetic disorders associated with aortic dissection.

1Manufactured by Cryolife Inc., 1655 Roberts Blvd. NW, Kennesaw, GA 30144.
A genetic basis of nonsyndromic familial thoracic aortic aneurysm and dissection has recently been defined. A genetic basis of nonsyndromic familial thoracic aortic aneurysm and dissection has recently been defined. **Anuloectasia** without Marfan syndrome is present in some patients in whom acute dissection of the ascending aorta develops. It is important to recognize anuloectasia when it coexists, because aortic root replacement rather than cusp resection is indicated (see “Indications for Operation, Selection of Technique, and Choice of Device” in Chapter 12).

A bicuspid aortic valve is frequently associated with acute aortic dissection. Larson and Edwards, in the study of Larson and Edwards, the process of acute dissection occurred nine times as frequently in patients with bicuspid as in those with tricuspid aortic valves. There may be a higher prevalence of congenital abnormalities of the aortic wall in patients with bicuspid than in those with tricuspid valves.

A dilated ascending aorta (>5.0-5.5 cm) occurring in combination with anuloectasia (with or without Marfan syndrome), with a bicuspid aortic valve, or with previous aortic valve replacement is associated with increased risk of aortic dissection. The role of arteriosclerosis in development of acute aortic dissection has been debated. It is probably not a predisposing lesion, although occasionally an intimal tear may develop in a penetrating arteriosclerotic ulcer, resulting in dissection of the media.

Aortic coarctation is associated with acute dissection, but this is likely due to systemic arterial hypertension, an important risk factor for developing acute aortic dissection. Bicuspid aortic valve and an abnormal ascending aorta, frequently present in patients with coarctation, may also be contributing factors.

The role of pregnancy in genesis of acute aortic dissection is unresolved. Closed chest trauma may rarely result in true aortic dissection, as may aortic cannulation and aortic clamping during operations employing CPB.

Intramural hematoma may be a precursor of aortic dissection. It likely results from rupture of vasa vasorum and may, in its initial stages, exist in the absence of an intimal tear (see text that follows).

**Intimal Tear**

Controversy exists as to whether an intimal tear is consistently present in acute aortic dissection and, thus, whether an intimal tear is a requisite for dissection. One point of view is that rupture of aortic vasa vasorum is the inciting event and that it initiates an intramural hemorrhage and subsequent dissection. This hypothesis is supported by studies of the role of intramural hematoma as a precursor of aortic dissection and by intraoperative and postmortem observations of aortic dissection without the presence of an intimal tear. However, Larson and Edwards found an intimal tear in each of 158 specimens personally examined, supporting the hypothesis of the primacy of an intimal tear, a view held by Murray and Edwards and by Roberts. The intimal tear develops commonly in the ascending aorta but also in the upper descending aorta just beyond the origin of the left subclavian artery. In the latter instance, dissection usually proceeds only distally (antegrade) but may extend proximally (retrograde) as far as the ascending aorta. Proximal dissection occurred in 48% (CL 29%-47%) of autopsied cases studied by Larson and Edwards. The intimal tear originates in the aortic arch in about 10% to 20% of patients and dissection is both retrograde into the ascending aorta and antegrade into the descending thoracic aorta. Rarely, the intimal tear is low in the descending thoracic or abdominal aorta.

**Dissection**

When medial dissection occurs, the walls of any of the branches of the aorta may be involved with the dissection, may be sheared off from the lumen and occluded by the dissecting media and intima, may stay in communication with the aorta but only by the false lumen, or may be uninvolved. Extension of dissection into the branch wall is more common in large arteries such as the brachiocephalic, carotid, subclavian, and renal than in smaller ones. Dissection more frequently involves the left rather than right iliac artery. Extent and nature of involvement of the branches, including coronary and iliac arteries, is an important determinant of the clinical syndrome with which the patient presents.

**False Lumen**

The false lumen develops in the outer half of the aortic media; as a consequence, its external wall is thinner than the internal wall (dissecting membrane). The false lumen usually involves half to two thirds of the circumference of the aorta and rarely the entire circumference. Although the false lumen may be contained initially by the thin outer layer of media and adventitia, it often ruptures into the pericardium, the pleural space (usually the left), or less commonly, the abdomen. Even when initial rupture does not occur, blood from the false lumen may extravasate through weak areas of media and adventitia to form a mediastinal or pericardial hematoma.

Usually, the false lumen gradually enlarges as time passes, producing a marked increase in wall thickness and size of involved portions of the aorta. In many instances, aortic enlargement in the acute stage is diffuse and does not reach aneurysmal proportions. In the ensuing years, the thin outer wall of the false aneurysm tends to weaken, the lumen tends to become aneurysmal, and eventually rupture may occur. The false lumen may become partially or totally thrombosed.

**Types of Aortic Dissection**

Two classifications of aortic dissection are widely used (Fig. 25-1): DeBakey and Stanford (Box 25-1). DeBakey type I or Stanford type A dissection, the intimal tear is usually located in the anterior wall of the proximal portion of the ascending aorta. Occasionally it is in the aortic arch and less commonly in the descending aorta distal to the left subclavian artery. Aortic valve regurgitation and myocordial infarction (MI) may result from extension of the dissection into the most proximal portion of the ascending aorta and the aortic root. In DeBakey type II dissection, only the ascending aorta is involved, and dissection terminates proximal to the brachiocephalic artery. This type may be found incidentally during operations for ascending aortic aneurysms. In DeBakey type III or Stanford type B dissection, the dissecting hematoma may involve only the descending thoracic aorta (DeBakey type IIIa), but most commonly extends into the abdominal aorta and occasionally into the iliac arteries (DeBakey type IIIb). It may also extend proximally into the aortic arch and the ascending aorta. In these types, the
**Box 25-1 Classification of Aortic Dissection**

**DeBakey Classification**
- Type I. Intimal tear usually originates in the proximal ascending aorta and dissection involves ascending aorta, arch, and variable lengths of descending thoracic and abdominal aorta.
- Type II. Dissection is confined to ascending aorta.
- Type III. Dissection may be confined to descending thoracic aorta (type IIIa) or may extend into the abdominal aorta and iliac arteries (type IIIb). Dissection may also extend proximally to involve the arch and the ascending aorta.

**Stanford Classification**
- Type A. All cases in which ascending aorta is involved by dissection, with or without involvement of the arch and descending thoracic aorta.
- Type B. Cases in which only descending thoracic aorta is involved; however, occasionally, dissections originating in the descending thoracic aorta extend proximally (retrograde) to include the aortic arch but not the ascending aorta, and others originating in the aortic arch remain localized or extend distally (antegrade) without involving the ascending aorta; in this text these are included in type B.

intimal tear is usually located just distal to the left subclavian artery. The proportion of patients with the various types of dissection depends on the nature of the series reported. In the large surgical series of DeBakey and colleagues, which contained both acute and chronic dissections, type I and type II dissections comprised about 35% of cases. In other clinical and autopsy series, acute dissections involved the ascending aorta in 62% to 85% of cases.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Hemodynamic State**

*Sudden death* may be the presenting feature, occurring shortly after onset of dissection, with free rupture of the false lumen through the thin outer wall into the pericardial, pleural, or peritoneal space. Sudden death can also follow shearing off of the coronary arteries from their aortic origins.

Alternatively, the presentation may be *hypovolemic shock* of varying degree. It may be the immediate result of acute dissection with loss of a considerable amount of blood from the false lumen into periaortic tissues and spaces. It may also result from development of acute aortic regurgitation when the dissection shears off the aortic attachment of valve commissures, which occurs in 35% to 60% of patients with acute dissection involving the ascending aorta. It may also be the result of acute cardiac tamponade after the site of rupture into the pericardium has temporarily sealed off. As time passes after the acute event, often with some improvement in arterial hypotension, further extravasation of blood can occur from the false lumen into periaortic tissues or spaces, leading to further hypovolemia and a worsening hemodynamic state.

In some patients, the *hemodynamic state is good* after the immediate event, and acute extravasation from the false lumen or rupture of the lumen may not occur for hours, days, or years, if at all. In a few patients, acute dissection results in *no symptoms* and passes unnoticed.

**Demographics and Syndromes**

Most patients (80%-90%) presenting with acute aortic dissection are age 60 or older and have a history of arterial hypertension. Severe acute arterial hypertension, such as occurs in weight lifters, appears to predispose to acute dissection, particularly of the ascending aorta. Use of cocaine, which induces hypertension and vasoconstriction, has also been associated with acute aortic dissection. Patients with acute dissection involving the ascending aorta tend to be younger than those with more distal dissections; thus, the mean age of patients with ascending aortic dissections in the experience of Fann and colleagues was 56 ± 14 years (range 15-85 years), whereas that of patients with involvement of only the descending aorta and beyond was 64 ± 13 years (range 32-86 years). Some patients have evidence of Marfan syndrome; in others, dissection develops during pregnancy. A few have a history of coarctation or its repair or previous aortic valve
surgery (see Morphology earlier in this chapter). Occasionally, acute aortic dissection occurs in patients with Turner, Noonan, vascular Ehlers-Danlos, and Loeys-Dietz syndromes. In patients with these syndromes, dissection develops at a younger age, generally during the third or fourth decade of life. In them, and in younger persons in general, there is likely to be no history of hypertension, and dissection usually originates in the ascending aorta. Patients with nonsyndromic familial thoracic aortic aneurysm and dissection present at a younger age than patients with sporadic (non-genetically mediated) disease, but are older than patients with Marfan or Loeys-Dietz syndrome.

Symptoms and Signs

Although dissection may be painless and at times unknown to the patient, most patients experience sudden severe pain at the moment of dissection and a feeling of impending death. The pain is often interscapular, but it may be precordial and radiate into the neck or arms. It is at times difficult to distinguish from angina pectoris. Once acute dissection occurs, symptoms and signs can be produced by occlusion of a major vessel. Arch vessel occlusion causes stroke in 5% to 10% of patients with type I dissection. One leg (more commonly the left than right) may suddenly become numb, pale, and pulseless as dissection occludes the iliac artery or aortic bifurcation. Occasionally, the same process causes pulses to diminish or disappear in an upper extremity. Uncommonly (2%-5% of patients), paraplegia suddenly develops as intercostal arteries are separated from the aortic lumen by dissection. Oliguria or anuria may appear with occlusion of the aortic origin of the renal arteries.

Chest Radiography

The chest radiograph frequently exhibits widening of the mediastinal shadow, particularly in its upper part and toward the left in DeBakey types I and III dissections. There may be cardiomegaly secondary to pericardial effusion or signs of pleural effusion, particularly in the left hemithorax. The aortic shadow is frequently prominent. However, as a diagnostic test, chest radiography is inadequately sensitive to definitively exclude the presence of aortic dissection in all but the lowest-risk patients. Sensitivity is lower for pathology confined to the ascending aorta than for disease involving distal aortic segments.

Imaging Studies

Echocardiography

Transesophageal echocardiography (TEE) with Doppler color flow imaging is emerging as the most useful and accurate diagnostic technique. It is distinctly superior to transthoracic echocardiography (TTE) and can be performed relatively rapidly with minimal morbidity. When TEE was compared with aortography or with findings at operation or autopsy, its sensitivity and specificity for type A dissection ranged from 88% to 100% and from 86% to 100%, respectively, and for type B dissection from 98% to 100% and from 96% to 100%, respectively. In addition to identifying the dissecting membrane (Fig. 25-2, A), TEE can identify pericardial fluid, evidence for pericardial tamponade, aortic regurgitation, involvement of proximal coronary arteries in the dissection process (Fig. 25-2, B), and wall motion abnormalities of right and left ventricles.

TTE may be useful in critically ill patients to establish a diagnosis rapidly. However, absence of positive findings does not preclude the presence of an acute dissection, and other diagnostic studies become necessary.

Computed Tomography

Computed tomography (CT) with use of contrast material is useful for diagnosing and delineating acute aortic dissection. It produces excellent images with relatively short scanning times (Fig. 25-3). Because CT scanning equipment
is available in emergency departments of most hospitals, CT is the most widely used diagnostic technique for aortic dissection. Advantages include ability to image the entire aorta including lumen, wall, and periaortic regions; identify anatomic variants and branch vessel involvement; and distinguish between the various acute aortic syndromes (intramural hematoma, penetrating arteriosclerotic ulcer, and acute aortic dissection). Electrocardiographic-gated techniques have made it possible to generate motion-free images of the aortic root and coronary arteries. Reports using new-generation multidetector helical CT scanners have noted sensitivities of up to 100% and specificities of 98% to 99%. In comparative studies, however, CT has lower sensitivity and specificity than either TEE or magnetic resonance imaging (MRI) (see later). Dissection may be obscured by complete thrombosis of one lumen or similar opacification in both true and false lumens. Location of entry site and presence of aortic regurgitation cannot always be accurately determined. The technique requires use of contrast medium for accurate delineation of aortic pathology and may be contraindicated in patients with allergies to contrast agents or with renal insufficiency.

Magnetic Resonance Imaging
MRI is emerging as a premier imaging method for diagnosing diseases of the thoracic aorta, including acute aortic dissection. It does not require use of contrast medium. In some situations, a single study can provide information similar to that obtained from a combination of echocardiography, CT, and aortography, with high sensitivity and specificity. It provides superb imaging of both ascending and descending thoracic aortic dissections and can accurately identify sites of entry and thrombus formation (Fig. 25-4). MR angiography (MRA) using gadolinium, a contrast agent, further enhances its utility. Disadvantages of MRI compared with CT and TEE include a longer time to complete the study, greater cost, inaccessibility to patients who are connected to ventilators and monitoring devices, and limited availability.

Aortography
Despite advances in noninvasive and minimally invasive techniques for diagnosing acute aortic dissection, aortography remains an important and highly accurate method for establishing the diagnosis. It is the benchmark against which other diagnostic studies are measured. The false lumen can be visualized, as can at times the intimal tear (Fig. 25-5). It provides accurate information about branch artery involvement and presence of aortic valve regurgitation. It is an essential component of interventional procedures to treat acute aortic dissection, such as fenestration and endovascular stent-grafting (see “Special Situations and Controversies” later). Disadvantages of aortography compared with other diagnostic methods include need for arterial access and introduction of wires and catheters into the aorta, potential for false-negative results if the false lumen is thrombosed, risk of allergic reactions to contrast medium, and renal failure in patients with impaired renal function.

In the International Registry of Acute Aortic Dissection (IRAD), which included 618 patients with acute aortic dissection who had imaging studies between January 1996 and December 1999, the order for which the imaging studies were performed was known in 604 patients (98%). Among these, CT was performed first in 379 (63%), TEE in 192 (32%), aortography in 24 (4%), and MRI in 9 (1%). Among the 396 patients with a second study, TEE was performed in 229 (58%), CT in 68 (17%), aortography in 61 (15%), and MRI in 38 (10%). Data from the IRAD centers demonstrated a high diagnostic sensitivity for all four imaging modalities. However, false-negative CT, TEE, and aortography studies were frequent, so diagnosis of acute aortic dissection could not be confidently excluded on the basis of negative findings of a single test. The authors strongly recommended a second imaging study if the initial diagnostic test did not identify aortic dissection when the diagnosis was suspected clinically.
Chapter 25 Acute Aortic Dissection

25%–39%) patients analyzed by Weiss and colleagues. Thus, thrombolytic therapy can be safely administered to patients with ST-segment elevation and no physical signs of aortic dissection without need for further diagnostic studies. Additional studies may be indicated before thrombolytic agents are given to patients with ST-segment depression or other ECG evidence of myocardial ischemia.

Several serum markers have been investigated for their utility in diagnosing acute aortic dissection and differentiating it from other conditions associated with acute onset of chest pain, such as MI and pulmonary embolism. D-dimer, a degradation product of cross-linked fibrin in thrombus, is sensitive for ongoing intravascular thrombosis. It is highly elevated in patients with acute aortic dissection, with a sensitivity in pooled studies of 94% (95% CL, 91%-96%).

Using 64-slice CT scanners, it is possible to establish or exclude a diagnosis of acute aortic dissection, acute pulmonary embolism, and obstructive coronary artery disease (the so-called triple rule-out CT), and this diagnostic study is being used with increasing frequency.

Coronary Angiography

Selective coronary angiography to identify coronary artery involvement in acute ascending aortic dissection is not usually indicated, because this can be determined by TEE preoperatively or intraoperatively (see Fig. 25-2, B) and by direct examination of the coronary arteries after the aorta has been opened. Use of coronary angiography to detect arteriosclerotic coronary artery disease in patients who are to undergo surgical treatment of acute ascending aortic dissection is arguable (see Special Situations and Controversies later in this chapter).

Differential Diagnosis

Symptoms associated with acute aortic dissection can mimic those of acute MI. The electrocardiogram (ECG) may demonstrate myocardial ischemia, and serum creatine kinase may be elevated. Because thrombolytic therapy is frequently administered to patients with acute MI and ST-segment abnormalities, thrombolytic agents might be administered to patients with acute aortic dissection with potentially disastrous results. ST-segment elevation occurs rarely in acute aortic dissection; however, ST-segment depression occurs more commonly and was noted in 16 of 50 (32%; CL 25%-39%) patients analyzed by Weiss and colleagues. Thus, thrombolytic therapy can be safely administered to patients with ST-segment elevation and no physical signs of aortic dissection without need for further diagnostic studies. Additional studies may be indicated before thrombolytic agents are given to patients with ST-segment depression or other ECG evidence of myocardial ischemia.

Several serum markers have been investigated for their utility in diagnosing acute aortic dissection and differentiating it from other conditions associated with acute onset of chest pain, such as MI and pulmonary embolism. D-dimer, a degradation product of cross-linked fibrin in thrombus, is sensitive for ongoing intravascular thrombosis. It is highly elevated in patients with acute aortic dissection, with a sensitivity in pooled studies of 94% (95% CL, 91%-96%).

The lower specificity (40%-100%) in the pooled studies is not of sufficient magnitude to exclude the diagnosis, however, and in general, other diagnostic studies are required. Using 64-slice CT scanners, it is possible to establish or exclude a diagnosis of acute aortic dissection, acute pulmonary embolism, and obstructive coronary artery disease (the so-called triple rule-out CT), and this diagnostic study is being used with increasing frequency.
NATURAL HISTORY

Acute aortic dissection is a serious event, and the natural history of patients who have sustained it is related primarily to type and extent of the dissection and to the nature and severity of complications that may follow.

Survival

Information about survival of nonsurgically treated patients is sparse, but some general inferences may be drawn. Between 40% and 90% of patients survive 24 hours or more after the dissection, but this generalization ignores the well-established difference in prognosis between type A and type B dissections (Fig. 25-6, A). The hazard function for death also appears to be different in these two types of dissection (Fig. 25-6, B). Type B has a rapidly declining early hazard phase, a constant phase, and a rising late hazard phase beginning about 2 years after dissection; type A dissection has a rapidly declining early hazard phase and only a constant phase thereafter.

Involvement of the ascending aorta or aortic arch is, then, a risk factor for early death in patients with acute dissection.

Modes of Death

Most patients who die acutely succumb from false lumen rupture with hemopericardium, hemomediastinum, or hemothorax. Deaths later in the early period after dissection can result from delayed rupture or organ dysfunction secondary to arterial occlusions.

Course after Surviving Acute Aortic Dissection

Patients surviving acute dissection continue to be at greater risk of dying than the general population. This is because the false lumen generally persists (see Morphology [earlier] and Results [later]), usually and gradually becomes aneurysmal, and may rupture months or years after the acute episode. Also, a new dissection (redissection) may occur in a previously uninvolved portion of the wall of the aorta and present new risks.

TECHNIQUE OF OPERATION

Purpose of Surgical Treatment

Operation for acute aortic dissection is performed to prevent death from cardiac tamponade or exsanguination by excising and repairing or replacing areas of actual or impending rupture and, wherever possible, restoring blood flow to branches of the aorta that have been occluded by the dissection. Operation does not remove the entire false lumen in most patients. To this extent, operation is palliative rather than curative. Another purpose of operation when dissection involves the ascending aorta is to correct acutely developed or chronic coexisting aortic valve regurgitation. Resuspending detached commissures or replacing the aortic valve may be necessary. Replacing the aortic root may be required in some instances, and this is accomplished with a composite graft, an aortic allograft, or a stentless xenograft.

Repair of Acute DeBakey Type I or II (Type A) Dissection

General Considerations

Usual preparations are made for operations in which CPB is used (see Sections III and IV in Chapter 2). Pressures are monitored in the right radial artery and in the femoral artery opposite the cannulation site to promptly detect obstruction to retrograde flow within the aortic arch after CPB is established. Doppler sonography of the extracranial carotid arteries and monitoring of cerebral oxygen saturation are useful techniques for detecting compromised blood flow in brachiocephalic arteries.

The common femoral artery with the most normal pulse is exposed through a small vertical or oblique incision in the inguinal fold. If dissection is present upon opening it, the lumen in which blood is flowing should be cannulated. This may be either the false or the true lumen. In some cases,
effective retrograde arterial perfusion may not be possible, because the aorta becomes obstructed (see “Malperfusion Syndromes” later under Special Situations and Controversies). In this situation, provisions should be made for antegrade aortic perfusion through the ascending aorta, aortic arch, or apex of the left ventricle, or for perfusion of an axillary artery or the opposite femoral artery (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” under Special Situations and Controversies in Section III of Chapter 2).  

If it is necessary to establish CPB urgently, the right common femoral vein should be used because the long venous cannula can be more easily positioned in the right atrium from the right side.

After median sternotomy, the pericardium is incised and stay sutures placed. The often hemorrhagic ascending aorta is not disturbed at this point (Fig. 25-7, A). If dissection is confined to the ascending aorta (DeBakey type II) and hypothermic circulatory arrest is not needed, a single two-stage

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**Figure 25-7** Repair of acute DeBakey type I or II (type A) aortic dissection.  

A, Dashed line indicates proposed line of incision into dissected and often hemorrhagic ascending aorta. B, After cardiopulmonary bypass is established, aorta is clamped proximal to origin of brachiocephalic artery. After incising outer layer of aorta, origin of intimal tear is often visualized just distal to aortic valve. Cardioplegic solution is infused directly into coronary arteries whenever possible for optimal myocardial management.  

C, Aortic wall is transected circumferentially 4 to 5 mm above level of aortic commissures.

Continued
PART V Diseases of the Thoracic Arteries and Veins

D. Pledgeted, double-armed, polypropylene sutures are placed across each detached commissure and through outer layer of aorta, and are tied over a second pledget. Inset: Gelatin-resorcinol-formaldehyde or other glue may be used to obliterate false lumen. E, Disrupted layers of aorta are approximated between strips of polytetrafluoroethylene (PTFE) felt or pericardium and are secured with multiple polypropylene mattress sutures.

In Section III of Chapter 2). A balloon-tipped catheter is placed into the coronary sinus through a purse-string suture in the right atrium for delivery of retrograde cardioplegia (see “Technique of Retrograde Infusion” in Chapter 3).

Limited dissection is carried out, carefully separating the ascending aorta from the pulmonary trunk proximal to the origin of the brachiocephalic artery, and the aorta is clamped at this point after transiently reducing CPB flow to a low level \( (0.5 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}) \). Whenever possible, the clamp should be placed several centimeters proximal to the brachiocephalic artery to avoid further injury and fragmentation of the aorta at a site where an anastomosis to a graft may be performed. A longitudinal incision is made in the ascending aorta extending to, but not into, the noncoronary sinus (Fig. 25-7, B). This incision often enters into the false lumen, which is
This cuff is sutured to a prepared woven polyester graft using a continuous polypropylene suture. Note that cut ends of layers of aorta extend beyond bolster. 

With DeBakey type II dissection, intact ascending aorta beyond dissection is completely transected and sutured to distal end of aortic graft with a continuous polypropylene suture incorporating a strip of PTFE felt or pericardium.

Completed procedure. A pledgeted polypropylene suture is used to seal site of insertion of a needle vent for aspiration of air.

Figure 25-7, cont’d
usually anterior and to the right of the true lumen. If clot is present in the false lumen, it is carefully removed. The dissecting membrane is incised, and retraction sutures are placed in the aortic wall. Cardioplegic solution is promptly infused into the coronary ostia. Retrograde cardioplegia should be administered if the coronary ostia are compromised by the dissection (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). Cardioplegic solution is infused every 12 to 15 minutes. External cooling of the ventricles with topical slush or a cooling jacket may also be used. The interior of the ascending aorta is examined and the aortic wall transected circumferentially 4 to 5 mm above the level of the aortic commissures (Fig. 25-7, C).

Management of Aortic Root

Repair of Disrupted but Nonectatic Aortic Root If one or more aortic valve cusps have been separated from the outer aortic wall by the dissecting hematoma with consequent cusp prolapse, a pledgeted 4-0 double-armed polypropylene mattress suture is placed across each affected commissure and through the outer layer of the aorta, and is tied over a second felt pledget (Fig. 25-7, D). The coronary arteries are carefully examined, and if dissection extends to one or both ostia but the coronary artery is intact, divided layers of the aorta surrounding the ostium are approximated with pledgeted 4-0 polypropylene sutures. Aortic wall surrounding the involved coronary artery is mobilized, and these sutures are tied on the outside of the aorta. If dissection completely surrounds a coronary ostium, a 3- to 4-mm button of both layers of the aorta surrounding the ostium is excised, and the divided layers are approximated with a 5-0 or 6-0 running polypropylene suture. This button can be attached to the ascending aortic graft or to an interposed segment of saphenous vein or 8-mm collagen- or gelatin-impregnated woven or knitted polyester graft (see “Ascending Aorta Replacement” under Technique of Operation in Chapter 26).

If dissection extends into the coronary artery, most commonly the right, repair may be possible. Alternatively, an interposition or bypass graft of saphenous vein or polyester is sutured to the unininvolved artery beyond the dissection in an end-to-end or end-to-side fashion, and the proximal end is anastomosed to the ascending aortic graft. If the end-to-side technique is used, the coronary artery is ligated proximal to the anastomosis. Disrupted layers of the aorta are approximated using 4- to 5-mm strips of polytetrafluoroethylene (PTFE) felt placed in the lumen and outside the aorta. This is accomplished with multiple mattress sutures of 4-0 or 5-0 polypropylene (Fig. 25-7, E).

Alternatively, strips of autologous or bovine pericardium may be used. This cuff, containing the two strips of felt (or pericardium) and the two layers of the aorta, is sutured to a collagen- or gelatin-impregnated woven polyester graft with a continuous 3-0 or 4-0 polypropylene suture (Fig. 25-7, F). Occasionally, use of 5-0 polypropylene suture may be indicated because of thinness and friability of aortic tissue. Diameter of the graft should be 10% to 15% smaller than the diameter of the aortic anulus to ensure adequate coaptation of the aortic cusps. The separated layers of the aorta can also be approximated using GRF or other glue (see Fig. 25-7, D, inset).

Replacement of Structurally Abnormal or Diseased Aortic Valve Occasionally, resuspension of the aortic valve is inadequate and replacement is necessary. The aortic valve may also require replacement if it is structurally abnormal. If the aortic root is not dilated, the aortic valve is excised and replaced (see “Replacement of Aortic Valve and Ascending Aorta, En Bloc” under Technique of Operation in Chapter 12). Dissected layers of the aorta in the region of the coronary sinuses and the coronary ostia are managed as described earlier under “Repair of Disrupted but Nonectatic Aortic Root.” The ascending aortic graft is sutured to the reinforced cuff of aorta at or just above the level of the aortic commissures, as shown in Fig. 25-7, F.

Management of Ectatic Aortic Root In patients with preexisting dilatation of the aortic sinuses and sinutubular junction, combined replacement of the aortic valve, aortic sinuses, and ascending aorta is the preferred method of treatment. These abnormalities are frequently encountered in patients with Marfan syndrome but may also be present in patients without this condition. Replacement with a composite graft containing a mechanical valve and a polyester tube graft is the most widely used technique. Conduits containing xenograft valves may be used in elderly patients or those in whom long-term anticoagulant therapy is contraindicated or inadvisable. Aortic root allografts and pulmonary root autografts can also be used. Valve-sparing procedures in combination with reconfiguration of the aortic root are only rarely indicated in patients with acute aortic dissection, because these operations are lengthy and complex. Such procedures are described under “Repair of Aortic Valve Regurgitation Caused by Aortic Dilatation or Aneurysm” in Chapter 12.

Occasionally, aortic root replacement may be advisable in the absence of ectatic aortic sinuses when there is marked disruption of layers of the aorta in this area. The aortic anulus is generally unaffected by the dissection and provides a secure area for attaching a composite graft or an aortic allograft. The coronary arteries are repaired, if necessary, and attached to the graft directly or to interposed segments of saphenous vein or polyester grafts.

DeBakey Type II Dissection

In these infrequent cases, dissection is confined to the ascending aorta, and the distal graft-to-aorta anastomosis is made to undissected aortic tissue. If dissection involves only the proximal ascending aorta, the aortic clamp is placed just proximal to the origin of the brachiocephalic artery (Fig. 25-7, G). The aorta is completely transected and sutured to the aortic graft with a continuous 3-0 or 4-0 polypropylene suture incorporating a strip of PTFE felt (see Fig. 25-7, G-H).

The interposition method of graft insertion is preferred for replacing the ascending aorta. Use of collagen- or gelatin-impregnated polyester grafts, fine suture (4-0 or 5-0 polypropylene), strips of PTFE felt or pericardium (see Fig. 25-7, G), and biological glue has substantially reduced severity of bleeding through graft interstices and from anastomotic suture lines. The older graft inclusion technique favored by some surgeons (see “Historical Note” in Chapter 26) is not recommended, because hemostasis and approximation of dissected layers of the aorta may be less secure, and because wrapping the aorta around the graft to reduce bleeding through graft interstices is no longer necessary.

Intraluminal sutureless prostheses have been used to treat both acute and chronic dissections of the ascending aorta. Woven polyester grafts of varying lengths with
a felt-covered metal spool at each end are available for this.\textsuperscript{2} Cloth tapes are placed around the aorta proximal and distal to the incision in the ascending aorta. After the aorta is clamped distally and opened longitudinally, the device is inserted into the aorta and is secured with the tapes, which are tied over the grooves in the proximal and distal spools. Obstruction of orifices of the coronary arteries and brachiocephalic artery must be avoided. The aorta can be sutured over the graft to minimize bleeding. Complications with these prostheses include dislodgment or buckling, pressure gradients when the prostheses buckle or are too small, and erosion of the aortic wall. The authors have observed all of these complications, as have others.\textsuperscript{8,12} For these reasons, intraluminal prostheses have a limited role in treating acute ascending aortic dissection. Occasionally, end-to-end anastomosis of the ascending aorta is possible after resecting the area containing the aortic tear.\textsuperscript{13}

As repair of whatever type is being completed, suction on the intracardiac venting catheter is discontinued, and the venous line is partially occluded to fill the heart with blood and evacuate air. The lungs are temporarily inflated to assist in this maneuver. Anastomosis of the aortic graft to the distal ascending aorta is completed, and a venting catheter or needle is inserted through a small stab incision in the graft guarded by a pledgeted mattress suture. With suction on the vent, the aortic clamp is opened briefly to remove any remaining air and reapplied. Infusion of warm blood cardioplegia retrogradely through the coronary sinus or controlled aortic root reperfusion can be performed at this time (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). When this is completed, suction is placed on the aortic vent, and the aortic clamp is released and may be reapplied to the aortic graft distal to the vent in a partially occluding position. Standard de-airing procedures are carried out (see “De-airing the Heart” in Section III of Chapter 2). CPB is then discontinued. TEE can be used to assist in evacuating air from the cardiac chambers and to assess competency of the aortic valve or valve substitute.\textsuperscript{24} Operation is completed in the usual manner.

\textit{DeBakey Type I Dissection}

When it is known from preoperative diagnostic studies or intraoperative TEE that dissection involves the distal ascending aorta, aortic arch, and remainder of the thoracic aorta, provisions are made for hypothermic circulatory arrest. An open technique for performing the distal aortic anastomosis is recommended because it provides the opportunity for directly inspecting the aortic arch and proximal descending thoracic aorta and permits distal anastomosis of the aorta to the aortic graft to be made at the most appropriate level.

If retrograde brain perfusion is to be used (for alternative methods, see “Brain Protection during Operations on the Aortic Arch” under Special Situations and Controversies in Chapter 26), separate cannulae are placed in the superior and inferior venae cavae and are connected to venous return tubing of the pump-oxygenator. Tapes are placed around both venae cavae but are not secured. Cannulating the femoral artery and placing left-heart venting and retrograde cardioplegia catheters are performed as described earlier under “General Considerations.”

\textsuperscript{2}Maquet Inc., 45 Barbour Pond Drive, Wayne, NJ 07470.
Figure 25-8 Repair of acute DeBakey type I (type A) aortic dissection. A, After circulatory arrest is established, aortic clamp is removed and aorta is completely transected proximal to origin of brachiocephalic artery. Disrupted layers of aorta are approximated between strips of polytetrafluoroethylene (PTFE) felt or pericardium and secured with multiple polypropylene mattress sutures. B, This cuff is sutured to a prepared woven polyester graft using a continuous polypropylene suture. C, After infusing cold blood into superior vena cava and briefly restoring retrograde arterial flow (arrows) (see "Brain Protection during Operations on the Aortic Arch" under Special Situations and Controversies in Chapter 26), proximal end of graft is elevated and gently massaged to evacuate air.

Malperfusion of brachiocephalic vessels and may reduce flow in the false lumen, thus reducing the possibility of late aneurysmal changes in the remaining aorta. The remaining steps in managing the proximal extent of the dissection and discontinuing CPB are completed as described earlier for DeBakey type II dissection. After removing the cannula in the aortic graft, the purse-string suture is secured (Fig. 25-8, E). If a sidearm graft was used for arterial return, it is suture-ligated as close to the aortic graft as possible and the remaining portion excised.

If it is necessary to include the aortic arch in the repair, the incision already made in the ascending aorta is extended into the arch and, if necessary, into the upper descending thoracic aorta to just beyond the origin of the left subclavian artery (Fig. 25-9, A). If an intimal tear is present in the arch, is located beneath the origins of the brachiocephalic arteries, and does not involve them or extend into the descending thoracic aorta, the aorta is transected obliquely beneath the brachiocephalic arteries (Fig. 25-9, B). The area containing the tear is excised. Disrupted layers of aorta are approximated between strips of PTFE felt or pericardium using mattress sutures of 4-0 polypropylene as previously described (Fig. 25-9, C). A prepared polyester graft of appropriate size is cut obliquely with a wire cautery and is sutured to the aortic cuff with 3-0 or 4-0 polypropylene suture (see Fig. 25-9, C). If the bevel created in the aorta at the level of transection is short, the graft is sutured so that it is vertically aligned with respect to the aortic arch (Fig. 25-9, C-D). If the aortic bevel is long, the graft is beveled in the reverse direction and sutured in a more horizontal position (see Fig. 25-9, D, inset).

As this anastomosis is being completed, cold oxygenated blood is infused into the superior vena cava as previously described, and air is evacuated from the brachiocephalic arteries and distal aorta. A cannula connected to the arterial return line of the pump-oxygenator is inserted into the graft close to the suture line and is secured with a purse-string suture. Alternatively, an aortic graft containing a sidearm can be used as previously described. Air is evacuated from the graft, the graft clamped proximal to the cannula (Fig. 25-9, E), and the procedure completed as previously described.

If the inner layer of the aorta is disrupted over the entire length of the aortic arch or if the arch has ruptured or is aneurysmal, replacing the entire arch is indicated. After the aorta has been incised, the phrenic and vagus nerves are dissected free from the anterior surface of the arch. The aorta is transected distal to the origin of the left subclavian artery. If dissection is present at this level, the disrupted layers of the aorta are approximated with strips of PTFE felt or pericardium. A prepared polyester graft is sutured to the distal aortic
Figure 25-8, cont’d  D. A perfusion cannula that has been attached to the arterial return tubing from the pump-oxygenator is inserted into aortic graft through a purse-string suture, and antegrade perfusion is reestablished (arrows). A soft-jawed clamp is placed on the graft. Graft is then anastomosed to proximal prepared aortic cuff with a continuous polypropylene suture. E. Completed procedure. Aortic cannula is removed and a pledgeted polypropylene suture used to seal this site and site of insertion of needle vent for aspirating air.

Figure 25-9  Repair of acute DeBakey type I (type A) aortic dissection when aortic arch is included in repair. A. Dashed line indicates line of incision that is extended onto anterior surface of aortic arch. B. Dashed line indicates site of transection of aorta when the aortic tear does not involve distal aortic arch or origins of brachiocephalic arteries and inner layer of aorta is intact in these areas. 

Continued
cuff with a 3-0 or 4-0 polypropylene suture (Fig. 25-10, A). After this anastomosis is completed, the graft is temporarily clamped, and retrograde aortic perfusion is established briefly to detect leaks in the anastomotic suture line. These are repaired with mattress sutures of 3-0 or 4-0 polypropylene. Alternatively, a ringed intraluminal prosthesis can be inserted into the true lumen of the descending thoracic aorta and secured with tapes, which are tied over a strip of PTFE felt.

A full-thickness elliptical incision is made in the aorta surrounding the origins of the brachiocephalic arteries (see Fig. 25-10, A). If dissection is present, the layers of the aorta are approximated between strips of PTFE felt or pericardium. An opening is made in the aortic graft opposite the aortic cuff with a wire cautery, and the cuff is sutured to the graft with a continuous 3-0 or 4-0 polypropylene suture (Fig. 25-10, B). As this suture line is being completed, cold oxygenated blood is infused retrogradely into the superior vena caval cannula to evacuate air from the brachiocephalic vessels. The open end of the graft is elevated to assist in evacuating air. A purse-string suture is placed in the graft beneath the brachiocephalic arteries, and an aortic cannula attached to the arterial return tubing is inserted into the graft through a small incision. Alternatively, as noted previously, an 8- or 10-mm polyester graft that is attached to the aortic graft and positioned beneath the anastomosis to the brachiocephalic arteries can be used for arterial return. A soft-jawed clamp is placed across the graft just proximal to the brachiocephalic artery. Antegrade flow is established and rewarming begun (Fig. 25-10, C). The remainder of the procedure is completed as described earlier.

If dissection extends into the brachiocephalic arteries and there are no intimal tears, disrupted layers of aorta adjacent to these arteries are approximated as described earlier and sutured to the aortic graft. If intimal tears are present in these arteries, they are transected, and the disrupted layers are
injury is a serious complication following descending thoracic clamping, distal aortic perfusion is routinely employed (see "Methods for Perfusing the Distal Aorta during Aortic Clamping" under Special Situations and Controversies in Chapter 24). If only a short segment of the proximal descending thoracic aorta requires replacement, left atrial–to–femoral artery bypass or partial CPB can be used. If the distal aortic arch requires replacement, or if extensive resection of the descending thoracic or thoracoabdominal aorta is necessary, full CPB with profound hypothermia (with or without circulatory arrest) is preferred.

Replacement of Descending Thoracic Aorta

After positioning the patient in the lateral decubitus position with the pelvis rotated posteriorly to allow access to the left femoral vessels, a posterolateral thoracotomy incision is made and the pleural cavity entered through the bed of the fifth rib, which

Figure 25-10 Repair of acute DeBakey type I (type A) aortic dissection when replacing entire aortic arch is necessary (see Indications for Operation in text). A, Aorta is completely transected distal to origin of left subclavian artery. Disrupted layers of aorta are approximated with strips of polytetrafluoroethylene (PTFE) felt or pericardium. A full-thickness elliptical incision is made in aorta surrounding origins of brachiocephalic arteries. If aorta is dissected in this area, disrupted layers are approximated with strips of PTFE felt or pericardium. A prepared polyester graft is sutured to distal aortic cuff with a continuous polypropylene suture. B, An opening is made into aortic graft with a wire cautery corresponding to size of aortic cuff surrounding the brachiocephalic arteries. Graft is sutured to aortic cuff with a continuous polypropylene suture. C, After evacuating air from the distal aorta and brachiocephalic arteries (see Fig. 25-8, C), aorta is clamped, a perfusion cannula attached to arterial return tubing from pump-oxygenator is inserted into the aortic graft through a purse-string suture, and antegrade perfusion is reestablished. Procedure is completed as shown in Fig. 25-8, D and E.
can be retracted or resected. This incision provides adequate exposure of the distal aortic arch and proximal two thirds of the descending thoracic aorta. If exposure of the more distal thoracic aorta is required, the incision can be extended anteriorly, dividing the cartilage at the costal arch; alternatively, a separate incision through a lower interspace can be made using the same skin incision. After placing a retractor, the left lung is collapsed and retracted anteriorly. Often there is an extensive mediastinal hematoma, and the mediastinal pleura is incised only where clamps are to be placed (Fig. 25-11, A; see also Fig. 24-8, A-D, in Chapter 24). Distal aortic perfusion is then established.

Whenever possible, control of the proximal aorta should be obtained at a level proximal to the origin of the disease, which is usually located just distal to the origin of the left subclavian artery. This is achieved by placing a clamp on the distal aortic arch between the left carotid and left subclavian arteries. The mediastinal pleura is opened in this area, and the aorta is circumferentially freed from surrounding tissue. The left subclavian artery is also freed from adjacent tissue near its origin. Intraoperative TEE and epiaortic scanning as well as preoperative CT or MRI can be used to detect presence of retrograde dissection in this area.

If placing clamps in these areas is inadvisable, total CPB with hypothermic circulatory arrest is used, and anastomosis of the aortic graft to the proximal aorta is performed using an open technique (see “Technique Using Hypothermic Circulatory Arrest” under Technique of Operation in Chapter 26). The vagus nerve is identified and protected (see Fig. 25-11, A-D). The site for clamping the distal aorta is identified, the mediastinal pleura is incised in this area, and the aorta is freed from surrounding tissue. Every effort should be made to limit resection to as short a segment of the upper descending thoracic aorta as possible to minimize risk of spinal cord ischemic injury. Clamps are then placed on the aorta between the left carotid and left subclavian arteries, on the left subclavian artery, and on the descending aorta just distal to the proposed area of resection (see Fig. 25-11, A).

The aorta is opened longitudinally (Fig. 25-11, B), thrombus removed from the false lumen, and the true lumen entered. Orifices of any bronchial arteries and of the intercostal arteries above the level of the sixth intercostal space are suture-ligated. Intercostal arteries below this level should be preserved and can be temporarily occluded with bulldog clamps if necessary. The aorta is completely transected below the origin of the left subclavian artery. The recurrent laryngeal nerve should be identified and protected. The aortic cuff below the proximal aortic clamp is carefully examined. If no dissection is present, this cuff is sutured to a prepared polyester tube graft of appropriate size using a continuous 3-0 or 4-0 polypropylene suture, incorporating a small cuff of PTFE felt that is placed on the external surface of the aorta (Fig. 25-11, C). If the layers of the aorta are separated in this area, they are approximated between strips of PTFE felt, and the resulting cuff is sutured to the aortic graft using the technique shown in Fig. 25-8, A and B. (If an intimal tear is present and extends proximally beyond the aortic clamp into the aortic arch, an alternative procedure is used as described in text that follows.) The completed suture line can be tested by placing a soft-jawed clamp on the graft and temporarily releasing the clamp on the proximal aorta. Bleeding sites on the suture line can be controlled with interrupted sutures.

The appropriate site for transection of the aorta above the distal clamp is selected. If this is above the level of the sixth intercostal space, the dissected layers are approximated between strips of PTFE felt using mattress sutures (Fig. 25-11, D). This cuff is sutured to the aortic graft with a continuous 3-0 or 4-0 polypropylene suture. If the site of transection is below the sixth intercostal space, the aorta is divided obliquely whenever possible to preserve lower intercostal arteries, and the cuff containing the strip of PTFE felt is sutured to the aortic graft. If it is necessary to transect the

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**Figure 25-11** Repair of acute DeBakey type III (type B) aortic dissection. A, Aorta is approached through a left posterolateral thoracotomy incision, and preparations are made for distal perfusion and protection of spinal cord (see “Methods to Minimize Spinal Cord Injury” under Special Situations and Controversies in Chapter 24). Clamps are placed on aorta between left carotid and left subclavian arteries, on left subclavian artery, and on the descending aorta just distal to proposed area of resection. Dashed line indicates site of incision. B, Aorta is opened and true and false lumens identified. Bulldog clamps are placed on exposed intercostal arteries.
Chapter 25  Acute Aortic Dissection

Polyester graft

C, Aorta is completely transected below origin of left subclavian artery. If layers of aorta are separated in this area, they are approximated between strips of polytetrafluoroethylene (PTFE) felt or pericardium (see Fig. 25-8, A and B). Aortic cuff is sutured to a prepared polyester graft with a continuous polypropylene suture. D, Appropriate site for transection of distal aorta is selected. Dissected layers are approximated between strips of PTFE felt or pericardium, and aortic cuff is sutured to distal end of aortic graft. E, If aorta must be transected at or above level of left subclavian artery, the aortic graft is sutured to the aorta at this level, and transected subclavian artery is sutured to the aortic graft directly or to a prepared, interposed 8- or 10-mm polyester graft using a continuous polypropylene suture.

Figure 25-11, cont’d  C, Aorta is completely transected below origin of left subclavian artery. If layers of aorta are separated in this area, they are approximated between strips of polytetrafluoroethylene (PTFE) felt or pericardium (see Fig. 25-8, A and B). Aortic cuff is sutured to a prepared polyester graft with a continuous polypropylene suture. D, Appropriate site for transection of distal aorta is selected. Dissected layers are approximated between strips of PTFE felt or pericardium, and aortic cuff is sutured to distal end of aortic graft. E, If aorta must be transected at or above level of left subclavian artery, the aortic graft is sutured to the aorta at this level, and transected subclavian artery is sutured to the aortic graft directly or to a prepared, interposed 8- or 10-mm polyester graft using a continuous polypropylene suture.

If it is necessary to transect the aorta proximally at or above the level of the left subclavian artery, the aortic graft is sutured to the aorta at this level using the technique previously described, and the transected subclavian artery is sutured to the aortic graft directly or with an interposed prepared 8- or 10-mm polyester graft using 4-0 or 5-0 polypropylene suture (Fig. 25-11, E).

After the distal anastomosis is completed, the distal aortic clamp is removed and air evacuated from the graft using an 18-gauge needle. Proximal clamps are removed, and if no major bleeding points are identified, CPB is discontinued. Cannulae used for distal perfusion are removed, heparin is neutralized with protamine, and the femoral vessels are

descending aorta below the level of the eighth or ninth intercostal space, intercostal arteries between the level of transection and the sixth intercostal space are isolated with a full-thickness cuff of aorta using the electrocautery, and this button of aorta is sutured to an opening in the graft with a continuous 4-0 polypropylene suture (see Fig. 26-18, F in Chapter 26). Alternatively, a separate prepared polyester graft can be sutured to the cuff of aorta surrounding the intercostal arteries. This graft is then sutured to an opening in the aortic graft with 5-0 polypropylene. If the aortic tissue surrounding the intercostal arteries is too friable to support sutures, these arteries are suture-ligated. Anastomosis of the graft to the distal aorta is completed as described previously.
Involvement of Aortic Arch  Occasionally, a DeBakey type III dissection extends retrogradely, involving the aortic arch and even the ascending aorta. If arch involvement is recognized preoperatively or intraoperatively, hypothermic CPB and circulatory arrest are used (see “Technique Using Hypothermic Circulatory Arrest” in Chapter 26). During cooling, the left phrenic and vagus nerves are identified and protected. After the desired temperature has been reached, the patient is placed in the head-down position, a clamp is placed on the aorta near the site selected for the distal anastomosis, and circulation is arrested.

The aorta is opened anteriorly distal to the origin of the left subclavian artery, and the incision is extended proximally beneath the origins of the brachiocephalic arteries. The site for the anastomosis must be proximal to the site of any intimal tears or rupture, although separation of layers of the aorta may be present. The aorta is completely transected, divided layers of the aorta are approximated with strips of PTFE felt or pericardium, and a prepared aortic graft containing a 10-mm sidearm is sutured to this cuff as described previously. Most often, the aorta can be transected obliquely beneath the origins of the brachiocephalic arteries so that only a single anastomosis is required.

Rarely, separate anastomoses to the aorta proximal to the origins of the brachiocephalic arteries and to a cuff of aorta surrounding these arteries are necessary. Once these anastomoses are completed, the sidearm of the aortic graft is attached to a second arterial line from the pump-oxygenator. After evacuation of air, flow is established through the aortic graft as well as through the femoral arterial cannula to assist in evacuating air from the upper body. Once this has been accomplished, a clamp is placed on the graft just distal to the sidearm, and CPB is reestablished (see Fig. 26-19, D-E in Chapter 26). Anastomosis of the graft to the distal aorta is completed as described earlier under “Replacement of Descending Thoracic Aorta.”

If dissection extends more proximally to involve the ascending aorta and the false lumen is not thrombosed or there is evidence for hemopericardium, the aorta should be approached through a midline sternotomy. The technique is described earlier under “DeBakey Type I Dissection.” The area of the aorta containing the intimal tear in the descending thoracic aorta may not be accessible with this anterior approach. In this situation, exposure of the proximal one third to one half of the descending thoracic aorta can be achieved by transverse extension of the midline sternotomy incision into the left third intercostal space, retracting the left lung anteriorly and inferiorly. If involvement of the ascending aorta with dissection is determined after a left thoracotomy has been performed, the thoracotomy can be extended anteriorly, and the sternum divided transversely at this level to facilitate exposure.

Involvement of Thoracoabdominal Aorta  Extension of operation to the thoracoabdominal aorta is indicated when rupture of this segment of the aorta has occurred or is imminent and when there is evidence for malperfusion of distal organs. This is only rarely necessary. Techniques for replacement of the thoracoabdominal aorta are discussed under “Thoracoabdominal Aorta Replacement” in Chapter 26.

Repair of Intraoperative Aortic Dissection  Intraoperative dissection of the ascending aorta is an infrequent complication of cardiac operations that require use of CPB. In two large series of patients operated on between 1980 and 1990, intraoperative dissection recognized intraoperatively or early postoperatively occurred in about 0.5% of patients. It is also a recognized complication of off-pump coronary artery bypass grafting (CABG), occurring in up to 1% of patients. Actual prevalence is likely higher, because diagnosis is not made perioperatively in all patients, and because some patients present late after operation with evidence for dissection that likely occurred intraoperatively. If unrecognized, this complication is associated with substantial mortality. Prompt diagnosis and surgical treatment are essential for survival.

Intraoperative aortic dissection should be suspected when a subadventitial or intramural hematoma develops in the ascending aorta, particularly in association with excessive bleeding from suture lines or needle holes. TEE and epiaortic ultrasonographic imaging are especially useful in establishing presence and extent of the dissection. Dissection originates most commonly at sites of partial or complete aortic clamping and aortic cannulation, and less frequently at sites of proximal anastomoses to venous or arterial bypass grafts and of needle venting.

Disrupted layers of aorta must be approximated and the false lumen, if present, obliterated. If dissection is localized to a small part of the aorta, such as the site of a venting or cardioplegia needle, it can be repaired by plicating the aorta using mattress sutures placed over strips of PTFE felt to exclude the area of dissection. This type of repair should be performed at a low level of aortic pressure to avoid tension on the suture line and possible extension of the dissection. This is best accomplished with the patient on CPB. Clamping the aorta with a partially occluding clamp surrounding the area of the tear should be avoided.

If the tear occurs at the anastomotic site of a bypass graft, the graft should be relocated to another area of the aorta or anastomosed to an adjacent graft. After the aorta is clamped in a nondissected area, divided layers of the aorta are approximated, usually with strips of PTFE felt or pericardium placed inside and outside the aorta. If dissection is not circumferential, the defect can be repaired with a patch of polyester or pericardium. If dissection is more extensive or extends beyond the ascending aorta, as is often the case when it originates from the aortic clamp or aortic cannulation site, resection and graft replacement of the ascending aorta are usually required. When dissection originates at the aortic cannulation site, the cannula is removed, and a common femoral artery exposed and cannulated. Unless dissection is confined to the proximal two thirds of the ascending aorta, aortic clamping should be avoided and preparations made for hypothermic circulatory arrest. Repair is accomplished using the techniques described earlier under “Repair of Acute DeBakey Type I or II (Type A) Dissection.”

SPECIAL FEATURES OF POSTOPERATIVE CARE  Early postoperatively, standard protocols are used (see Chapter 5). Control of hypertension is particularly important because hypertension predisposes the patient to excessive bleeding and early redissection or rupture of the residual false
lumen. Because malperfusion of major branches of the aorta may occur or become apparent postoperatively (see Special Situations and Controversies later), peripheral pulses and organ function should be monitored frequently.

Periodic evaluation following surgical repair or medical management of acute aortic dissection is mandatory. Stringent control of arterial hypertension is essential and is accomplished with calcium channel blocking agents, β-adrenergic blocking agents, and angiotensin-converting enzyme inhibitors used singly or in combination. β-Adrenergic blocking agents reduce rate of dilatation of the aorta and development of aortic complications in patients with Marfan syndrome and thus may provide an additional protective effect in patients with acute aortic dissection.514

Long-term follow-up is also necessary to detect false lumen enlargement and development of aneurysms that may require surgical treatment to prevent rupture. Currently, contrast-enhanced CT is the most widely used and cost-effective diagnostic study for evaluating the dissected aorta postoperatively. It provides accurate measurement of aortic diameter at various levels. MRI provides similar information, but is presently less readily available and more expensive than CT. Aortography may be indicated if additional surgery is contemplated or if compromise of branch vessels is suspected. TTE may be used to assess competency of the aortic valve after its resuspension as well as the size of the ascending aorta. TEE provides this information as well as information regarding flow and thrombosis in the false lumen. A protocol proposed by Borst and colleagues for follow-up of patients with aortic dissection is shown in Table 25-1.518 Patients with Marfan syndrome should be examined at 6- to 12-month intervals for the duration of their lives. Follow-up examinations are best performed by cardiovascular specialists who are knowledgeable about the sequelae and complications of aortic dissection.

<table>
<thead>
<tr>
<th>Table 25-1 Follow-up Studies after Acute Aortic Dissection</th>
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<tr>
<td><strong>Time of Study</strong></td>
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<tr>
<td><strong>Before Hospital Discharge</strong></td>
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<td>CT or MRI</td>
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<td>TTE</td>
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<td>Arteriography</td>
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<td><strong>After Hospital Discharge</strong></td>
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<td>3 months</td>
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<td>9 months</td>
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<td><strong>Subsequent Examinations</strong></td>
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<td>Every 6 months</td>
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<td>TTE</td>
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<tr>
<td>Every 12 months</td>
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<td>Every 24 months</td>
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Modified from Borst and colleagues.518

Key: CT, Computed tomographic scan; MRI, magnetic resonance imaging; TTE, transthoracic echocardiogram.

### RESULTS

#### Acute Dissection Involving Ascending Aorta (DeBakey Types I and II)

**Early (Hospital) Death**

Hospital mortality for heterogeneous groups of patients undergoing repair for various types of acute dissection of the ascending aorta has been 5% to 33%,85,B11,B12,C7,F5,G1,G4,G5,G11,M14,N2,O4,T4,Y4,Y7,Z1 A report by IRAD, established in 1996 and consisting of 18 large international referral centers, assessed the current presentation, management, and outcomes of patients with acute aortic dissection; hospital mortality was 25% among 526 patients (CL 23%-27%) with acute type A aortic dissection treated surgically between January 1, 1996, and December 31, 2001.74

**Time-Related Survival**

In the study of Crawford and colleagues of a heterogeneous group of patients undergoing repair of acute ascending aortic dissection, 1-month, and 1-, 5-, 10-, and 15-year survival was 79%, 66%, 46%, 46%, and 37%, respectively (Fig. 25-12, A).57 The hazard function for death had a rapidly declining early phase and a constant phase (see Fig. 25-12, B). Among 174 patients treated by the Stanford group and followed up to 30 years, 1-, 5-, 10-, and 15-year survival was 67%, 55%, 37%, and 24%, respectively.38

**Modes of Death**

In earlier years, hemorrhage and acute cardiac failure were the principal modes of death early after operation. In more recent experience, which reflects improved perioperative management, brain injury and malperfusion syndromes have emerged as important contributors to early death. B11,G1,G5,G11 Cardiac failure, MI, and stroke are other common modes of early death.37 Approximately 20% to 30% of late deaths are related to aortic rupture or new dissection. C9,F5,17

**Incremental Risk Factors for Premature Death**

**Acuity** The event of acute dissection itself is the dominant patient-specific risk factor, as is need for preoperative resuscitation. C7,G5 Predissection functional class (New York Heart Association class) of the patient was a surprisingly weak risk factor, which interacts with extent of operation to become more powerful when the arch is included in repair (Fig. 25-13).67 However, Sabik and colleagues, who combined acute and chronic dissections and used both analysis of interactions with dissection acuity and propensity score adjustment (see “Clinical Studies with Nonrandomly Assigned Treatment” in Section I of Chapter 6), concluded that it was hemodynamic state rather than acuity of dissection that was the risk factor for early mortality.51 In the IRAD study, preoperative shock or cardiac tamponade was an independent predictor of operative mortality.74

**Location of Dissection** Five-year survival is appreciably better for patients with DeBakey type II as compared with DeBakey type I ascending aortic dissection (87% vs. 56%, respectively). G4

**Comorbidity** In the IRAD study, age 70 years or older was a risk factor for hospital mortality.74 Older age was a risk...
factor for late-phase risk in the studies by Sabik and colleagues and Zierer and colleagues. In the IRAD study, previous aortic valve replacement and preoperative limb ischemia were risk factors for premature death. Presence of diabetes is a risk factor, as is preoperative renal insufficiency. Procedural Risk Factors Earlier date of operation is a predictor of early death in some series (Fig. 25-14), reflecting the major improvements in technique and perioperative management not seen in other series. Failure to include the area of the intimal tear has not been, with any certainty, a risk factor for death early or late after repair. Inclusion of the arch in the repair is a risk factor for death within 30 days and late after operation in some series (see Fig. 25-14) but not in others. Sabik and colleagues found that need to use a composite graft technique was a risk factor.

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those involving the aortic arch and proximal descending thoracic aorta. Among operative survivors, aneurysmal dilatation of the remaining dissected aorta occurs in up to 50% to 60% within 10 years, and up to 25% require reoperation (see later section on “Reoperation”). Risk factors for aneurysmal dilatation include patent or wide false lumen, larger aortic diameter early after repair, Marfan syndrome, hypertension, younger age, and male sex. In the study of Park and colleagues, shrinkage of the false lumen occurred in 36 (29%) of 122 patients with serial CT imaging who were followed a mean of 34 months. Shrinkage occurred in 23 of 24 patients (96%) who had thrombosed and narrow false lumens in the thoracic aorta.

Redissection

Redissection (i.e., new aortic dissection in a different part of the aortic wall) may develop years after surgical or medical treatment of an acute aortic dissection. Marfan syndrome is believed to increase the probability of redissection.

Aortic Valve Competence after Commissural Resuspension

Successful resuspension of the aortic valve, rather than replacement, does not increase risk of operation in patients with acute aortic dissection and aortic regurgitation. Furthermore, in most patients, the aortic valve is competent or shows only mild regurgitation after this procedure. Late reoperation and valve replacement occur infrequently. Meng and colleagues reported 55 of 60 patients (92%; CL 86%-95%) in a collected series to be free of the need for valve replacement 2 to 10 years later, virtually the same as that reported by Borst and colleagues, Fann and colleagues, Jex and colleagues, and Sabik and colleagues. Among 123 patients with acute type A dissection treated at Stanford University who had resuspension of the aortic valve (n = 82), composite graft replacement (n = 21), or separate valve and ascending aortic replacement (n = 20), actuarial freedom estimates for reoperation on the aortic valve at 6 years were 94% ± 4%, 100% ± 2%, and 88% ± 12%, respectively (P = NS). A new dissection proximal to the ascending aortic graft or development of a sinus of Valsalva aneurysm late postoperatively predisposes patients to developing important aortic valve regurgitation that may require reoperation.

Reoperation

Need for reoperation is relatively common. It is required most often for enlarging aneurysms of the false lumen but also for a new dissection, false aneurysms at the original suture lines, sinus of Valsalva aneurysms, or aortic valve regurgitation (described in the preceding text). In the experience from Stanford with 174 patients with acute type A dissections, 30 patients (17%; CL 14%-20%) required reoperation. Freedom from reoperation at 1, 5, 10, and 15 years was 94%, 83%, 65%, and 65%, respectively. In the multivariable analysis, younger age was the only risk factor predicting a higher likelihood of reoperation over time. Similar prevalence of reoperation has been observed by other groups. However, Sabik and colleagues reported 5- and 10-year freedom from reoperation of 91% and 85%, with a rate of 2% per year after the first 3 months. Freedom from reoperation for distal false-lumen aneurysm only, in the series of Crawford and colleagues, is shown in Fig. 25-15. Kirsch and colleagues identified severe preoperative aortic regurgitation as the only risk factor for proximal reoperation. Reoperation is required with greater frequency in patients with Marfan syndrome. Other important risk factors for reoperation include patent false lumen, large initial aortic diameter distal to the repair, hypertension, and non-resection of the primary tear.

Surgical Techniques to Reduce the Frequency of Late Aneurysm Formation and Reoperation

Total Aortic Arch Replacement

Total aortic arch replacement at the time of repair of acute DeBakey type I (type A) aortic dissection has been performed in experienced surgical centers and has been accomplished without increasing the risk of operation in selected patients. It has been proposed as a mechanism to promote thrombosis of the distal false lumen and reduce the frequency of late aneurysm formation and reoperation. Extended follow-up, however, has not conclusively demonstrated that this procedure improves survival or reduces frequency of reoperation.

Elephant Trunk Technique

Addition of an elephant trunk to ascending aorta and total arch replacement has been proposed as a method to ensure a more secure distal aortic anastomosis and to promote thrombosis of the false lumen in the descending thoracic and abdominal aorta. This can be accomplished with either a polyester graft (see section on Elephant Trunk Technique in Chapter 26) or an endovascular stent-graft inserted through the open aortic arch (Fig. 25-16). The putative advantages of an elephant trunk include promoting thrombosis of the false lumen, reducing the frequency of subsequent operations for aneurysm formation of the residual dissected aorta, and simplifying any subsequent operative procedure on the distal aorta. In contrast to a polyester elephant trunk, use of a stent-graft permits fixation of the distal end of the elephant trunk to the aortic wall. Thrombosis of the false lumen surrounding the elephant trunk has been demonstrated in a high percentage of patients undergoing either technique (Fig. 25-17). Thrombosis of the more distal thoracic and abdominal aorta, however, has not consistently occurred. It has not been conclusively demonstrated in a large series of patients undergoing either procedure.
demonstrated that the frequency of reoperations on the remaining dissected aorta has been reduced. Unique complications of extending the aortic graft into the descending thoracic aorta include paraplegia/paraparesis, creation of a new dissection by the stents of the endovascular graft, endoleak, and compression or collapse of the graft, creating important obstruction to aortic flow.

Functional Status
Most patients return to their predissection functional status after surgical repair of the acute dissection.

Acute Dissection Involving Descending Thoracic Aorta

Early (Hospital) Death
When operation is performed as a routine for acute dissections involving the descending aorta, early mortality can be as low as 10%. However, in most centers, operation is commonly performed in patients with specific indications (see Indications for Operation later) such as a failed initial course of medical treatment, and for them, early mortality has ranged from 28% to 49%. An IRAD study, independent predictors of early death following surgical treatment in 82 patients were age older than 70 years (odds ratio 4.3; CL 2.4-7.9) and preoperative shock/hypotension (odds ratio 6.0; CL 2.6-14.0).

Time-Related Survival
Time-related survival following operation appears to be similar to that of patients with acute dissection involving the ascending aorta. In the Stanford University experience, 1-, 5-, 10-, and 15-year survival for 46 patients with acute type B dissections was 56%, 48%, 29%, and 11%, respectively. In a more recent IRAD study of patients treated surgically and discharged alive, 3-year survival was 83% ± 19%.

Morbidity
Paralysis of the lower extremities and renal failure are more frequent postoperative complications following operations on the descending aorta than on the ascending aorta.

INDICATIONS FOR OPERATION

Acute Dissection Involving Ascending Aorta (DeBakey Types I and II)

When dissection involves the ascending aorta with or without involvement of the proximal portion of the aortic arch, immediate operation is indicated. This policy is the result of comparison of the natural history (see Fig. 25-6) with results of surgical treatment (see Figs. 25-12 and 25-18) and the knowledge that rupture or fatal cardiac tamponade is likely to occur. Contraindications are markedly advanced age and frailty, severe incurable disease such as malignancy or chronic dementia, and evidence of irreversible brain injury. Stroke occurring as a result of dissection is a risk factor for death after operation, but among survivors, symptoms and signs of stroke may resolve considerably. Thus, a new stroke is not necessarily a contraindication to operation. MI induced by the dissection, coma, paraplegia, renal failure, and ischemia of the extremities and abdominal viscera are
not contraindications to operation. These complications may disappear or improve following repair of the aorta, or they may be surgically treated at the time of or after the aortic procedure.

The aortic arch should be included in repair when the intimal tear is located in the arch, the inner layer of the aorta is fragmented, the outer wall of the aorta is tenuous or aneurysmal, or rupture of the arch has occurred. Although replacement of all or, more commonly, a part of the arch to eliminate the site of the intimal tear is arguable, it should usually be performed, because prevalence of late reoperation is greater when the site of the intimal tear is not resected, and because recent experience with resection of the aortic arch in the setting of acute dissection is associated with acceptable operative risk. Replacement of the arch may also be advisable in patients with acute ascending aortic dissection when the tear is located in the proximal descending thoracic aorta.

Acute Dissection Involving Descending Thoracic Aorta (DeBakey Type III)

Whereas indications for operation for acute aortic dissections involving the ascending aorta are fairly well standardized, those for acute dissections involving the descending aorta are not. When only the descending thoracic aorta is involved in acute dissection, with or without involvement of the abdominal aorta and iliac vessels, and there have been no clinically evident complications of the acute dissection, medical treatment is indicated. This plan is supported by comparisons of results in comparable patients treated medically vs. surgically, which show no differences. With medical treatment only, approximately 90% of selected patients survive for 30 days (Fig. 25-18) and 80% survive at least 1 year after acute dissection. Medical treatment is directed toward maintaining normal (not elevated) arterial blood pressure with sodium nitroprusside, reducing force of left ventricular ejection with β-adrenergic receptor blockade, and maintaining good urine flow and good overall subsystem function.

When initial medical treatment results in survival without important complications, close patient follow-up after hospital discharge is essential. This need is emphasized by the experience of Wheat and colleagues and of McFarland and colleagues, who found that 50% of such patients die during the subsequent 3 to 5 years. Follow-up is conducted to obtain the same information, and for the same reasons as required after surgical treatment (see Special Features of Postoperative Care earlier in this chapter).

Complications occurring in patients with acute aortic dissection involving only the descending thoracic and abdominal aorta require immediate surgical treatment by open operation, endovascular grafting, or interventional procedures to manage malperfusion (see “Malperfusion” and “Endovascular Grafts” later under Special Situations and Controversies). These include aortic rupture; dissection superimposed upon a preexisting aneurysm; rapid expansion of aortic diameter; ischemia of limbs, visceral organs, or kidneys; progression of dissection; uncontrolled hypertension; intractable pain despite medical therapy; and extensive hemothorax. Marfan syndrome is considered by some to be an indication for early operation because of poorer results with medical therapy.

Paraplegia occurring as an isolated complication is not an indication for intervention, because recovery of spinal cord function following repair of aortic dissection does not commonly occur. However, neither is it a contraindication to operation, because relief of distal ischemia, particularly when femoral pulses are absent, may result in return of sensory and motor function. Although there are no absolute contraindications to operative treatment, mortality may be prohibitively high in very elderly patients and those with comorbid conditions such as ischemic heart disease, pulmonary disease, and extensive arteriosclerosis.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Malperfusion Syndromes**

Major branches of the aorta are commonly involved in dissection, and the presenting clinical picture may be influenced by symptoms that result from ischemia of one or more affected organs. Thus, patients may present with myocardial ischemia, stroke, paralysis of the lower extremities, symptoms and signs of acute abdomen, renal failure, or ischemia of the extremities. In the large autopsy study of Hirst and colleagues, dissection was observed in the carotid arteries in 28%; in the celiac, mesenteric, or renal arteries in 28%; in the iliac and femoral arteries in 26%; in the subclavian arteries in 14%; in the coronary arteries in 7%; and in the spinal arteries in 1.8% of cases.

In large clinical studies of aortic dissection, symptomatic malperfusion of the major aortic branches was present in 15% to 33% of patients. Malperfusion and ischemia can result from compression of the true lumen of the aorta by the expanding false lumen, extension of the dissection into the branch artery with compression of the true lumen, intussusception of the inner wall of the aorta into a branch artery, or occlusion of a branch vessel by a flap of dissected aorta. Managing malperfusion of the coronary arteries during repair of acute dissection involving the ascending aorta was discussed earlier under “Repair of Disrupted but Nonectatic Aortic Root.” If malperfusion of the brachiocephalic arteries
is detected after establishing CPB using the femoral artery or after placing a clamp on the ascending aorta, urgently establishing antegrade flow in the ascending aorta is indicated. This can be accomplished by direct cannulation of the ascending aorta or aortic arch guided by TEE, or by cannulating the left ventricular apex or right axillary artery.\textsuperscript{B20,R10,S22}

Occasionally, extraanatomic bypass grafts to the carotid or subclavian arteries may be necessary to correct persisting malperfusion after repair of ascending aortic dissection. In most cases of acute ascending aortic dissection, graft replacement of the ascending aorta will correct malperfusion syndromes of visceral, renal, and lower extremity arteries, and this should be expeditiously performed.\textsuperscript{F4,G2} If ischemia persists, fenestration of the dissecting membrane or direct revascularization of the occluded arteries may be necessary.\textsuperscript{G2} In patients with acute descending aortic dissection, fenestration or direct revascularization procedures may be indicated to relieve ischemia when other indications to resect and replace a segment of the descending thoracic aorta are not present.\textsuperscript{G6} Alternatively, these procedures can be performed using endovascular techniques.\textsuperscript{C2,K6,L1,P5,W1}

Endovascular Grafts

Endovascular grafts have been used to treat acute complicated DeBakey type I (type A) and DeBakey type III (type B) aortic dissections when the primary intimal tear is located in the descending thoracic aorta.\textsuperscript{D2,K3,K4,P1} Use of an endovascular stent-graft eliminates need for thoracotomy and for clamping the thoracic aorta. Other putative advantages of endovascular repair include restoration of true lumen flow with closure of the primary tear, thrombosis of the false lumen, restoration of flow to distal organs and lower extremities, and lower early mortality than reported for open repair. Results of endografting from recently reported series and from a single meta-analysis are shown in Table 25-2. Early mortality appears to be lower than for open repair, although no randomized trials comparing the two forms of therapy for complicated descending thoracic aortic dissection have been reported. Conversion to open operation has been infrequent (0.6% among the 942 patients [CL 0.4%-1.0%] included in the meta-analysis of Parker and Golledge\textsuperscript{P3}).

The complications of aortic rupture, stroke, spinal cord ischemic injury (paralysis or paraparesis), and renal failure have not been eliminated, and adjunctive procedures to manage endoleaks and persisting malperfusion are often required (see Table 25-2). Type A aortic dissection following endovascular repair occurred in 2% of patients (18 of 918; CL 1.5%-2.6%) in the meta-analysis of Parker and Golledge.\textsuperscript{P3} Complete thrombosis of the false lumen has not been consistently observed.\textsuperscript{C6,K7,R10,S24}

A randomized multicenter trial comparing endovascular stent-grafting with medical therapy for patients with uncomplicated acute type B aortic dissection who were randomized 2 weeks after onset of symptoms was performed by the INvestigation of STEnt-grafts in Aortic Dissection (INSTEAD) group.\textsuperscript{N6} There was no difference in 30-day mortality between the two groups. One-year survival was 91% in the stent-graft group and 97% in the medically treated group (\(P = .16\)).\textsuperscript{C6} Follow-up from one of the earliest series of patients with acute type B dissection treated with endovascular stent-grafts by Palma and colleagues\textsuperscript{P3} demonstrated that at a mean of 36 ± 28 months, late mortality was 18%; subsequent endovascular grafting was required in 6 of 28 patients (21%); and late failure, defined as sudden or aortic-related death, surgical conversion, or reintervention, occurred in 12 patients (43%).\textsuperscript{A3}

Detecting and Managing Coexisting Coronary Artery Disease

With increased use of CT and TEE to diagnose acute ascending aortic dissection, routinely performing preoperative angiography, including coronary angiography, has been questioned.\textsuperscript{G1,K9,R3} Rizzo and colleagues suggest that rapid noninvasive diagnosis and avoidance of routine angiography appear to improve survival by expediting surgical intervention and thus decreasing risk of aortic rupture.\textsuperscript{R3} In contrast, Creswell and colleagues documented the presence of arteriosclerotic coronary artery disease (>50% stenosis) in 8 of 23 patients (35%; CL 25%-45%) with acute ascending aortic

---

Table 25-2  Early Results of Endovascular Repair of Acute DeBakey Type III (Type B) Dissection

<table>
<thead>
<tr>
<th>Individual Series</th>
<th>No. of Patients</th>
<th>30-Day Mortality</th>
<th>Stroke (%)</th>
<th>SCI\textsuperscript{1} (%)</th>
<th>Renal Failure\textsuperscript{b}</th>
<th>Adjunctive Intervention\textsuperscript{c}</th>
<th>1-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verhoye et al., 2008\textsuperscript{k2}</td>
<td>16</td>
<td>25%</td>
<td>0</td>
<td>0</td>
<td>19%</td>
<td>25%</td>
<td>73%</td>
</tr>
<tr>
<td>Szeto et al., 2008\textsuperscript{k24}</td>
<td>35</td>
<td>2.8%</td>
<td>2.8%</td>
<td>8.5%</td>
<td>20%</td>
<td>34%</td>
<td>93%</td>
</tr>
<tr>
<td>Sayer et al., 2008\textsuperscript{k6}</td>
<td>38</td>
<td>2.6%</td>
<td>5.3%</td>
<td>0</td>
<td>NA</td>
<td>21%</td>
<td>93%</td>
</tr>
<tr>
<td>Pearce et al., 2008\textsuperscript{k7}</td>
<td>15</td>
<td>13%</td>
<td>6.7%</td>
<td>13%</td>
<td>13%</td>
<td>47%</td>
<td>NA</td>
</tr>
<tr>
<td>Conrad et al., 2009\textsuperscript{k6}</td>
<td>33</td>
<td>12%</td>
<td>12%</td>
<td>6.1%</td>
<td>12%</td>
<td>NA</td>
<td>76%</td>
</tr>
<tr>
<td>Feezor et al., 2009\textsuperscript{k7}</td>
<td>33</td>
<td>21%</td>
<td>12%</td>
<td>24%</td>
<td>12%</td>
<td>48%</td>
<td>61%\textsuperscript{e}</td>
</tr>
<tr>
<td>Khoynezhad et al., 2009\textsuperscript{k10}</td>
<td>28</td>
<td>11%</td>
<td>3.3%</td>
<td>0</td>
<td>10%</td>
<td>18%</td>
<td>82%</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Temporary or permanent paralysis.

\textsuperscript{b}Temporary or permanent dialysis.

\textsuperscript{c}Concomitant or early postoperative.

\textsuperscript{d}Six-month survival.

\textsuperscript{e}Paraplegia.

NA, Not available; SCI, spinal cord injury.
dissection. Four of these patients with the most severe disease had CABG at the time of repair of acute dissection, and all survived the operative procedure. Mean age of the four patients was 73 years, whereas age of the entire cohort of patients with acute dissection was 59 years. These observations suggest that coronary angiography and CABG, when indicated, should be considered for hemodynamically stable patients with a known history of coronary artery disease, previous CABG, or acute changes on preoperative ECGs.

Use of Biological Glues to Reduce Bleeding and Obliterate the False Lumen

GRF and other biological glues have been used in an attempt to reduce bleeding during operations for acute aortic dissection. Although several groups have reported satisfactory early outcomes with use of GRF and other glues with low mortality and reduced bleeding, no prospective or randomized trials have been reported. In contrast to the findings of Bachet and colleagues, Goossens and colleagues did not observe a reduction in hospital mortality or need for reoperation for bleeding following introduction of GRF glue. Although several groups have reported satisfactory early outcomes with use of GRF and other glues with low mortality and reduced bleeding, no prospective or randomized trials have been reported. Biological glues have also been used to facilitate reconstruction of the aortic root by obliterating the false lumen and reinforcing the aortic layers.

Although initial results have been satisfactory, need for reoperation for aortic root dissection and for aortic regurgitation attributed to use of various glues has been observed in several centers.

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DEFINITION

This chapter considers true aortic aneurysm, false aortic aneurysm, chronic aortic dissection, penetrating arteriosclerotic ulcer, intramural hematoma, and diffuse arteriosclerotic disease. Methods for protecting the brain during operations on the aortic arch are also discussed.

True aortic aneurysm is a permanent localized dilatation of the aorta, of a diameter 50% or greater than normal, contained by walls that although attenuated, have all layers of the normal wall.15 False aortic aneurysm is a localized dilatation whose wall consists of adventitia, some or all of the media, and compressed periaortic tissue. Chronic aortic dissection is a separation for more than 14 days of the outer from the inner layer of the media, caused by blood leaving the normal aortic channel through a point of exit (intimal tear). Penetrating arteriosclerotic ulcer is an arteriosclerotic lesion that penetrates the internal elastic lamina of the aortic wall. Intramural hematoma is an extravasation of blood into the aortic wall, commonly in the absence of an intimal disruption. Diffuse arteriosclerotic disease is sessile, mobile, or pedunculated atheroma involving lipid deposition in large areas of the intimal layer of the aorta.

HISTORICAL NOTE

An important contribution to modern aneurysm surgery was made by Rudolph Matas in New Orleans in 1902 when he described the basic maneuver of “getting inside the aeurysm” with minimal external dissection and after obtaining control of the artery above and below the aneurysm.37 Interestingly, this basic maneuver was ignored as aortic aneurysm surgery began to develop, and in early work with abdominal aortic aneurysms at the Mayo Clinic, the aneurysm was dissected away from surrounding tissues, often with a long and difficult operation and considerable hemorrhage from lumbar arteries.9,21 DeBakey and Cooley described this same tedious method in their classic paper of 1953.37 Javid and colleagues in 1962 and Crecel in 1966 are generally credited with reintroducing the technique of working within the aneurysm.33,12 However, DeBakey and colleagues in Houston had reintroduced this concept into abdominal aortic aneurysm surgery by 1958.48 The inclusion technique of sewing the graft in place from within the aneurysm is an embodiment of this concept.43

Throughout the first half of the 20th century, sporadic attempts were made to treat aortic aneurysms, almost all in the abdominal aorta. Treatment was by proximal partial or complete ligation of the aorta. Results were generally unsatisfactory.11,12 Various other palliative procedures had also been used unsuccessfully. In 1950, Estes at the Mayo Clinic published a classic paper that demonstrated the poor prognosis of patients with abdominal aortic aneurysms, only 50% of whom survived 3 years after diagnosis, with two thirds of the deaths attributable to aneurysmal rupture.12 In response to that study, the Mayo Clinic began a surgical approach to this condition in 1951, and in 1953 reported the results of aneurysm reinforcement and the tedious operation of aortoplasty and complete wrapping with fascia lata.10 In 1952, Schafer and Hardin in Kansas City reported resection and grafting with an aortic allograft of an abdominal aortic aneurysm, only to have the patient die of numerous complications 28 days after operation.59 In that same year, Dubost and colleagues, working in Paris, reported the first successful case of aortic resection for aneurysm and restoration of blood vessel continuity (in their case, an abdominal aortic aneurysm that was approached retroperitoneally and replaced by a preserved aortic allograft).22 In 1953, reports of similar successes came from DeBakey and Cooley in Houston and from the Mayo Clinic.47,66,10 Aortic allograft banks were subsequently established in some centers to provide aortic replacement grafts.47,48,20,26

In 1944, Alexander and Byron successfully resected a thoracic aortic aneurysm secondary to coarctation, although without restoration of aortic continuity.85 Aortic allografts were developed in 1948 by Gross and colleagues in Boston to replace resected aortic segments.47,48,26 On May 24, 1948, they resected a coarctation in a 7-year-old boy, restoring aortic continuity with an aortic allograft. When the clamps were released, the distal vasculature dilated, and the patient became hypotensive and died. This led to a recommendation to slowly release the clamps following repair of aortic coarctation.47,48 They performed four more allograft replacements of the aorta for coarctation in 1948, five in 1949, and eight in 1950, including the first frozen and irradiated graft, which functioned for at least 30 years (Dr. Robert Replogle, personal communication, July 19, 2002). In 1950, Swan and colleagues also reported successful clinical use of allografts for treating complex coarctations, including those with aneurysms.31 Adopting this technique, Lam and Aram in 1951 reported resection and allograft replacement of a descending thoracic aortic aneurysm in an adult.4,5 Prophetically, paraparesis developed in their patient, who died 6 weeks after operation of empyema. About this time, Bahnsen reported successful management of a saccular aneurysm of the descending thoracic aorta by lateral resection and aortorrhaphy.52 In 1953, DeBakey and Cooley reported the first successful application of resection and grafting to a descending thoracic aortic aneurysm.58

Ascending aortic aneurysms were also approached surgically before the advent of cardiopulmonary bypass (CPB). In 1952, Cooley and DeBakey reported removal of sacciform ascending aortic aneurysms by lateral resection and aortorrhaphy, as did Bahnsen and Johnston and colleagues in 1953.52,8,9 In 1956, Cooley and DeBakey reported the first successful modern operation for ascending aortic aneurysm, consisting of resecting the ascending aorta and grafting with an aortic allograft, with the aid of CPB.52,8,9 Wheat and colleagues then reported successful simultaneous but separate replacement of the ascending aorta and aortic valve with implantation of the coronary ostia into the graft.56 Bentall and De Bono in 1968 and Edwards and Kerr in 1970 reported accomplishing this replacement with a composite valve and polyester tube graft.8,9 Wheat and colleagues subsequently demonstrated long-term patency of their anastomoses between grafts and coronary ostia.56

Aneurysms of the arch of the aorta presented a more difficult surgical challenge. By 1952, Cooley and DeBakey had removed some sacciform aneurysms in this portion of the aorta by lateral resection, as had Bahnsen by 1953.52,8,9 The next year, DeBakey and Cooley reported successful resection of the distal aortic arch and replacement by a graft for an aneurysm that had resulted from acute traumatic aortic transection.58 The case is of interest in that the patient’s temperature was reduced to 28°C by surface cooling before thoracotomy. The aorta was clamped proximal to the left
subclavian artery (which was also individually clamped) for 1 hour, and paraplegia did not develop (see “Paraplegia” under Special Situations and Controversies in Chapter 24 for the significance of this finding). In 1955, Cooley and colleagues reported unsuccessful resection of an aneurysm of the entire aortic arch, using the cumbersome method of temporary shunts without CPB, as did Stranahan and colleagues in a 15-hour operation in 1955 and Creech and colleagues in 1956. In 1957, DeBakey and colleagues reported the first successful repair of an aortic arch aneurysm using CPB and allograft replacement.

Thoracoabdominal aneurysms also presented difficult surgical challenges, not only because of the magnitude of the operation but also the propensity of patients to develop renal and spinal cord dysfunction after repair. In 1952 during Bahnsen’s pioneering work with aneurysms of the aorta, he successfully repaired a saccular thoracoabdominal aneurysm by lateral resection and aortorrhaphy. Ellis and colleagues at the Mayo Clinic first reported repair of such an aneurysm involving a visceral artery (in their case, the renal artery) by resection and grafting in 1955. Etheredge and colleagues reported successful repair of a more complex thoracoabdominal aneurysm including the celiac axis and superior mesenteric artery in the same year. In 1956, DeBakey and colleagues reported successful repair of such an aneurysm involving all the visceral arteries (celiac, superior mesenteric, and both renal). Subsequently, they devised the technique of permanent aortic bypass with a synthetic graft and visceral arterial reattachment to appropriately located side-arm grafts, and in 1965 they reported 26% mortality among 42 patients. Crawford and colleagues modified and simplified the operation by applying the inclusion technique, reducing hospital mortality to 8% by 1978.

During this developmental phase, there was controversy about the lethality of thoracic aortic aneurysms. Some reports indicated that patients with thoracic aneurysms fared better than those with abdominal aneurysms. In 1964, Joyce and colleagues established that this was not the case. A series of technical improvements evolved into many of the techniques currently used for surgical treatment of thoracic aortic aneurysms. Even after successful repair of aneurysms of the arch had been accomplished using CPB, methods remained complex, often involving separate cannulation of the brachiocephalic arteries. In 1964, Bosr and colleagues reported repair of a traumatic aneurysm of the distal portion of the aortic arch through a left thoracotomy, using CPB to produce profound hypothermia and performing the repair during an interval of circulatory arrest.

In 1975, Griep and colleagues established the value of profoundly hypothermic circulatory arrest for resecting and grafting of more proximal and more extensive aneurysms of the aortic arch. Among the technical improvements was use of a single anastomosis between an oval opening in the graft and the aortic wall around all three brachiocephalic arteries in replacing aortic arch aneurysms, reported by Bloodwell and colleagues in 1968 and by Pearce and colleagues the following year. Later, Ott and colleagues reported tailoring the arch resection and graft so that a single distal anastomosis could be made. Crawford and Saleh applied the inclusion technique to arch aneurysms, working entirely within the aneurysm and wrapping the graft with aneurysm wall.

Technical improvements have also been made in the aortic replacement devices required for treating aortic aneurysms and dissections. Soon the search for synthetic aortic substitutes was revived despite the unsuccessful pioneering efforts of Carrel and others. The first satisfactory synthetic aortic substitute was a fabric tube made of polyvinyl chloride cloth, and the first clinical application of this device was reported by Blakemore and Voorhees in New York City in 1954. Shumaker and King in Indianapolis also used these fabric tubes for aortic replacement in the same year. For the next several years, surgeons autoclaved and used fabric grafts made on the sewing machines of wives and friends, with generally good results. Intensive study of prosthetic grafts was quickly undertaken by several groups, and in 1955, Deterling and Bhonslay reported that polyester was the best material then available for aortic replacement. Knitted and woven grafts of various types, mostly polyester, have been widely used since then. Subsequent development of polyester grafts impregnated with collagen, gelatin, or albumin has resulted in a substantial reduction in blood loss through the grafts (particularly in fully heparinized patients), a major cause of postoperative morbidity (see “Grafts for Use in Aortic Surgery” under Special Situations and Controversies in Chapter 24.)

Stent-grafting of descending thoracic aortic aneurysms was introduced by Duke and colleagues at Stanford University in the early 1990s using custom-designed grafts. Since then, a number of commercially developed grafts have become available for clinical use.

MORPHOLOGY AND MORPHOGENESIS

Classification

Diseases of the thoracic aorta that are amenable to surgical treatment are listed in Box 26-1. Acute traumatic aortic transection and acute ascending and descending aortic dissection are discussed in Chapters 24 and 25.

Aneurysm

Aneurysm is the most common condition of the thoracic aorta that requires surgical treatment. This category includes congenital or developmental, degenerative, chronic traumatic, inflammatory, infectious, mechanical, and anastomotic aneurysms.

Congenital or Developmental

Marfan syndrome is an autosomal dominant disorder resulting from mutations in the FBN1 gene that lead to defective synthesis of the glycoprotein fibrillin (a component of elastic tissue in the medial layer of the aorta). The aorta becomes aneurysmal as a result of a reduced number of microfibrils in this layer. The dilated aortic segments are prone to rupture or dissection.

Loeys-Dietz syndrome is an autosomal dominant aortic aneurysm disorder with involvement of other systems. It results from mutations in either the transforming growth factor receptor type I or II (TGFBR1 or TGFBR2) genes. The majority of patients have aortic root aneurysms that result in aortic dissection. These patients also develop aneurysms of other vessels.

Ehlers-Danlos syndrome comprises a group of heterogeneous conditions characterized by various defects in the synthesis of type III collagen. Development of aneurysms is
uncommon, but rupture or dissection of the aorta or other arteries (often abdominal) can occur as a catastrophic event. Tissue fragility and poor healing can complicate surgical treatment.\textsuperscript{512} Ehlers-Danlos type IV (vascular form) is generally sporadic, but when familial is usually an autosomal dominant disorder.

Other genetically mediated conditions associated with aneurysm development and aortic dissection include Turner syndrome, Beals syndrome (contractural arachnodactyly), Noonan syndrome, autosomal dominant polygenic disease, and the nonvascular form of Ehlers-Danlos syndrome.\textsuperscript{A5,I4,M18,S12,W3}

Degenerative Cystic medial degeneration is the most frequent pathologic condition that results in aneurysms of the ascending aorta.\textsuperscript{515} Characteristic features are fragmentation and loss of elastic tissue and loss of smooth muscle cells. Inflammation and apoptosis may be components of this process as well.\textsuperscript{517} Enlargement is usually confined to the proximal portion of the ascending aorta. Dilatation of the sinuses of Valsalva and aortic anulus (anulooaortic ectasia) may result in aortic regurgitation. (See “Anulooaortic Ectasia” under Morphology in Chapter 12 for discussion of this entity in patients with aortic valve regurgitation.)

Degenerative aneurysms, often associated with arteriosclerosis of the aorta, are the most frequently occurring aneurysms of the thoracic and abdominal aorta and most commonly involve the descending thoracic or thoracoabdominal segments.\textsuperscript{C41,C56} Abnormal proteolysis, presence of elastolytic serum enzymes, and deficiencies of collagen and elastin have been implicated as factors contributing to development of these aneurysms.\textsuperscript{B21,B24,C4,N2,R2} Although atheromatous changes are frequently present in and around such aneurysms, the causative role of arteriosclerosis in their development is not clearly established.\textsuperscript{C41,E11,J5}

**Chronic Posttraumatic** Aneurysms resulting from blunt trauma most frequently involve the proximal descending thoracic aorta and may present many years after the acute injury. When neither death nor operation follows the acute transection, disruption of at least part of the aortic circumference, usually at the level of the ligamentum arteriosum, results in extravasation of blood into the periaortic tissues (see Chapter 24). This blood may remain in communication with the aorta and form a pulsating hematoma that is contained by aortic adventitia or the mediastinal tissues. The resulting false aneurysm may enlarge and rupture from increased wall stress (Laplace law). Chronic posttraumatic aneurysms represent a small percentage of patients with aneurysms of the thoracic aorta.

**Inflammatory** Patients with Takayasu arteritis, Behçet disease, Kawasaki disease, and giant cell arteritis may develop aneurysms of the thoracic aorta that require surgical treatment.\textsuperscript{A6,A14,D1,E15,I1,I2,K11,T1,W4} Other inflammatory disorders, such as ankylosing spondylitis, psoriatic arthritis, polyarteritis nodosa, and Reiter syndrome, may result in dilatation of the aortic root and aortic valve regurgitation that require surgical intervention.\textsuperscript{I2}

**Infected** Primary infected (mycotic) aneurysms of the thoracic aorta are rare. A frequent cause is direct deposition of circulating bacteria in a diseased, arteriosclerotic, or traumatized aortic intima following an episode of endocarditis or infection of an aortic jet lesion.\textsuperscript{F3,G4} Infection of intraluminal clot in a preexisting degenerative aneurysm may occur after an episode of bacteremia or other infectious process.\textsuperscript{C10} Organisms can also infect previously inserted prosthetic grafts, causing false aneurysms. Other risk factors for development of infected aneurysm include congenital cardiac or vascular defects, trauma, and impaired immunity.\textsuperscript{B22,G4,G16} \textit{Staphylococcus aureus} is the most frequent causative organism, followed by \textit{Staphylococcus epidermidis}, \textit{Salmonella}, and \textit{Streptococcus} species.\textsuperscript{B22,C10,M24,G10} Infected aneurysms may be multifocal.

**Mechanical** Aneurysmal changes can occur in the aorta distal to stenotic aortic valves and aortic coarctation and proximal to arteriovenous fistulae. Dilatation of the ascending aorta in patients with a bicuspid aortic valve and of the descending thoracic aorta in patients with aortic coarctation is more likely the result of structural abnormalities of the aortic wall rather than turbulent flow produced by the stenotic lesions.\textsuperscript{I10}

**Anastomotic** Aneurysms (usually of the false type) can develop at the site of aorta-to-aorta or aorta-to-graft anastomoses.

**False Aneurysm** False aneurysms are most commonly associated with trauma, infection, and previous operations on the aorta.

**Chronic Aortic Dissection** Morphologic features of acute aortic dissection, including classification, are discussed in Chapter 25. When the false lumen persists after an acute aortic dissection, as it usually
does, its outer wall, consisting of the outer layer of the media and the adventitia, has a tendency to weaken and enlarge. A saccular or fusiform aneurysm may result. Chronic aortic dissection with persisting false lumen is a common substrate for development of chronic thoracic or thoracoabdominal aneurysms.

**Penetrating Arteriosclerotic Ulcer**

Arteriosclerotic lesions involving the intimal layer of the aorta may ulcerate and penetrate the internal elastic lamina of the aortic wall (Fig. 26-1). Penetrating arteriosclerotic ulcers occur most commonly in the descending thoracic aorta.\(^{220,244}\) They can result in separation of the layers of the media and formation of intramural hematoma.\(^{315,317}\) Saccular and fusiform aneurysms may develop, and dissection, rupture, and embolization can occur.

**Intramural Hematoma**

Intramural hematoma can occur in the absence of an intimal tear and may result in dissection\(^{14,26,81}\) (Figs. 26-2 and 26-3). Rupture of an arteriosclerotic plaque and spontaneous rupture of vasa vasora have been postulated as mechanisms for development of the hematoma.\(^{26}\)

**Diffuse Arteriosclerotic Disease**

Sessile, mobile, or pedunculated atheroma is an important risk factor for stroke after operations that require cannulating and clamping the ascending aorta or aortic arch\(^{214,24,91,92}\) (Fig. 26-4). Severe arteriosclerosis of the ascending aorta, aortic arch, and descending thoracic aorta is also an important cause of embolic stroke and embolization to the abdominal organs and lower extremities in patients who do not undergo cardiac or thoracic surgical procedures.\(^{49,93}\) In some situations, the latter condition is amenable to surgical treatment.\(^{233,98,332}\)

**Prevalence**

During the first half of the 20th century, thoracic aneurysms were far more common than abdominal aneurysms because of the predominance of syphilitic aneurysms. In 1952, the ratio of thoracic to abdominal aortic aneurysms was 2:1 in autopsy studies.\(^{315}\) By 1964, this ratio had declined to less than 1:1, primarily as a result of the decline in syphilitic aneurysms.\(^{46}\) In a study from England and Wales that examined mortality statistics, the number of deaths resulting from thoracic aneurysms increased 17% between 1974 and 1984.\(^{55}\) This increase was substantially less than that for abdominal aneurysms (53%).

Prevalence of thoracic and thoracoabdominal aortic aneurysms is difficult to determine because of underreporting of these aneurysms in mortality statistics.\(^{63}\) Between 1958 and 1985 in Malmo, Sweden, which has a stable urban population and an autopsy prevalence of 83%, thoracic aortic aneurysms were found in 489 per 100,000 autopsies in men and 437 per 100,000 autopsies in women.\(^{823}\) Prevalence of asymptomatic thoracic aneurysms was about 400 per 100,000 autopsies in 65-year-olds and about 670 per 100,000 autopsies in 80-year-olds. In a study by Bickerstaff and colleagues in Rochester, Minnesota, the prevalence of thoracic aneurysms between 1951 and 1980 was 5.9 per 100,000 population per year.\(^{811}\) In a subsequent study from the same institution, prevalence of thoracic aneurysms between 1980 and 1994 had increased to 10.4 per 100,000 population per year.\(^{316}\) A study of the entire population of Sweden by Olsson and colleagues\(^{37}\) from 1987 to 2002 found the prevalence of thoracic aortic disease (nonruptured or ruptured thoracic aneurysm, acute or chronic aortic dissection) to be 10.7 per
100,000 per year for men and 7.1 per 100,000 per year for women in 1987. By 2002, the prevalence had increased to 16.3 per 100,000 per year for men and 9.1 per 100,000 per year for women. The number of operations on the thoracic aorta increased sevenfold over this interval for men and 15-fold for women.

Penetrating arteriosclerotic ulcer and intramural aortic hematoma without an intimal tear are being diagnosed with increasing frequency, primarily because of aging of the population and more frequent use of imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI). Among older patients who undergo cardiac surgical procedures, moderate or severe arteriosclerosis of the ascending aorta and aortic arch is present in approximately 15% to 20% of those older than 50 years and 33% of those 80 years of age or older.\textsuperscript{92}

**Location**

The true anatomic distribution of thoracic aortic aneurysms is not known with certainty. In 72 individuals with aneurysms, Bickerstaff and colleagues found that 37 (51%) involved the ascending aorta, 8 (11%) the aortic arch, and 27 (38%) the descending thoracic aorta.\textsuperscript{811} The cause was aortic dissection in 53%, degenerative disease in 29%, aortitis in 8%, cystic medial necrosis in 6%, and syphilis in 4%. Svensjo and colleagues found that thoracoabdominal aneurysms made up 5% of asymptomatic thoracic aneurysms.\textsuperscript{823}

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Symptoms**

Many patients with thoracic aortic aneurysms are asymptomatic at presentation, and the aneurysms are detected during testing for other disorders. Symptoms relating to the aneurysm usually develop later in the course of enlargement of the aorta and result from impingement of the aneurysm on
adjacent structures. Patients with aneurysms involving the ascending aorta associated with dilatation of the aortic anulus frequently present with symptoms referable to the aortic regurgitation that develops as a result of progressive aortic enlargement. Patients with aneurysms of the aortic arch may present with pain in the neck and jaw. Hoarseness results from stretching of the left recurrent laryngeal nerve, stridor from compression of the trachea, dysphagia from impingement on the lumen of the esophagus, dyspnea from compression of the lung parenchyma, and plethora and edema from compression of the superior vena cava. Patients with aneurysms of the descending thoracic aorta may report pain in the interscapular area or left-sided pleuritic pain. Aneurysms of the thoracoabdominal aorta may be associated with back pain, abdominal pain, and pain in the left shoulder resulting from irritation of the left hemidiaphragm.

Acute onset of severe pain in the anterior part of the chest or neck or between the shoulders is the typical presenting symptom of acute aortic dissection, although it may occur with rupture or sudden expansion of a chronic dissecting or nondissecting aneurysm (see Chapter 25). Acute chest pain may also result from a nondissecting intramural hematoma of the aorta or erosion of a penetrating arteriosclerotic ulcer into the surrounding tissues. Stroke or evidence of ischemia of the kidneys, abdominal viscera, and lower extremities may result from embolization of atheroma or thrombus from a severely arteriosclerotic aorta.

Signs
Direct physical signs of the presence of a thoracic aortic aneurysm are uncommon. In earlier times, a pulsating mass of the anterior chest was the first evidence of a syphilitic aneurysm of the ascending aorta; rarely, such an aneurysm eroded the sternum and ruptured, resulting in fatal hemorrhage. Signs of aortic regurgitation (bounding peripheral pulses, an aortic diastolic murmur) may be present in patients with large ascending aortic aneurysms that involve the aortic sinuses. A pulsatile mass in the upper abdomen may be present in patients with thoracoabdominal aortic aneurysms. Evidence for embolization of atheroma or thrombus from an aneurysm or from a severely arteriosclerotic aorta to the lower extremities (blue toe syndrome) may occasionally be the first indication of severe aortic disease.

Diagnostic Techniques
Chest Radiography
Findings on the chest radiograph may be diagnostic of a thoracic aortic aneurysm. Ascending aortic aneurysms produce a convex shadow to the right of the cardiac silhouette (Fig. 26-5), those of the arch an anterior and left-sided shadow (Fig. 26-6), and those of the descending aorta a shadow to the left and posteriorly (Fig. 26-7). However, approximately 17% of patients with documented aneurysms or dissections have no abnormalities on chest radiography.\(^{K3}\) Pooling data place the sensitivity of detecting a widened mediastinum or abnormal aortic contour in patients with aortic dissection at 64% and 71%, respectively.\(^ {K3}\) Substantial enlargement of the ascending aorta may be confined to the retrosternal area, so that the aortic silhouette appears normal. Aneurysms that involve the ascending aorta and aortic arch cannot always be differentiated from tumors or other masses.\(^ {C11,E1}\)

Computed Tomography
CT is the most widely used noninvasive technique for diagnosing thoracic aortic disease. It provides information about size, location, and extent of disease (Fig. 26-8). It is of particular value in documenting the growth rate of aneurysms, determining timing of operative intervention in asymptomatic patients, and evaluating patients postoperatively.\(^ {D5,G14,H11,T3}\) It is useful in identifying anatomic variants and branch vessel involvement, and provides three-dimensional (3D) data (Fig. 26-9). Because approximately 25% of patients have aneurysms in more than one area of the aorta, both the thoracic and the abdominal aorta should be examined.\(^ {B1,P10}\) CT is also useful for detecting intramural hematoma (see Fig. 26-2) and penetrating arteriosclerotic ulcers, and for determining severity and extent of thickening of the aortic wall in patients with severe aortic arteriosclerosis.\(^ {L11,C20,L14,N6}\) It is of particular value in diagnosing thoracic aortic dissection.\(^ {C37,P7}\) The principal disadvantage of CT is that it requires use of contrast medium for precise delineation of aortic disease, which may be contraindicated in patients with allergies to contrast agents or with renal insufficiency.

Radiation-induced malignancy in patients with thoracic aortic disease who require periodic CT imaging is a concern. Techniques to reduce radiation exposure (e.g., appropriate shielding, radiation dose reduction and management, algorithms to improve system efficiency) have been implemented to minimize this risk.\(^ {M10}\)

Magnetic Resonance Imaging
MRI is emerging as a premier imaging method for diagnosing diseases of the thoracic and thoracoabdominal aorta.\(^ {L11,M17}\) Standard techniques do not require contrast agents (Fig. 26-10, A). In certain applications, a single study can provide
information similar to that obtained from a combination of echocardiography, CT, and angiography. It provides excellent imaging of aortic dissections and can accurately identify thrombus formation and sites of entry.\textsuperscript{N4,N5} It can also differentiate periaortic hematoma from thrombosis of a false aneurysm. Breath-holding and 3D magnetic resonance angiography permit examination of the entire thoracic aorta, its major branches, the pericardium, the aortic valve, and the contractile pattern of the left ventricle.\textsuperscript{H5} Contrast-enhanced, time-resolved, 3D magnetic resonance angiography using agents such as gadolinium provide excellent images of the aorta and its major branches, comparable with those obtained by conventional aortography (Fig. 26-10, B).

Compared with CT, current disadvantages of MRI include a longer time to complete the study, greater cost, inaccessibility to patients who are connected to ventilators
and monitoring devices, contraindication in patients with metallic implants, pacemakers, and defibrillators, and limited availability. Use of MRI with a contrast agent (gadolinium compounds) is associated with a risk of nephrogenic systemic sclerosis.

**Transesophageal Echocardiography**

Transesophageal echocardiography (TEE) with Doppler color flow imaging is being used with increasing frequency for diagnosing thoracic aortic disease and caring for patients who undergo operations on the thoracic aorta. It is superior to transthoracic echocardiography for these purposes. It can be performed rapidly, with minimal morbidity, and has emerged as the most useful and accurate technique for diagnosing acute aortic dissection (see Chapter 25).

Before and during operations on the thoracic aorta, TEE is invaluable for assessing presence of arteriosclerosis, including mobile or pedunculated atheroma in the thoracic aorta, hemopericardium, malperfusion, competency of the aortic valve before CPB is established, and adequacy of reparative procedures on the valve. It also provides information about ventricular function and function of the mitral and tricuspid valves.

Disadvantages of TEE include lack of availability at small centers and during off hours, need for sedation, and occasionally endotracheal intubation.
Aortography
Aortography can be performed in patients who are to undergo elective operations on the thoracic aorta. It provides information about location of aneurysms, particularly in relation to major branches of the aorta in the chest and upper abdomen (Fig. 26-11). It also defines areas of relatively normal aorta proximal and distal to aneurysms. It can detect presence of aortic regurgitation. Selective injections of the coronary, brachiocephalic, visceral, and renal arteries provide important information that permits more accurate assessment of operative risk and may demonstrate need for modifications in operative technique.\(^{C8,3}\)

A disadvantage of aortography is that the size of large aneurysms may be underestimated because of the presence of thrombus. Other disadvantages include risk of allergic reactions after injection of contrast medium and risk of renal failure in patients with impaired renal function.\(^{N5}\) Multidetector CT has largely replaced angiography for anatomic studies that are required for treating and monitoring aortic disease.\(^{B5}\)

Epiaortic Ultrasonography
Intraoperative epiaortic ultrasound imaging of the ascending and descending thoracic aorta is useful for detecting arteriosclerosis. Presence of severe arteriosclerosis, including mobile or pedunculated atheroma, may necessitate alterations in surgical technique to avoid embolization of atheromatous debris to the brain and other organs during cardiac and thoracic aortic operations (see Fig. 26-4, A). Epiaortic imaging is more accurate than palpation of the aorta and, in comparative studies, more accurate than TEE for detecting atheromatous disease in the ascending aorta.\(^{D6, N8}\)

Preoperative Evaluation
Because myocardial infarction, respiratory failure, renal failure, and stroke are the principal causes of mortality and morbidity after operations on the thoracic aorta, preoperative assessment of the function of these organ systems is essential.\(^{K2,8,7, S7}\)

Cardiac Function
Because of the high prevalence of ischemic heart disease in older individuals, particularly those with degenerative aneurysms, assessment of cardiac function is necessary when elective operation is contemplated, especially for those with a history of myocardial infarction or angina pectoris and those older than 50 years. Patients with symptoms or electrocardiographic (ECG) changes indicative of myocardial ischemia should undergo stress testing and coronary angiography when indicated. Patients with valvar heart disease are evaluated with echocardiography and cardiac catheterization. Clinically important coronary artery disease should be treated with percutaneous catheter interventional techniques or bypass grafting, and valvar heart disease by valve repair or replacement before or, in some cases, at the time of the procedure on the thoracic aorta.

Pulmonary Function
History of smoking and presence of chronic pulmonary disease are important predictors of respiratory failure, and they are frequently present in patients who require operations on the descending thoracic and thoracoabdominal aorta.\(^{C2, K23, S7}\) Pulmonary function tests should be performed in patients with these risk factors. Spirometric tests and arterial blood gas analysis should be performed in patients with chronic pulmonary disease.\(^{C2}\) If reversible restrictive disease or excessive sputum production is present, antibiotics and bronchodilators should be administered preoperatively. Cessation of smoking is advisable.
Rupture is often preceded by symptoms. Bickerstaff and colleagues reported that once symptoms developed, the mean time to rupture was 2 years.111 Medical treatment is of limited value in managing thoracic aneurysms. Control of systemic hypertension, when present, is important to reduce wall stress even though no clear correlation between expansion rate of thoracic aneurysms and presence of hypertension has been demonstrated.154 Hypertension is a risk factor for aortic enlargement and need for reoperation after repair of type A aortic dissection, however.21 Administration of β-adrenergic blocking agents decreases progression of aortic dilatation in Marfan syndrome patients and may slow the rate of aortic dilatation in those with chronic aortic dissection in the absence of this syndrome.13 Angiotensin receptor blockers and angiotensin-converting enzyme inhibitors may slow the growth rate of aneurysms in patients with Marfan syndrome.226 Whether these agents can similarly affect other diseases of the aorta is unknown. Although statin therapy has been associated with decreased long-term mortality in patients with abdominal aortic aneurysms, no similar effect has been observed in patients with thoracic aneurysms.138 No prospective trials have demonstrated a beneficial effect of cessation of smoking on rates of progression of thoracic aortic disease.

Other Conditions

The natural history of penetrating arteriosclerotic ulcers is variable. In the largest reported series, the majority of ulcers detected by CT imaging were not associated with symptoms and remained stable or regressed.155,221 A small percentage progressively enlarged, with formation of saccular aneurysms. Intramural hematoma, dissection, embolization, and rupture can also occur.134,221

Intramural hematoma is a dynamic entity that may regress, expand, or progress to aortic dissection. Its natural history varies according to location of the hematoma in the thoracic

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**Figure 26-12** Survival of patients with thoracic aortic aneurysms (TAA; n = 57), thoracoabdominal aortic aneurysms (T-AAA; n = 53), and abdominal aortic aneurysms (AAA; n = 60) who did not undergo operative treatment. (From Perko and colleagues.96)
aorta and geographic location. A higher prevalence of dissection and death has been observed among patients with hematomas in the ascending aorta and arch than in those with hematomas in the descending aorta.52,57,58 The experience from Asia suggests more frequent resolution of the hematomas with conservative management than that reported from Western countries.56

Patients with severe arteriosclerotic plaques (>4 mm in thickness) involving the ascending aorta and aortic arch have a high prevalence of atheromatous emboli in the cerebral circulation.81,14 These emboli are probably a major cause of cerebral infarction.10,18,14 Patients with severe ascending aortic arteriosclerosis are at risk for embolization and stroke after manipulation of the ascending aorta during coronary artery bypass grafting and other cardiac surgical procedures.14,75,91,92 When severe atheromatous disease is present in the distal aortic arch and descending thoracic aorta, embolization to the visceral, renal, and peripheral arteries may occur.

Among patients with the conditions just described, death due to coexisting cardiovascular disease is common.

**TECHNIQUE OF OPERATION**

**Preparations for Thoracic and Thoracoabdominal Aortic Surgery**

After anesthesia induction, venous access is obtained with a large-bore central catheter and several large peripheral catheters. A radial arterial catheter is inserted for monitoring blood pressure and withdrawing blood samples. This is placed in the left radial artery in patients with ascending aortic and proximal arch disease, and in the right radial artery in patients with descending thoracic or thoracoabdominal aortic disease. If chronic aortic dissection is present and the potential for malperfusion exists (see “Malperfusion Syndromes” under Special Situations and Controversies in Chapter 25), a second arterial catheter is placed in a femoral artery or the opposite radial artery. If entrance into the left chest after a median sternotomy is anticipated, or if a lateral thoracotomy or thoracoabdominal incision is used, a double-lumen endotracheal tube is inserted. Alternatively, an occlusive balloon can be placed through a single-lumen endotracheal tube. Leads II and V5 of the ECG are continuously monitored. A pulmonary artery catheter is placed to measure pulmonary artery pressure, oxygen saturation, and cardiac output. Thermistor probes are placed for measuring nasopharyngeal and bladder temperature. If an interval of hypothermic circulatory arrest is planned, electroencephalographic monitoring is also necessary, and monitoring of cerebral oxygen saturation is advisable. Cerebrospinal fluid drainage is performed in patients with extensive descending thoracic aortic disease and thoracoabdominal aneurysms.84 TEE is performed intraoperatively to assess function of the cardiac valves, size of the aorta, and type and extent of aortic disease, and to monitor myocardial function.82,83

**Ascending Aorta Replacement**

**Aneurysm**

The aneurysmal segment of the ascending aorta is excised and replaced with a tube graft. When the aortic valve is diseased and requires repair or replacement, the techniques are those described under Technique of Operation in Chapter 12. A full median sternotomy or a partial upper sternotomy is used. If the aneurysm does not involve the distal ascending aorta or proximal aortic arch, these sites can be used for cannulation (Fig. 26-13, A). If this is not possible, the common femoral artery or axillary artery may be used for arterial return from the pump-oxygenator.51 A single two-stage venous cannula is inserted into the right atrium. After CPB is established, a venting catheter is inserted through the right superior pulmonary vein, although this is not always necessary. A balloon-tipped catheter is inserted into the right atrium and positioned in the coronary sinus for delivery of retrograde cardioplegia (see Fig. 26-13, A). Moderate hemodilution (hematocrit 20%-30%) and moderate systemic hypothermia (28°C-32°C) are used.

A standard approach involves replacing the ascending aorta from the level of the aortic commissures to just proximal to the brachiocephalic artery. The aorta is clamped proximal to the origin of the brachiocephalic artery. Cardioplegic solution is administered into the aortic segment proximal to the aortic clamp if there is no aortic regurgitation. Alternatively, it can be infused directly into the coronary arteries after the aorta is incised (see Chapter 3).

The aorta is completely transected just proximal to the aortic clamp and just above the commissures of the aortic valve (Fig. 26-13, B). A collagen- or gelatin-impregnated (prepared) woven polyester tube graft of appropriate size is sutured to the distal aorta with a continuous 3-0 or 4-0 polypropylene suture incorporating a 4- to 5-mm strip of polytetrafluoroethylene (PTFE) felt (Fig. 26-13, C). Use of the PTFE felt is not essential, but is of value in minimizing blood loss when the aorta is thin. If aortic valve replacement or repair is necessary, this is performed (Fig. 26-13, D and E). The aortic graft is then cut to the appropriate length and sutured to the proximal aorta with a 3-0 or 4-0 polypropylene suture incorporating a strip of PTFE felt (Fig. 26-13, F). If there is appreciable cephalad displacement of the ostium of the right coronary artery, an opening is created in the graft with a wire cautery, the artery is detached from the aorta with a cuff of aortic tissue and sutured to the graft with a 4-0 or 5-0 polypropylene suture incorporating a small strip of PTFE felt.

As the proximal aortic suture line is being completed, suction on the intracardiac vent is discontinued, warm blood cardioplegic solution is administered through the coronary sinus catheter, and CPB flow is reduced to permit filling of the heart and the aortic graft with blood. The lungs are temporarily inflated to facilitate removal of air. A venting needle or catheter is inserted into the graft through a small stab incision and secured with a pledged suture and a tourniquet (Fig. 26-13, F). After the suture line is completed, controlled aortic root reperfusion can be performed (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). Standard de-airing procedures are carried out, CPB is discontinued, and the cannulae are removed (Fig. 26-13, G).

If coronary artery disease that requires bypass grafting is present, anastomoses of grafts to the coronary arteries are performed after infusion of cardioplegic solution. During rewarming, the proximal ends of the bypass grafts are sutured to the aortic graft with 5-0 or 6-0 polypropylene suture after openings in the graft are made with a wire cautery (Fig. 26-13, H).
Other Conditions
Penetrating arteriosclerotic ulcers that result in formation of saccular or fusiform aneurysms in the ascending aorta are treated by resecting the involved segment and replacing it with a polyester graft using the technique described in the preceding text. Managing patients with intramural hematoma involving the ascending aorta is similar to managing patients with ascending aortic dissection (see “Repair of Acute DeBakey Type I or II [Type A] Dissection” in Chapter 25). Severe diffuse arteriosclerosis or mobile atheroma involving the ascending aorta that is encountered during coronary artery bypass grafting or valve replacement can be managed by resection and graft replacement or by endarterectomy. Surgical management of mycotic aneurysms, false aneurysms, and infected grafts is discussed under Special Situations and Controversies later in this chapter.

Figure 26-13  Ascending aorta replacement. A, After cardiopulmonary bypass is established and venting and cardioplegia catheters have been inserted, aorta is clamped just proximal to origin of brachiocephalic artery. B, Aorta is transected just proximal to aortic clamp and just above commissures of aortic valve.
Alternative to Replacement

Resection of a portion of the dilated ascending aorta and closure of the aortotomy longitudinally, with or without external reinforcement (usually with a synthetic graft), is an alternative to resection and graft replacement when the aorta is less than 6 cm in diameter. Rupture of the aorta following aortoplasty has been reported both with and without external reinforcement. B4,D16,R4 Atrophy of the aortic wall beneath an external wrap has also been observed. B4,N1

Aortic Arch Replacement

Although aortic disease can be confined to the aortic arch (segment of the thoracic aorta that extends from the proximal origin of the brachiocephalic artery to the distal origin of the
left subclavian artery), most aneurysms in this area are associated with aneurysmal disease of the ascending aorta or the adjacent descending thoracic aorta. In rare circumstances, the aneurysm may be localized to a discrete area of the arch with a small opening into the aneurysm from the aortic lumen. Excising the aneurysm and closing the defect in the aortic wall with a synthetic patch may be possible.

Hypothermic circulatory arrest is the most widely used technique for protecting the brain during operations on the aortic arch. The technique is described in “Clinical Methodology of Hypothermic Circulatory Arrest” in Section IV of Chapter 2. Alternative techniques are discussed in “Brain Protection during Operations on the Aortic Arch” under Special Situations and Controversies later in this chapter.

Figure 26-13, cont’d  
E, Aortic valve is replaced when necessary with a mechanical or biological valve. F, Aortic graft is cut to appropriate length and sutured to proximal aorta with continuous 3-0 or 4-0 polypropylene suture incorporating a strip of PTFE felt.
Because of the increased risk of dislodging and embolizing atheromatous material from retrograde perfusion associated with femoral artery cannulation, axillary artery cannulation is used with increasing frequency for operations that involve the aortic arch. Alternative sites for establishing return of arterial blood from the pump-oxygenator include the ascending aorta, brachiocephalic artery, and carotid artery. Separate cannulae are placed in the superior and inferior venae cavae for venous return to the CPB circuit (Fig. 26-14, A). Cooling is initiated immediately after CPB is established, and a venting catheter is inserted into the left ventricle through the right superior pulmonary vein. A balloon-tipped catheter is inserted in the right atrium and positioned in the coronary sinus for delivery of retrograde cardioplegia. The superior vena cava is encircled with a tape that is secured around the cava and the cannula with a tourniquet (see Fig. 26-14, A). The ascending aorta is clamped if possible, and if the aortic valve is competent, cardioplegic solution is infused into the aortic root. If the aortic root is opened, cardioplegic solution can be infused directly into the coronary arteries. If coronary artery bypass grafting is required, anastomoses of grafts to the coronary arteries are performed during cooling.

Nasopharyngeal, bladder, and perfusate temperatures are continuously monitored. Temperature gradients between the water bath of the heat exchanger in the CPB circuit and the blood, and between the blood and the tissues, are maintained below 12°C. Hematocrit is maintained between 15% and 20%. During cooling, methylprednisolone (7 mg · kg⁻¹) and...
Figure 26-14  Partial replacement of aortic arch. A, After separate cannulation of superior and inferior venae cavae (SVC, IVC) and placement of venting and cardioplegia catheters, superior vena cava is encircled with a tape. Dashed line indicates line of incision in ascending aorta and aortic arch. B, If only proximal arch replacement is necessary, aorta is transected obliquely beneath brachiocephalic vessels. Dashed line indicates line of incision.

Continued
Prepared polyester graft is cut at appropriate angle with a wire cautery. If bevel of aorta is relatively short, graft is sutured to aorta so that it is aligned vertically with respect to aortic arch, using 3-0 or 4-0 polypropylene suture incorporating a strip of polytetrafluoroethylene felt. If aortic bevel is long, graft is beveled in reverse direction and sutured to aorta in a more horizontal position (inset).

Figure 26-14, cont'd

Thiopental (10-15 mg · kg$^{-1}$) are administered to enhance the neuroprotective effect of hypothermia.$^{12,12}$ Mannitol (0.3-0.4 g · kg$^{-1}$) and furosemide (20-60 mg) are infused to preserve renal function.$^{35}$

Continuous electroencephalographic monitoring is used, and the head is packed in ice. Because hyperglycemia is associated with an increased prevalence of central nervous system dysfunction following hypothermic circulatory arrest, blood glucose levels are monitored, and insulin is administered intravenously to maintain the blood glucose level below 140 mg · dL$^{-1}$.$^{18}$

When nasopharyngeal temperature reaches 12°C to 14°C, bladder temperature reaches 15°C to 18°C, and the electroencephalogram becomes isoelectric, circulatory arrest can be
The patient is placed in Trendelenburg position, the superior vena caval cannula is occluded (to distend the venous system of the upper body so that air will not be sucked into the brachiocephalic arteries when the aorta is opened), and perfusion from the CPB circuit is discontinued. From 20% to 25% of the patient’s calculated blood volume is withdrawn from the venous line into the reservoir of the oxygenator. The clamp is removed from the ascending aorta. If hypothermic circulatory arrest is the sole means of brain protection (in addition to the agents noted previously), no clamps are placed on the distal aorta or brachiocephalic arteries.

After circulatory arrest is established, the ascending aorta is opened (dashed line, Fig. 26-14, A) and the incision is extended beneath the brachiocephalic arteries. The extent of aortic disease is assessed (Fig. 26-14, B). Aneurysms of the aortic arch vary in size and extent, and techniques of repair vary.

**Partial Arch Replacement**

If the aneurysm involves only the proximal portion of the arch (often the disease is contiguous with disease in the ascending aorta), a single anastomosis between the tube graft and the distal aorta can be performed by beveling the incision in the aorta beneath the brachiocephalic arteries (see Fig. 26-14, B). A prepared polyester graft of appropriate size is correspondingly beveled and sutured to the distal aorta with a continuous 3-0 or 4-0 polypropylene suture incorporating a 3- to 4-mm strip of PTFE felt (Fig. 26-14, C and D). As the suture line is being completed on the anterior aspect, a shunt from the arterial line of the perfusion circuit is opened to the venous line, the inferior vena caval cannula is occluded with a clamp, and cold (18°C-20°C) oxygenated blood is infused into the superior vena caval cannula at a flow rate of 350 to 500 mL · min⁻¹ (Fig. 26-14, E). The jugular venous pressure is monitored and should not exceed 30 to 35 mm Hg. Flow is continued until the suture line is completed. This maneuver removes air and particulate matter from the brachiocephalic arteries. Flow through the arterial line from the pump-oxygenator (femoral or axillary) is reestablished, and air is evacuated from the distal aorta. The aortic graft is gently massaged to facilitate evacuating any remaining air, a clamp is placed across the graft close to the brachiocephalic artery, and CPB is reestablished (Fig. 26-14, F). If the femoral artery has been cannulated, dislodging atheromatous debris into the lumen of the aorta is a concern. Therefore, a perfusion cannula is inserted into the aortic graft through a stab wound and secured, the arterial line from the pump-oxygenator is disconnected from the femoral artery cannula and connected to this cannula, air is evacuated from the graft, the clamp is applied, and flow is established in the antegrade direction. This maneuver substantially reduces the possibility of embolizing atheromatous debris into the brachiocephalic arteries and embolic stroke.

Rewarming is accomplished using temperature gradients of 12°C or less between the water bath of the heat exchanger and the blood, and between the blood and the tissues. The perfusate flow is gradually increased to a maximum of 2.4 to 2.6 L · min⁻¹ · m⁻². During rewarming, the aortic graft is anastomosed to the proximal ascending aorta. If aortic valve or aortic root replacement is required, it is performed at this time (see Fig. 26-13, D and E). If coronary artery bypass grafting has been performed, the grafts are sutured to the aortic graft (see Fig. 26-13, H). Procedures for evacuating air and reperfusing the myocardium are identical to those described previously under “Ascending Aorta Replacement.” When bladder temperature reaches 36°C, CPB is discontinued and the cannulae are removed.

**Total Arch Replacement**

If the aneurysm involves the entire aortic arch, the aorta is completely transected distal to the left subclavian artery. During cooling, the left phrenic and left vagus nerves are identified and protected by gentle dissection away from the anterior and posterior surface of the aorta. A prepared polyester graft is sutured to the ascending aorta with a 3-0 or 4-0 continuous polypropylene suture incorporating a strip of PTFE felt (Fig. 26-15, A). If chronic dissection is present, a portion of the septum between the true and false lumens of the descending thoracic aorta is excised and the graft sutured circumferentially to the outer wall of the aorta. This permits antegrade perfusion of both lumens. The origins of the

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**Figure 26-14, cont’d**

**E.** Cold oxygenated blood from pump-oxygenator is infused into superior vena cava to remove air and particulate matter from brachiocephalic arteries. If femoral artery has been cannulated, flow from pump-oxygenator is also initiated to evacuate air from distal aorta. **F.** Aortic graft is clamped, and cardiopulmonary bypass is reestablished.
Figure 26-15  Total aortic arch replacement. A, After circulatory arrest is established, aorta is transected distal to left subclavian artery (LSA). Aortic graft is sutured to descending thoracic aorta (DTA) with continuous 3-0 or 4-0 polypropylene suture incorporating a strip of polytetrafluoroethylene (PTFE) felt. Origins of brachiocephalic arteries are separated from diseased aorta with a small cuff of aortic tissue. B, Aortic graft is placed under tension, and an oval segment is excised with a wire cautery. Graft is sutured to cuff of aorta with continuous 3-0 or 4-0 polypropylene suture incorporating a strip of PTFE felt. Alternatively, the three brachiocephalic arteries can be individually transected, and separate prepared polyester grafts can be sutured to the arteries and to openings in aortic graft (inset).
brachiocephalic arteries are separated from the aneurysm with a small cuff of aortic tissue (see Fig. 26-15, A). If the layers of the aorta are separated in this area as a result of dissection, they are approximated. The graft is placed under tension, and an oval segment corresponding to the size of the aortic cuff is excised with a wire cautery. The graft is sutured to the cuff of aorta with a continuous 3-0 or 4-0 polypropylene suture incorporating a strip of PTFE felt (Fig. 26-15, B). Alternatively, the three brachiocephalic arteries can be individually transected, and separate polyester grafts can be sutured to these arteries and to openings in the aortic graft (see Fig. 26-15, B [inset]). Commercially prepared aortic grafts containing presewn branches are available and eliminate the need for the graft-to-graft anastomoses shown in the Fig. 26-15 inset. As the single suture line or the last branch anastomosis is being completed, retrograde brain perfusion is initiated, and the procedure is completed as described in the preceding text on partial arch replacement (Fig. 26-15, C-D).

If a prolonged period of circulatory arrest is contemplated, the brachiocephalic arteries can be perfused directly or they can be separately clamped, with perfusion of the brain occurring from the cannulated axillary artery (see “Antegrade Brain Perfusion” under Special Situations and Controversies later in this chapter).

**Elephant Trunk Technique**

When the aneurysm involves more than just the very proximal descending thoracic aorta, a two-stage procedure may be considered. Borst and colleagues introduced a useful technique for performing the first stage, the “elephant trunk” procedure. An important modification was introduced by Crawford and colleagues, whose technique is shown in Fig. 26-16. After establishing hypothermic circulatory arrest, the aorta is completely transected just beyond the origin of the left subclavian artery, and a cuff of aorta is fashioned around the brachiocephalic arteries (Fig. 26-16, A). The left phrenic and left vagus nerves are identified and protected. A polyester tube graft slightly smaller in diameter than the transected aorta is selected. Its length should be 5 to 8 cm (the length of the segment that will be positioned in the descending thoracic aorta) plus an amount sufficient for attachment to the aortic arch and to part or all of the ascending aorta. A stay suture is placed at the proximal (ascending aortic) end of the graft and secured with a clamp (Fig. 26-16, B). The proximal end of the graft is then inverted into the distal 5- to 8-cm segment that will be positioned in the descending thoracic aorta (see Fig. 26-16, B). The entire graft is inserted into the descending thoracic aorta (Fig. 26-16, C). The stay suture permits easy withdrawal of the inverted segment after anastomosis of the graft to the transected aorta is completed. If chronic dissection is present in the descending thoracic aorta, the septum between the true and false lumens is excised to permit full expansion of the segment of graft that will remain in the descending thoracic aorta. This segment of graft is kept relatively short to avoid compromising the lower intercostal arteries and development of paraplegia or paraparesis. The aorta is sutured to the double-layer edge of the aortic graft with a continuous 3-0 polypropylene suture. If the aorta is thin or dissected, this suture line can be reinforced with a strip of PTFE felt placed around the outside of the aorta (see Fig. 26-16, C). The invaginated portion of the graft is then...
withdrawn from the descending thoracic aorta by traction on the stay suture (Fig. 26-16, D). The procedure is then completed as just described under “Total Arch Replacement.” It is essential that aortic flow be reestablished in the antegrade direction following the interval of circulatory arrest to avoid malperfusion of the brachiocephalic and coronary arteries. This can result from resumption of retrograde aortic flow from the femoral artery cannula and compression of the elephant trunk. For this reason, an aortic cannula is inserted into the aortic graft beneath the anastomosis to the brachiocephalic arteries and connected to the arterial line of the pump-oxygenator. Alternatively, an 8- or 10-mm prepared graft can be sutured to the aortic graft and connected to the arterial line. Use of the right axillary artery for arterial return obviates the need for these maneuvers.

Arch First Technique
In some situations, a staged procedure may not be feasible or safe. Extensive thoracic aortic disease, particularly when there is marked (>4.5 cm) dilatation of the aorta just distal
Entire graft is positioned into DTA, and aorta is sutured to doubled-over edge of aortic graft with continuous 3-0 polypropylene suture incorporating a strip of polytetrafluoroethylene felt. Invaginated portion of graft is then withdrawn from DTA by traction on stay suture. Procedure is completed as shown in Fig. 26-15, B through D. It is necessary, however, to reestablish aortic flow in antegrade direction to avoid compression of the elephant trunk and malperfusion of brachiocephalic and coronary arteries (see text).

Key: BR, Brachiocephalic artery; LCA, left carotid artery.
intercostal space, combined with anastomosis of the graft to the brachiocephalic arteries first, facilitates exposure and minimizes duration of circulatory arrest. This approach also permits satisfactory exposure of the aortic root and provides access to the mitral valve and coronary arteries.\(^{21,16,87}\) It may be of particular value in patients with chronic type A aortic dissection who require reoperation.\(^{21,22}\)

After inserting the appropriate monitoring devices and cannulae for vascular access and a double-lumen endotracheal tube, the patient is placed in the supine position with the left hemithorax rotated 20 to 30 degrees to the right. The right arm is secured around the head, and the left arm is positioned over the head (Fig. 26-17, A [inset]). Bilateral submammary anterior thoracotomy incisions are made in the fourth intercostal space, with the left incision extending laterally to the midaxillary line and the right to the anterior axillary line. The left lung is collapsed. Both internal thoracic vascular pedicles are ligated and divided, and the sternum is divided transversely. The pericardium is incised over the aorta and over the right atrium, but only enough to permit separate cannulation of the superior and inferior venae cavae, insertion of a venting catheter through the right superior pulmonary vein, and placement of a cannula in the coronary sinus for delivery of cardioplegic solution (see Fig. 26-17, A). A tape is placed around the superior vena cava. Arterial return is established through a common femoral artery or the right axillary artery.

CPB is established, and cooling is initiated. Exposure of the ascending aorta, aortic arch, and descending thoracic aorta is obtained. Left phrenic and left vagus nerves are identified and protected (Fig. 26-17, B). The left inferior pulmonary ligament is divided. When the heart fibrillates, the ascending aorta is clamped. If there is no aortic regurgitation, cardioplegic solution is administered through a needle into the aortic root at 12- to 15-minute intervals. If clamping of the aorta is not possible, retrograde cardioplegia is used; it is administered as soon as the ascending aorta is opened after circulatory arrest has been established, and every 12 to 15 minutes thereafter. This may be supplemented by direct perfusion of the coronary arteries. When coronary artery bypass grafting is required, distal anastomoses are performed during cooling. Aortic valve or aortic root replacement or reconstruction can be performed at this time, if indicated. Circulatory arrest is established when the appropriate temperatures are reached and the electroencephalogram becomes isoelectric (see “Aortic Arch Replacement”). The patient’s head is packed in ice and placed in a dependent position. The tape around the superior vena cava is secured, the superior vena cava cannula is clamped to distend the veins of the upper body and avoid suctioning of air into the opened aorta, and 20% to 25% of the calculated blood volume of the patient is drained from the inferior vena cava cannula into the venous reservoir of the bypass circuit. A clamp is placed on the distal descending thoracic aorta to minimize blood loss into the operative field when the aorta is opened and to permit perfusion of the lower body and lower intercostal arteries.

The ascending aorta is incised and transected proximally. Origins of the brachiocephalic arteries are separated from the aneurysm with a small cuff of aortic tissue. The descending aorta is incised distal to the arch (see Fig. 26-17, B). A prepared tube graft to which a 10-mm limb is attached is passed into the opened arch beneath the pedicle containing the left phrenic and vagus nerves, and into the opened descending aorta (Fig. 26-17, C). The 10-mm graft is positioned opposite the site where anastomosis of the aortic graft to the brachiocephalic arteries will be performed. An opening is made in the aortic graft with a wire cautery at the site of the arch vessels, and the cuff of aorta surrounding them is sutured to the graft (see Fig. 26-17, C). All aortic anastomoses are constructed with a continuous 3-0 or 4-0 polypropylene suture buttressed with a strip of PTFE felt.

As anastomosis to the arch vessels is being completed, cold (18°C-20°C) oxygenated blood is infused into the superior vena cava cannula to evacuate air and atheromatous debris (see “Partial Arch Replacement”). The aortic graft is clamped just distal to the arch anastomosis with a long, straight atraumatic vascular clamp, and the proximal portion of the graft is allowed to fill with blood. A second arterial line from the pump-oxygenator is attached to the 10-mm graft, and flow is initiated to evacuate air from the proximal segment of the graft. If the axillary artery was used for arterial return, flow is initiated through this vessel rather than the 10-mm graft. Retrograde perfusion through the superior vena cava cannula is discontinued, and the aortic graft is clamped proximal to the aortic arch with a large straight or angled vascular clamp. Antegrade perfusion into the brachiocephalic arteries is then established at a flow of 800 to 1200 mL · min\(^{-1}\) at a temperature of 20°C (Fig. 26-17, D).

An alternative technique involves use of a branched graft and separate suture of the three brachiocephalic arteries to branches of the graft (see Fig. 26-15, B [inset]). Right axillary artery perfusion is used, and after establishing circulatory arrest, the three arteries are transected at their origins from the aorta. They are flushed by a brief period of perfusion from the axillary artery to evacuate air and are occluded separately with clamps. Flow to the brain is established through the axillary artery (10-15 mL · kg\(^{-1}\) · min\(^{-1}\) at a temperature of 20°C to 22°C. The brachiocephalic arteries are then sequentially attached to the branches of the aortic graft, beginning with the left subclavian artery. When these anastomoses are completed, the aortic graft is clamped just distal to the left subclavian branch, the clamps on the brachiocephalic arteries are released, and after evacuation of air from the aortic graft, it is clamped just proximal to the brachiocephalic artery. Flow to the brain is then established in the antegrade direction through the three brachiocephalic arteries.

During hypothermic low flow to the upper body with either of the techniques described in the previous text, the distal clamp on the descending aorta is removed and the aorta is transected at the appropriate level (see Fig. 26-17, D). The aorta is beveled whenever possible to preserve the origins of the intercostal arteries below the sixth intercostal space. In the presence of chronic dissection, a large segment of the septum between the true and false lumens is removed to permit perfusion of both. The graft is cut to the appropriate length and sutured to the distal aorta (see Fig. 26-17, D and E). As this anastomosis is being completed, perfusion through the femoral arterial line (if present) is initiated to remove air and debris. After the anastomosis is completed, air is removed from the graft through several puncture holes created by an 18-gauge needle. The clamp on the aortic graft distal to the left subclavian artery is released, flow from the femoral arterial line is discontinued, and antegrade flow is established through the 10-mm graft or the axillary artery (see Fig. 26-17, E). Rewarming is begun at this time. The excluded, patent upper intercostal and bronchial arteries are ligated.
Figure 26-17  Arch first technique. A, [Inset] Patient is positioned supine with left chest elevated 20 to 30 degrees. Chest cavity is entered through a bilateral anterior thoracotomy incision in fourth intercostal space (dashed line). Bicaval cannulation is used, and superior vena cava (SVC) is encircled with a tape. Left phrenic and vagus nerves are mobilized and protected. B, After circulatory arrest is established, clamp is placed on proximal ascending aorta and distal descending aorta to minimize blood loss. Ascending aorta is incised and resected, and a cuff of aortic tissue containing brachiocephalic arteries is prepared.

Continued
Opening is made in aortic graft, and aortic tissue surrounding brachiocephalic arteries is sutured to graft with a continuous 3-0 or 4-0 polypropylene suture buttressed with a strip of polytetrafluoroethylene felt. A 10-mm prepared graft has been sutured to aortic graft opposite brachiocephalic arteries. After completing retrograde brain perfusion (see text) and evacuating air from brachiocephalic arteries and aortic graft, clamps are placed on graft just proximal and distal to arch anastomosis, and antegrade perfusion of arch vessels with cold blood is initiated. Clamp on distal descending aorta is removed, and open anastomosis of graft to distal descending aorta is performed.

The proximal end of the aortic graft is sutured to the ascending aorta or to an existing ascending aortic graft (see Fig. 26-17, E). Aortic valve or aortic root replacement, if indicated, can be completed during this time. If saphenous vein bypass grafts were placed, they are anastomosed to the aortic graft. The remaining clamp on the aortic graft is removed, and a needle vent is placed in the proximal portion of the graft and connected to suction. Procedures for reperfusion of the myocardium and evacuation of air are identical to those described under “Replacement of the Ascending
the top of the nonresected fifth rib. If the entire descending thoracic aorta is involved, a longer incision is made, curving slightly inferiorly at the anterior portion, and the pleural space is entered through the top of the nonresected sixth rib. Exposure can be enhanced by dividing the sixth rib or the fifth rib posteriorly. If the distal clamp must be placed at or near the diaphragm, a second entrance into the pleural space can be made through the top of the bed of the nonresected eighth rib. Alternatively, the costal margin can be divided. This will substantially enlarge the single opening into the chest, exposing the entire descending thoracic aorta.

The procedure varies according to location and extent of aortic disease. A limited dissection is performed around the aorta just proximal and distal to the diseased segment to permit placement of clamps. If the aortic disease begins at or
Figure 26-18 Descending thoracic aorta replacement. 

A, Patient is positioned in right lateral decubitus position with left hip rotated posteriorly to permit access to left femoral artery and vein. Left pleural space is entered through fourth or fifth intercostal space (dashed line). 

B, Left femoral artery (LFA) is cannulated. If femoral vein–to–femoral artery bypass is used, left femoral vein (LFV) is also cannulated. If left heart bypass is used, femoral artery and left atrial appendage or left inferior pulmonary vein are cannulated. Clamps are placed on aorta proximal and distal to site of entry into aneurysm. 

C, Aorta is opened between clamps and transected proximally (dashed line).
near the origin of the left subclavian artery, mobilizing the aortic arch between origins of the left common carotid and left subclavian arteries is required. The parietal pleura is incised between the left phrenic and left vagus nerves, and the aorta is isolated circumferentially. The left vagus and left recurrent laryngeal nerves are identified and protected. Access to the more proximal aorta can be improved by opening the pericardium, particularly if an aortic cannula is to be inserted proximal to the clamp site. Appropriate clamps are selected. The segment of aorta that is replaced should be no longer than necessary to avoid sacrificing patent intercostal arteries.

A suitable technique for protecting the spinal cord during aortic clamping is selected and implemented (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24). A prepared polyester tube graft of the proper size is chosen. The proximal aortic clamp and, when necessary, a left subclavian arterial clamp are placed (Fig. 26-18, B). When distal aortic perfusion is used, the distal aortic clamp is initially placed as close as possible to the
If intercostal arteries below sixth or seventh intercostal space are patent, they are excised from aorta along with a small cuff of aortic tissue, using a wire cautery (inset). Opening is made in graft, and aortic cuff is sutured to graft with continuous 3-0 or 4-0 polypropylene suture. Clamp on graft is repositioned below intercostal pedicle to permit perfusion of intercostal arteries. Graft is sutured to aorta with continuous 3-0 or 4-0 polypropylene suture buttressed with a strip of PTFE felt. Key: BR, Brachiocephalic artery; LCA, left carotid artery; LSA, left subclavian artery.

Figure 26-18, cont’d.
proximal clamp to permit perfusion of as many of the intercostal arteries as possible. The aorta is opened between the clamps and is transected proximally (Fig. 26-18, C). The patent intercostal and bronchial arteries in the aortic segment that will be excluded are ligated (Fig. 26-18, D). The graft is sutured to the proximal aorta with a continuous 3-0 or 4-0 polypropylene suture buttressed with a strip of PTFE felt. If the left subclavian artery has been occluded, the proximal aortic clamp is repositioned onto the aortic graft to permit early perfusion of the left subclavian artery (Fig. 26-18, E). After this anastomosis is completed, the distal clamp can be repositioned at a lower level if necessary, and the aorta opened longitudinally. Location and patency of intercostal arteries, particularly those below the sixth or seventh intercostal space, are determined. The distal aorta is transected obliquely whenever possible, to permit preservation of the lower patent intercostal arteries. The aortic graft is beveled appropriately and sutured to the aorta. If an oblique incision is not possible, the lower intercostal arteries are detached from the aorta with a small, full-thickness cuff of adjacent aorta using the electrocautery (Fig. 26-18, F). The aortic graft is stretched, and a segment opposite the intercostal artery pedicle is excised with a wire cautery. The aortic cuff is sutured to the graft with a continuous 3-0 or 4-0 polypropylene suture. The graft is flushed to remove air by removing the proximal clamp. This clamp is then repositioned below the pedicle to permit perfusion of the intercostal arteries (Fig. 26-18, G). The distal aorta is transected at the appropriate level, and the graft is sutured to the aorta with a continuous 3-0 or 4-0 polypropylene suture buttressed with a strip of PTFE felt. If distal perfusion is used, the distal aortic clamp is briefly removed to assist in evacuating air from the graft and to assess integrity of the anastomosis. Distal flow is then discontinued.

If partial or total CPB is used, it is discontinued, protamine is administered, and the central and peripheral cannulae are removed. Two intercostal drainage catheters are placed, one posteriorly and inferiorly and one anteriorly at the apex of the pleural cavity. The incision is closed.

If the location and severity of aortic disease are such that clamps cannot be safely placed on the aorta, particularly in the area of the distal aortic arch, the procedure is performed using hypothermic CPB and circulatory arrest without placing clamps on the proximal aorta (see “Technique Using Hypothermic Circulatory Arrest” in later text).

**Thoracoabdominal Aorta Replacement**

After standard preparations are completed, the patient is positioned in the right lateral decubitus position. The shoulders are positioned almost perpendicular to the operating table. The hips are rotated posteriorly at about 45 degrees from the table (Fig. 26-19, A). A thoracoabdominal incision is made, usually through the fifth or sixth intercostal space, entering the pleural cavity through the top of the bed of the lower rib. After dividing the costal margin, the incision is extended obliquely across the abdominal wall, and the muscles are divided to the level of the rectus abdominis fascia. The diaphragm is incised radially to the level of the aortic hiatus or circumferentially 2 to 3 cm from the chest wall. In some cases, it is possible to enlarge the aortic hiatus circumferentially and obtain sufficient exposure of the upper abdominal aorta so that division of the diaphragm is not necessary. The peritoneum is incised in the left gutter, and stomach, intestines, spleen, and left kidney are retracted anteriorly and to the right.

Because of the prevalence and clinical importance of paralysis of the lower extremities (paraplegia or paraparesis) following operations on the thoracoabdominal aorta, distal perfusion with some degree of systemic hypothermia (passive or induced), or regional hypothermia of the spinal cord induced by irrigation of the epidural space, is employed. Drainage of cerebrospinal fluid is also used (see “Paraplegia after Aortic Clamping” in Chapter 24).

**Technique Using Hypothermic Circulatory Arrest**

For purposes of illustration, the technique for thoracoabdominal aorta replacement using hypothermic CPB and circulatory arrest for protection of the spinal cord and the abdominal organs is shown in Fig. 26-19. The left common femoral artery and vein are exposed through an oblique or vertical incision in the groin crease. Heparin is administered, and a long 28F, 30F, or 32F cannula is inserted into the femoral vein over a guidewire system and positioned in the center of the right atrium. TEE is used to facilitate proper placement. With cannulae of these sizes and use of vacuum-assisted venous drainage, flows of 2.0 to 2.4 L · min⁻¹ · m⁻² can be easily achieved. If flow is limited, the pericardium is incised anterior and parallel to the left phrenic nerve and a second 28F or 30F angled cannula is inserted into the pulmonary trunk through a purse-string suture. The tip of the cannula is passed retrogradely through the pulmonary valve and positioned in the right ventricle. Unless there is severe atherosclerosis of the common femoral or external iliac artery, or if an abdominal aortic aneurysm is present, the femoral artery is cannulated with a 20F or 22F cannula. If this is not possible, the descending thoracic aorta, left subclavian artery, or left axillary artery can be used.

CPB is established immediately after the chest is entered, and perfusion cooling is initiated. Methylprednisolone (7 mg · kg⁻¹) and thiopental (10−15 mg · kg⁻¹) are administered to protect the central nervous system. No other adjuncts for spinal cord protection are used. During cooling, the abdominal portion of the incision is completed. The left lung is collapsed and gently retracted to minimize manipulation and injury. The left vagus and left recurrent laryngeal nerves are identified and protected. When the heart fibrillates, a venting catheter is inserted into the left inferior pulmonary vein for decompression (Fig. 26-19, B). If the vein is not accessible, the catheter is placed into the left ventricle through a stab wound near the apex. The aorta proximal to the diseased segment is not clamped, and no form of cardioplegia is used.

Preparations for circulatory arrest are made as described under “Aortic Arch Replacement.” Circulatory arrest is established after the patient is placed in Trendelenburg position and the venting catheter in the left heart has been occluded to prevent suction of air into the heart and proximal aorta. No clamps are placed on the proximal aorta. The aorta distal to the diseased segment is clamped. If a clamp cannot be safely placed on the distal aorta, it is opened and occluded with a balloon catheter. This is done to permit later perfusion of the iliac and hypogastric arteries, which may be important sources of blood flow to the lower spinal cord. The aorta is opened and transected proximal to the diseased segment (see Fig. 26-19, B). A prepared tube graft is selected and sutured to the proximal aorta with a continuous 3-0 or 4-0
Figure 26-19  Thoracoabdominal aorta replacement. A, Patient is positioned in right lateral decubitus position. Shoulders are positioned perpendicular to operating table, and hips rotated posteriorly to 45-degree angle. Left pleural space is entered through fifth or sixth intercostal space. Incision is extended obliquely across costal margin toward umbilicus (dashed line). Oblique muscles of abdomen are divided to level of rectus fascia, and peritoneal cavity is entered. Diaphragm is divided, peritoneum in left gutter is incised vertically, and abdominal viscera and left kidney are retracted anteriorly and to the right (see text). B, Technique employing hypothermic cardiopulmonary bypass and circulatory arrest. (See text for details.) Left femoral artery and vein (LFA, LFV) are cannulated, and a venting catheter is placed in left inferior pulmonary vein. After circulatory arrest is established, clamp is placed on lower thoracic aorta (if possible) to minimize blood loss. No clamps are placed on aorta proximal to diseased segment. Aorta is opened and transected proximally.

Polypropylene suture buttressed with a strip of PTFE felt (Fig. 26-19, C). When this anastomosis is completed, an aortic perfusion cannula or a 10-mm prepared polyester graft that has been attached to the aortic graft is connected to a second arterial line from the pump-oxygenator adjacent to the anastomosis. With the patient’s head in a dependent position, cold oxygenated (18°C-20°C) blood is infused retrogradely through the venous line until all air is evacuated from the brachiocephalic arteries and aortic arch. The aortic graft is clamped just distal to the proximal arterial line and flow into the upper and lower aorta (through the femoral artery) is established (Fig. 26-19, D). If the time of circulatory arrest is short (<20-25 minutes), it can be extended briefly so that the aorta can be widely opened to clearly identify patent lower intercostal and lumbar arteries and the origins of the visceral and renal arteries.

After flow through the upper and lower circuits has been established, 35% of the total arterial flow is directed through
C, Aortic graft, to which a 10-mm prepared polyester graft is attached, is sutured to aorta with continuous 3-0 or 4-0 polypropylene suture buttressed with a strip of polytetrafluoroethylene (PTFE) felt. Patent bronchial and intercostal arteries above sixth intercostal space are ligated. D, After evacuating air from circulation of upper body (see text), clamp is placed on graft just distal to the 10-mm graft, and flow into upper aorta is established. Lower aortic clamp is repositioned below segment of aorta to be resected, and flow into femoral arterial cannula is initiated.

Figure 26-19, cont’d  C, Aortic graft, to which a 10-mm prepared polyester graft is attached, is sutured to aorta with continuous 3-0 or 4-0 polypropylene suture buttressed with a strip of polytetrafluoroethylene (PTFE) felt. Patent bronchial and intercostal arteries above sixth intercostal space are ligated. D, After evacuating air from circulation of upper body (see text), clamp is placed on graft just distal to the 10-mm graft, and flow into upper aorta is established. Lower aortic clamp is repositioned below segment of aorta to be resected, and flow into femoral arterial cannula is initiated.

Continued

the upper arterial line and 65% through the lower line. The temperature of the perfusate is adjusted to maintain the nasopharyngeal temperature between 18°C and 20°C, and total flow is maintained between 750 and 1500 mL · min⁻¹ · m⁻². Drainage through the left heart vent is reestablished. During the period of hypothermic low flow, the intercostal and lumbar arteries that will be attached to the graft are isolated within a full-thickness cuff or cuffs of aorta that are excised from the diseased aortic segment with a cautery (Fig. 26-19, E). All patent intercostal and lumbar arteries below the sixth intercostal space should be attached to the graft if possible. A segment of graft opposite these arteries is excised with a wire cautery, and the rim of aortic tissue surrounding the arteries is sutured to the graft with a continuous 3-0 or 4-0 polypropylene suture (see Fig. 26-19, E and F). The aortic clamp is repositioned below the intercostal artery–to-graft anastomoses, air is evacuated from the graft with a needle vent, and flow to the intercostal arteries is established (see Fig. 26-19, F). Rewarming is begun at this time, and flow is gradually increased to the precooling level.

Anastomoses to the visceral and renal arteries are then completed. This can be accomplished using a cuff of aorta (see Fig. 26-19, F) or by suturing the arteries individually to the graft. Interposition of segments of polyester grafts between the aortic graft and these arteries may be necessary, particularly in patients with Marfan syndrome.¹²⁰,K¹² When these anastomoses are completed, the aortic clamp is repositioned below the level of the renal arteries, and anastomosis to the distal aorta is completed (Fig. 26-19, G).
With hypothermic low flow established above and below isolated aortic segment, intercostal and lumbar arteries that will be attached to graft are isolated with full-thickness cuff of aorta. This cuff is sutured to graft with continuous 3-0 or 4-0 polypropylene suture. Clamp on graft is repositioned below intercostal pedicle to permit perfusing intercostal arteries. Full-thickness cuff of aortic tissue surrounding celiac, superior mesenteric, and renal arteries is excised from aorta with a cautery, and cuff is sutured to graft with continuous 3-0 or 4-0 polypropylene suture. Clamp on graft is repositioned on aorta below renal arteries, and graft is sutured to distal aorta with 3-0 or 4-0 polypropylene suture buttressed with a strip of PTFE felt.

Figure 26-19, cont’d
During cooling, the heart spontaneously fibrillates and becomes quiescent; during rewarming, spontaneous defibrillation occurs in most patients when the nasopharyngeal temperature reaches 26°C to 28°C. The venting catheter is then removed. CPB is discontinued when the bladder temperature reaches 36°C. Peripheral cannulae are removed, protamine is administered, and hemostasis is obtained. A drain connected to suction is placed in the retroperitoneal space, and intercostal drainage catheters (two or three) are placed in the left pleural space. Edges of the divided diaphragm are approximated, and the incision is closed.

**Technique Using Left Heart Bypass**

A widely used alternative technique is left heart bypass (left atrium to left femoral artery) and mild (32°C–33°C) permissive hypothermia. The common femoral artery and the left atrium (or alternatively, the left inferior or superior pulmonary vein) are cannulated and partial cardiac bypass established using an in-line centrifugal pump. Bypass flows are adjusted to maintain a mean arterial pressure in the lower circulation of 60 to 70 mmHg while normal arterial pressure and central venous pressure are maintained in the upper circulation. Flows between 750 and 1500 mL · min⁻¹ · m⁻² are generally required. The aorta is clamped proximal to the diseased aortic segment, and a second clamp is placed on the descending aorta in the midportion. This maneuver maintains perfusion of the lower intercostal arteries, kidneys, abdominal organs, and lower extremities. As the operation proceeds, the distal aortic clamp is sequentially moved to lower positions to maintain distal perfusion. If distal clamping is not possible, separate balloon-tipped perfusion catheters can be introduced into the celiac, superior mesenteric, and renal arteries and connected to a cannula from the perfusion circuit to provide oxygenated blood to these organs. The procedure is then completed as shown in Fig. 26-19, E through G.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Patients who have undergone thoracic or thoracoabdominal aorta replacement receive the same care given to patients after major cardiac operations (see Chapter 5). Particular attention is paid to maintaining adequate ventricular preload by volume infusions. Amount of chest drainage is closely monitored, and the usual rules for reentry (see “Treatment of Bleeding” in Chapter 5) are observed because major bleeding can occur, and it is a risk factor for developing other complications.

When the procedure has been performed through a left thoracotomy or thoracoabdominal incision, pulmonary complications are more likely to develop than after a median sternotomy. Thus, close attention to pulmonary subsystem management is mandatory (see Chapter 5 for details). Because renal blood flow is often reduced or absent for a time during and early after repair, renal function must also be carefully monitored early postoperatively. Managing renal dysfunction and renal failure is discussed in Chapter 5.

Although most patients in whom paraplegia or paraparesis develops after operations on the descending thoracic or thoracoabdominal aorta have evidence of ischemic injury upon awakening from anesthesia, this complication sometimes develops later postoperatively. Prompt initiation of cerebrospinal fluid drainage may, in some instances, reverse the neurologic deficit, and if a drain is not already in place, it should be inserted when signs of spinal cord ischemia develop postoperatively. Avoiding prolonged periods of hypotension is also essential to ensure optimal spinal cord perfusion.

Because additional aortic disease frequently develops in patients who have had operations on the thoracic aorta, perioperative evaluation is an important feature of their postoperative care. This should be performed at 4- to 6-month intervals in the first postoperative year, and semiannually or annually thereafter. Two-dimensional echocardiography is useful for examining the aortic root and proximal ascending aorta. CT or MRI is required to accurately assess the aortic arch and descending thoracic aorta. Ultrasonography can be used to evaluate the abdominal aorta.

**RESULTS**

**Survival**

**Early (Hospital) Death**

**Ascending Aorta**

Early (hospital) mortality after elective repair of chronic ascending aortic disease in heterogeneous groups of patients ranges from 0% to 9%. Most patients in these series had aneurysms of the ascending aorta resulting from aortic medial degenerative disease and had concomitant aortic valve replacement, either as a separate procedure or using a composite graft. These series also included patients with Marfan syndrome and patients who had partial resection of the aortic arch with hypothermic circulatory arrest. Use of hypothermic circulatory arrest is not a risk factor for increased mortality among such patients. Resection of the ascending aorta for severe diffuse arteriosclerosis or calcification, usually performed in conjunction with coronary artery bypass grafting or aortic valve replacement, is associated with higher early mortality and morbidity. These procedures usually require hypothermic circulatory arrest. Endarterectomy is preferred by some groups for managing the severely calcified ascending aorta and has similar early mortality.

**Aortic Arch**

Early mortality after elective repair of aortic disease that involves the arch is higher, ranging from 5% to about 20%. This is related in part to greater complexity of the operative procedures compared with operations on the ascending aorta, and to higher prevalence of neurologic injury, which is associated with increased mortality. In general, resection of the entire or distal aortic arch is associated with higher mortality than operations involving only the proximal aortic arch (Table 26-1).

<table>
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<th>Extent Replaced</th>
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<th>No.</th>
<th>%</th>
<th>CL</th>
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<td>42</td>
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<td>14.6</td>
<td>8.7-20</td>
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<td>533</td>
<td>54</td>
<td>10.1</td>
<td>8.7-11.5</td>
</tr>
</tbody>
</table>

Data from Svensson and colleagues. Key: CL, 70% confidence limits.
In all the mentioned categories, emergency operation for rupture or acute dissection is associated with substantially higher early mortality.

### Time-Related Survival

#### Ascending Aorta

Among heterogeneous groups of patients, survival after ascending aorta replacement, usually in combination with aortic valve replacement, is approximately 70% at 5 years and 50% to 60% at 10 years (Fig. 26-20). In a collaborative study from 10 centers, excellent results were obtained for patients with Marfan syndrome. Five-year survival for elective repair was 86%, and 10-year survival was 80% (Fig. 26-21). Survival was lower for patients who required urgent or emergency operation.

#### Thoracoabdominal Aorta

With increasing experience, and with use of adjuncts such as distal aortic perfusion and hypothermia, early mortality for elective operations is approximately 3% to 15% (Table 26-2).

#### Descending Thoracic Aorta

When aortic disease is confined to the descending thoracic aorta, early mortality for elective procedures with currently used techniques is 4% to 10% (Table 26-2).
employing hypothermic CPB and circulatory arrest in 151 patients, 5- and 10-year survival was 71% and 45%, respectively. Survival was less favorable for patients with degenerative aneurysms than for those with nondegenerative aneurysms (Fig. 26-26).

Thoracoabdominal Aorta In one of the largest series of patients with surgical repair of thoracoabdominal aortic disease ($n = 1509$) reported by Svensson and colleagues in 1993, $S_{27}$ survival was 60% at 5 years and 32% at 10 years (Fig. 26-27). In a series of 1220 patients treated more recently reported by Coselli and colleagues, $C_{35}$ survival was 74% at 5 years (Fig. 26-28). As noted previously with descending thoracic aortic aneurysms, survival among patients with degenerative thoracoabdominal aortic aneurysms was substantially lower than for those with nondegenerative aneurysms ($K_{33}$) (Fig. 26-29).

Modes of Death

Myocardial failure and infarction, hemorrhage, neurologic dysfunction, and multiple system organ failure are common
operation are due to rupture of an anastomotic false aneurysm.

Incremental Risk Factors for Premature Death after Repair

Patient-Specific Risk Factors

Location of aneurysm on the aortic arch or thoracoabdominal aorta poses greater risks for early death than location on the ascending or descending thoracic aorta. Among patients with thoracoabdominal aortic disease, operations for extent II disease as defined by Crawford and colleagues (Fig. 26-30) are associated with increased risk compared with extent I or III (see Tables 26-3 and 26-4). These risks are related importantly to brain and spinal cord ischemic injuries, which occur more often after operations in these regions. Improved techniques of brain and spinal cord protection may ultimately neutralize these risks.

Older age and coexisting coronary arterial, renal, and pulmonary disease are associated with increased early and late death. Emergency operation for rupture of a thoracic or thoracoabdominal aortic aneurysm increases risk.

Diagnostic and Procedural Risk Factors

Although improved outcomes in recent years can be attributed to changes in preoperative, intraoperative, and postoperative management, the specific improvements that are responsible are difficult to quantify. They include a clearer understanding of the natural history of diseases of the thoracic aorta, improved diagnostic studies, increased knowledge of the determinants of operative risk, and critical analyses of early and long-term results.

Improved techniques for brain protection have reduced the risk of operations on the aortic arch. Increased use of distal perfusion and other adjuncts has substantially reduced spinal cord ischemic injury and death after operations on the descending thoracic and thoracoabdominal aorta. Availability of prepared grafts that are impervious to blood and improved methods for minimizing intraoperative and postoperative blood loss have also contributed to the improved outcomes.

Institutional Risk Factors

In institutions properly prepared for complex aortic surgical procedures, risks of repair are lower than in other institutions.

Complications

Brain Injury

Brain injury is an important complication of operations on the thoracic aorta, particularly those that involve the aortic arch. In a study of 183 patients following operations on the thoracic aorta in which hypothermic circulatory arrest was used, Ergin and colleagues identified two types of neurologic injury: (1) temporary neurologic dysfunction (agitation, lethargy, obtundation, disorientation, psychosis, choreoathetoid movements, and seizures) and (2) stroke. Temporary neurologic dysfunction occurred in 19% of patients and was correlated with duration of circulatory arrest and older age. Stroke was attributed to embolism and occurred in 11% of patients. Strokes correlated with older age, operations on the aortic arch, and presence of descending thoracic
Chapter 26  Chronic Thoracic and Thoracoabdominal Aortic Disease

Figure 26-30  Crawford classification for thoracoabdominal aortic aneurysms. Extent I: Most or all of descending thoracic aorta and upper abdominal aorta. Extent II: Most or all of descending thoracic aorta and most or all of abdominal aorta. Extent III: Distal half or less of descending thoracic aorta and varying segments of abdominal aorta. Extent IV: Most or all of abdominal aorta. (From Crawford and colleagues.

aneurysms that contained thrombus or atheroma. Improved methods of brain protection during operations on the aortic arch, including retrograde brain perfusion, avoidance of prolonged (>50-60 minutes) circulatory arrest, and antegrade cerebral perfusion are associated with lower occurrence of both temporary and permanent neurologic dysfunction.

Spinal Cord Injury
Paraplegia and paraparesis can occur after operations on the descending thoracic and thoracoabdominal aorta. Because of its clinical importance, preventing spinal cord ischemic injury is paramount (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24). Although considerable experience has been reported with the technique of simple aortic clamping, principally by Crawford and colleagues, there is emerging consensus that distal perfusion with some degree of systemic hypothermia (passive or induced), or regional hypothermia of the spinal cord induced by irrigation of the epidural space, reduces occurrence of spinal cord ischemic injury. Drainage of cerebrospinal fluid has also been associated with reduced occurrence of spinal cord ischemic injury.

Renal Dysfunction and Failure
Renal dysfunction can occur following operations on the descending thoracic and thoracoabdominal aorta. Because of variability of the criteria that are used to define it, the true prevalence is difficult to determine. Postoperative renal failure managed with dialysis occurs in 1% to 5% of patients having operations on the descending thoracic aorta and in 5% to 15% of those requiring replacement of the thoracoabdominal aorta. Preoperative renal dysfunction, as evidenced by elevated creatinine, is a predictor of postoperative renal failure when simple aortic clamping or normothermic distal perfusion is used for operations on the thoracoabdominal aorta.

Pulmonary Dysfunction
Pulmonary dysfunction of sufficient severity to require prolonged (>48-72 hours) mechanical ventilatory support occurs in 20% to 30% of patients undergoing repair of thoracic and thoracoabdominal aneurysms in which a lateral incision is used. Occurrence of this complication appears to be independent of operative technique (simple aortic clamping, distal perfusion, hypothermic circulatory arrest, epidural cooling). Incremental risk factors for prolonged ventilatory support after operations on the thoracoabdominal aorta include older age, division of the diaphragm, duration of aortic clamping, number of packed red blood cell units transfused, and current smoking.

Reoperation
Late reoperation is necessary in a substantial number of patients, particularly when there has been a previous aortic dissection or when Marfan syndrome is present. Thus, as in the case of acute aortic dissection (see Chapter 25), periodic evaluation with aortic imaging of patients following operations on the thoracic and thoracoabdominal aorta is essential.

INDICATIONS FOR OPERATION
Ascending Aorta
Patients with symptoms attributable to chronic aneurysm of the ascending aorta should, in general, have prompt surgical treatment whether the symptoms are from enlargement of
the aneurysm or from aortic valve regurgitation. Patients with cystic medial degenerative disease should undergo elective replacement of the ascending aorta and the aortic sinuses when the greatest diameter of the aorta exceeds 5.0 to 5.5 cm. If substantial aortic valve regurgitation is present, operation may be advisable before the aorta reaches this diameter. Surgical repair of the dilated aortic root or ascending aorta in patients with Marfan syndrome is usually performed at a threshold of 5.0 cm because of the greater tendency for aortic dissection at a smaller diameter. Rapid growth of the aneurysm (>0.5 cm · year⁻¹), family history of aortic dissection, and presence of moderate to severe aortic regurgitation are indications for operation at a smaller diameter. For patients with Loeps-Dietz syndrome or a confirmed TGFB1 or TGFB2 gene mutation, repair should be considered at a diameter of 4.4 to 4.6 cm as determined by CT or MRI. Asymptomatic patients with degenerative thoracic aneurysm, chronic aortic dissection, intramural hematoma, penetrating arteriosclerotic ulcer, and mycotic or false aneurysm with an aortic diameter of 5.5 cm or greater should be considered for surgical repair. Growth of 0.5 cm · year⁻¹ in aortas of smaller diameter is also an indication for repair. Patients who have dilatation of the ascending aorta in association with a congenitally bicuspid aortic valve and who require aortic valve replacement should have concomitant replacement of the ascending aorta when it measures more than 4.5 cm. These recommendations are based on evidence that combined operative and late mortality is less than mortality observed in patients managed without operation.

Aortic Arch

Patients who are symptomatic from chronic aneurysms that involve the aortic arch should, in most instances, undergo prompt surgical treatment, because the natural history of this condition is particularly unfavorable. Because of the complexity of operations that require replacement of the aortic arch and because neurologic complications are not uncommon (see “Brain Injury”), elective operation is generally advised only for aneurysms that are 5.5 to 6.0 cm in diameter or when there is documented progressive enlargement. Aneurysms of the aortic arch are often associated with aneurysmal disease of the ascending and descending thoracic aorta, and this may be the principal indication for operation.

Arteriosclerotic disease involves the aortic arch more frequently than other parts of the thoracic aorta. Because the presence of arteriosclerotic plaques with a thickness of more than 4 mm is an important predictor of brain infarction and because such plaques are also a source of embolization to other organs, graft replacement or endarterectomy of the involved segment of the arch should be considered when severe disease is detected in patients who are undergoing operations on the heart or ascending aorta. Occasionally, presence of pedunculated mobile atheroma in patients who have had a transient ischemic attack or stroke is an indication for operation.

Descending Thoracic and Thoracoabdominal Aorta

Patients with symptoms attributable to chronic aneurysms that involve the descending thoracic and thoracoabdominal aorta should, in general, have prompt operation, because rupture before operation substantially increases risk of the procedure (see “Incremental Risk Factors for Premature Death after Repair” under Results). The appearance of even mild symptoms, particularly in patients with thoracoabdominal aneurysms, may represent progression into a subacute phase that is associated with increased risk of rupture and higher operative mortality. Advising surgical treatment for asymptomatic patients with chronic descending or thoracoabdominal aortic aneurysms is less straightforward because of risks of stroke, spinal cord ischemic injury, renal failure, and a high prevalence of pulmonary complications postoperatively (see “Complications” under Results). Careful assessment of preoperative risk factors for death and for postoperative paralysis is essential before a recommendation for surgical intervention is made. These risk factors must be weighed against the probability of rupture of the aneurysm. In good-risk patients at experienced surgical centers, elective resection is advisable when the aneurysm exceeds 5.5 cm in the descending thoracic aorta and 6.0 cm in the thoracoabdominal aorta or when there is documented progressive enlargement. All asymptomatic patients in whom surgical treatment is deferred must have periodic follow-up, with determination of the size and extent of the aneurysm or other aortic disease by CT or MRI every 6 to 12 months, depending on the size of the aorta. In general, increase in size during the period of observation is a strong indication for surgical intervention.

Other Conditions

There is evidence from natural history studies to suggest that patients with chronic aneurysms resulting from type B aortic dissections are more likely to die of rupture of the aneurysm than patients with aneurysms not associated with dissection. In the study by Griep and colleagues, patients with rupture of chronically dissected aortas had significantly smaller maximal descending thoracic aortic diameters than patients with rupture of degenerative aneurysms. These observations indicate that a more aggressive surgical approach is indicated in patients with aneurysms associated with chronic type B dissection.

Patients with penetrating arteriosclerotic ulcers or intramural hematomas in whom symptoms and signs of impending rupture are present or in whom false aneurysms develop should undergo graft replacement of the involved segment of the aorta irrespective of size. Patients with severe arteriosclerosis and repeated episodes of embolization to the abdominal viscera, kidneys, or lower extremities should be considered for excision and graft replacement of the diseased aortic segment.

SPECIAL SITUATIONS AND CONTROVERSIES

Endovascular Grafts

Techniques have been developed for placing intraluminal stent-grafts into the descending thoracic aorta and aortic arch to treat patients with aortic aneurysms, dissections, intramural hematomas, penetrating arteriosclerotic ulcers, false aneurysm, and acute traumatic aortic disruption (see Chapter 24).
Descending Thoracic Aorta

Substantial experience has been accumulated with endovascular stent-grafts for aortic disease confined to the descending thoracic aorta. Availability of several commercially manufactured devices has facilitated implementation of this technology for a wide variety of conditions (Fig. 26-31).

Major requisites for graft placement are suitable landing zones proximal and distal to the diseased segment (1.5-2.0 cm in length), and diameters of these aortic segments greater than 20 mm and less than 40 mm. Possible deployment sites of the proximal end of endovascular grafts are shown in Fig. 26-32. There is emerging consensus that if coverage of the origin of the left subclavian artery is required, a left subclavian artery-to-left carotid artery bypass graft or transposition should be performed before deployment of the graft when feasible. Absence of revascularization of the left subclavian artery in this setting has been associated with a higher prevalence of left arm ischemia, vertebrobasilar ischemia, spinal cord ischemia, and anterior circulation stroke. Drainage of cerebrospinal fluid, when extensive coverage of the descending thoracic aorta is planned or when abdominal aortic aneurysm repair has been previously performed, is also advisable to reduce prevalence of spinal cord ischemic injury.

No randomized trials have compared endovascular treatment of descending thoracic aortic disease with open operation. Meta-analysis of large numbers of patients undergoing open or endovascular repair of isolated descending thoracic aortic disease has suggested lower (with endovascular repair) or comparable early (30-day or hospital) mortality. Patients treated with endovascular stent-grafts were generally older. Prevalence of postoperative complications in the aggregate was lower among these patients as well, and length of hospital stay was shorter. In the study by Gopaldas and colleagues of patients in the United States, hospital charges were substantially higher in the endovascular cohort, and the endovascular stent-graft patients were four times more likely to have a routine discharge to home.

There is no clear evidence from these and other studies demonstrating a substantial difference between the two methods of treatment in occurrence of postoperative stroke, spinal cord ischemic injury, or renal failure among patients with degenerative aneurysms or aortic dissection. Midterm survival of patients treated with the two techniques is comparable. Survival for the subset of patients with ruptured aneurysms is also comparable.

Complications unique to endovascular stent-grafting include endoleak, retrograde type A aortic dissection, aneurysm expansion and rupture, stent-graft collapse, graft migration, aortic valve perforation by a guidewire, dilatation of proximal and distal landing zones, injury to femoral and external iliac arteries, and erosion of the aorta resulting in aorto-bronchial or aortoesophageal fistulas. Periodic surveillance imaging studies are mandatory and add to overall cost of the procedure. Durability of the currently available devices beyond 10 years is unknown.

Endovascular stent-grafting should be considered for elderly patients with important comorbidity and limited life expectancy if the risk of intervention is judged to be lower than that for nonoperative or open surgical management. The precise role of endovascular stent-grafting in younger patients at lower risk for open operation remains incompletely defined.

Hybrid Operations

Aortic Arch

Hybrid procedures combining open surgical repair with endovascular grafting to treat aneurysmal disease involving the aortic arch and descending thoracic aorta include the “stented” or “frozen” elephant trunk technique and open debranching of the brachiocephalic arteries with repair of the aortic arch and descending thoracic aorta using a stent-graft (Fig. 26-34, A and B). The stented elephant trunk procedure was developed to eliminate the second stage of the conventional elephant trunk procedure or other procedures on the remaining thoracic aorta. To date, this objective has not been realized. The debranching procedure has been applied primarily to patients deemed to be at high risk for conventional aortic arch repair. Early results do not

Figure 26-31 Endovascular repair of a degenerative aneurysm of mid-descending thoracic aorta with a commercially prepared stent-graft.

Figure 26-32 Sites of proximal endovascular graft deployment for diseases of descending thoracic aorta. (From Adams and colleagues.)
**Figure 26-33** Survival following open and endovascular repair of (A) descending thoracic aorta or (B) descending thoracic and thoracoabdominal aortic aneurysms. (A modified from Stone and colleagues; B modified from Greenberg and colleagues.)

**Figure 26-34** Hybrid operation for aortic arch and descending thoracic aortic disease. **A**, Debranching of brachiocephalic arteries followed by insertion of stent-graft into distal ascending aorta, aortic arch, and descending thoracic aorta. **B**, Stent-graft can be deployed either through a limb of a multiple branched graft (shown) or through femoral artery. **C**, Debranching of celiac, superior mesenteric, and both renal arteries using a four-branch graft. Native aortic branches are ligated to prevent endoleak. Stent-graft can be deployed immediately after debranching or at a second procedure. (Modified from Hughes and colleagues.)
Brain Protection during Operations on the Aortic Arch

Early attempts to use temporary shunts to the brachiocephalic arteries during repair of aneurysms of the aortic arch are described under Historical Note in this chapter. By 1957, CPB was being used in some form for operations on the aortic arch, and this practice continues to this day. A small proportion of patients experience brain damage from CPB per se (see “Neurobehavioral and Neurologic Outcomes” under Results in Chapter 7, and see “Neuropsychological Subsystem” in Section I of Chapter 5) and from profound hypothermic circulatory arrest (see “Damage of Circulatory Arrest during Hypothermia” and “Safe Duration of Circulatory Arrest” in Section I of Chapter 2). However, prevalence of brain injury is greater after operations on the aortic arch than after other types of aortic or cardiac surgery. Brain injury is a frequent cause of death and complications after these operations and likely occurs as a result of embolization of particulate matter or severe global ischemia during the interval of circulatory arrest. Several methods are currently being used for protection of the brain during operations on the aortic arch.

Antegrade Brain Perfusion

During operations on the aortic arch, more or less continuous antegrade brain perfusion is possible only when two or more of the brachiocephalic arteries are separately perfused after the aortic arch has been opened. This technique was the first to be used for operations on the aortic arch, but survival was relatively low. Frist and colleagues perfused only one brachiocephalic artery, usually the trunk, and cannulated it directly. F7 Results with normothermic or mildly hypothermic brain perfusion were disappointing.

Crittenden and colleagues documented in a sheep model the clear superiority of antegrade brain perfusion over alternative methods of brain protection. They demonstrated that hypothermic, low-flow, antegrade brain perfusion preserved intracellular pH and energy stores. Bachet and colleagues and Kazui and colleagues have accumulated large series of patients in whom this technique has been used with satisfactory outcomes. B1,K7 Its advantage is that it allows an interval of safe, total body circulatory arrest because the brain is supplied with nutrients and oxygen during this period. The technique requires manipulation and direct cannulation of these arteries, with risk of dislodging arteriosclerotic debris and the potential for embolization of this material as well as air. In a study by Hagl and colleagues, this technique, compared with other methods of brain protection, was associated with the lowest prevalence of temporary neurologic dysfunction. H1 However, it may not be fully protective in patients who require antegrade perfusion for more than 80 minutes. H1

Although direct antegrade perfusion of all three brachiocephalic arteries is considered optimal, K7 substantial experience has been accumulated with perfusion of the brain only through the brachiocephalic or right axillary artery. F7,H2,J3,K16,K19,T4,T6 This technique eliminates need for direct cannulation and perfusion of the brachiocephalic arteries. Although concern has been expressed about inadequate perfusion of the left brain, K8 particularly in the absence of a complete circle of Willis, this has not proved to be an important problem. Perfusion at low temperature (20°C-25°C) likely contributes to the safety of this technique.

Hypothermic Circulatory Arrest

The simplest and currently the most widely used technique for brain protection during operations on the aortic arch is hypothermic circulatory arrest using CPB for cooling and rewarming of the patient (see “Replacement of Aortic Arch” for a description). A major advantage of this technique is its simplicity. It provides an operative field essentially free of blood and cannulae, and permits thorough inspection of the inside of the aorta and performance of secure distal aortic and arch anastomoses.

In carefully conducted clinical studies, neurologic complications are occasionally observed following use of hypothermic circulatory arrest for operations on the aortic arch in adults. B9 In addition to strokes, which are likely embolic in origin, temporary neurologic dysfunction occurs in approximately 20% of patients. Prevalence of temporary neurologic dysfunction increases with increasing age and with duration of circulatory arrest. B3,K9 Scrupulous implementation of techniques to ensure adequate cooling and rewarming of the brain is essential to minimize occurrence of this complication. B12 Because deterioration of cognitive function postoperatively occurs more often in patients with more than 25 minutes of hypothermic circulatory arrest, its safe duration in adults may be closer to 30 minutes rather than 40 to 50 minutes, as previously reported. D18,G12,S7 Recent studies in animals and humans suggest that cerebral metabolic suppression at clinical levels of hypothermia is less complete than had been previously assumed. G12,M11 Use of adjuncts such as retrograde brain perfusion (see “Retrograde Brain Perfusion” in text that follows) may increase the safe duration of hypothermic circulatory arrest beyond this limit and may reduce the prevalence of embolic stroke. C29,J9,K14,K22,K23

If hypothermic circulatory arrest is used for procedures that require a left thoracotomy, presence of severe aortic regurgitation may be a relative contraindication to its use because distention of the left ventricle may occur when the heart fibrillates. This may result in impaired subendocardial perfusion and ischemia of the left ventricle. If substantial aortic regurgitation is known to be present preoperatively and the procedure to be performed on the aorta is elective, the aortic valve should be replaced, and the procedure on the aorta should be performed 3 to 6 weeks later. If aortic regurgitation is not detected until time of the operation, an alternative technique should be used.

Retrograde Brain Perfusion

Protection of the brain during operations on the aortic arch by perfusing cold oxygenated blood into the superior vena
cava was first reported by Ueda and colleagues. This technique offers the potential advantages of delivering nutrients to the brain during an interval of hypothermic circulatory arrest and removing embolic material from the arterial circulation of the brain. Subsequent studies in animals have demonstrated that little or no effective blood flow occurs during retrograde perfusion, even with occlusion of the superior vena cava, to confer any meaningful metabolic benefit. Retrograde perfusion is, however, an effective method for washout of particulate emboli from the brain. Thus, its principal role is as an adjunct rather than as a primary technique for brain protection during hypothermic circulatory arrest.

False Aneurysms

False aneurysms are infrequent but serious complications after operations on the thoracic aorta and following infection or trauma. Their true prevalence after thoracic aortic procedures is unknown, but systematic surveillance suggests that false aneurysms may be present in up to 13% of patients after graft replacement of the ascending aorta for aneurysm or dissection. They have been observed in up to 7% of patients following operations on the descending thoracic and thoracoabdominal aorta and occur primarily at sites of attachment of intercostal, visceral, and renal arteries to the aortic grafts. Infection of grafts, with or without associated mediastinitis, progressive degeneration of the aortic wall, aortic dissection, and use of biological glue have been implicated as etiologic factors. Aneurysms have also occurred at aortic suture lines, sites of aortic cannulation and clamping, and sites of attachment of coronary arteries with buttons of aortic tissue and coronary artery bypass grafts.

Surgical treatment includes direct repair, resection, and graft replacement of the sites of the false aneurysm with synthetic or biological grafts, patch repair, and endovascular stent-graft repair. CPB is almost always necessary, and hypothermic circulatory arrest has been required in up to 60% of patients. In several large series, operative mortality did not exceed 10%, 5-year survival ranged from 74% to 79%, and freedom from reoperation at 5 years ranged from 72% to 77%.

Infected Aneurysms

Because infected (mycotic) aneurysms may be multifocal, the entire aorta should be evaluated. Because of the high probability of rupture, surgical treatment should not be delayed in an attempt to control the infection with antibiotic therapy.

Excision of the infected aortic segment is required to control sepsis and prevent rupture. The aorta can be replaced with an aortic allograft, autologous or heterologous pericardium, or a polyester graft. Aortic root allografts may be particularly advantageous for infections that involve the aortic root. Encouraging results have been reported with these techniques, with early survival exceeding 85%. Lifetime oral antibiotic therapy is recommended to prevent recurrence of infection.

Infected Aortic Grafts

Graft infections occur in 1% to 2% of patients who have undergone replacement of the thoracic aorta. Infection may appear at any time, but peak occurrence appears to be in the first month after operation. Important risk factors for infection include inadequate sterile technique, excessive transfusion of blood products, bacteremia, and reoperation. Grafts that are placed in the ascending aorta or aortic arch are particularly vulnerable because of the absence of muscle between the graft and the sternum and subcutaneous tissues. In the experience with infected aortic grafts reported by Coselli and colleagues, 33% of patients had a wound infection or sternal dehiscence, 27% had previous cardiac procedures, 17% had a distant infection, and 10% had delayed closure of their sternal wounds. Fifty-eight percent of the infectious organisms were gram-positive (primarily staphylococcal species), 23% were gram-negative, and 2% were fungal. No organisms were isolated in some patients despite local signs of infection.

Infected prosthetic grafts is usually associated with signs and symptoms of systemic infection. CT scanning may demonstrate pockets of air or air-fluid levels adjacent to the graft. MRI with gallium- or indium-labeled leukocytes or with indium immunoglobulin scintigraphy may be helpful. TEE may demonstrate false aneurysm formation. Diagnosis of graft infection is often based on a combination of bacteriologic and radiographic findings and a high index of suspicion.

Modern surgical principles for treating infected aortic grafts were described by Hargrove and Edmunds in 1984. They include prompt reoperation and débridement of all infected tissue, removal of infected prosthetic material if suture lines are involved (this may not always be possible), local antisepctic irrigation and systemic antibiotics, and use of pedicle flaps of muscle or omentum to cover the grafts. Extraanatomic rerouting of arterial blood flow is not practical in most cases of thoracic aortic graft infection. Omentum is the pedicle graft of choice for treating an infected ascending aortic graft. It is pliable, fills dead space well, and usually provides ample coverage. In addition, it absorbs fluid, secretes angiogenic factors, and results in no loss of function compared with muscle flaps.

Several groups have reported success using these methods. In a series of 40 patients reported by Coselli and colleagues, 70% were hospital survivors and were alive 4 months to 6.5 years postoperatively. Patients received 6 to 8 weeks of intravenous antibiotics followed by lifelong oral antibiotic therapy.

Ringed Intraluminal and Patch Grafts

Ringed sutureless intraluminal prostheses that are anchored to the aorta by tapes placed around them and tied tightly over rigid spools at each end of the graft have been successfully used to replace segments of the ascending and descending thoracic aorta. Potential advantages of this technique compared with conventional suture anastomotic technique include reduced aortic clamp time and blood loss. Erosion of the aortic wall at the site of the tapes, obstruction to flow from buckling or kinking of the prosthesis or from use of a small prosthesis, and hemolysis and anemia are complications of this technique that limit its usefulness.
Patch grafts rather than tube grafts can be used to treat saccular aneurysms located on the undersurface of the aortic arch and in the descending thoracic aorta when they have a small, discrete communication with the aortic lumen. However, the adjacent aorta is often abnormal and unsuitable for safe placement of sutures. This technique should be used only when the adjacent aorta is normal in appearance and thickness.

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In this chapter, five diseases involving the pulmonary arteries that are amenable to surgical treatment are discussed: acute massive pulmonary embolism, chronic pulmonary thromboembolic disease, pulmonary artery aneurysm, pulmonary artery dissection, and pulmonary artery tumors.

**Section I: Acute Massive Pulmonary Embolism**

**DEFINITION**

Acute massive pulmonary embolism is sudden entrapment in pulmonary arteries of dislodged thrombus, usually from deep veins of the legs, pelvis, or arms. It is life threatening and can result in right heart failure, low cardiac output, and sudden death.

**HISTORICAL NOTE**

The first pulmonary embolectomy was performed by Trendelenburg in 1908, but long-term survival using his technique was not achieved until 1924. It is prophetic and of great significance that Dr. John Gibbon, who in 1953 performed the first successful operation in which a patient was totally supported by cardiopulmonary bypass (CPB) using a pump-oxygenator, envisaged use of CPB to treat massive pulmonary embolism. In 1931, while working as a research fellow for Dr. Edward Churchill, he wrote the following words in a patient’s chart at Massachusetts General Hospital:
During that long night’s vigil, watching the patient struggling for life, the thought naturally occurred to me that the patient’s life might be saved if some of the blue blood in her veins could be continuously withdrawn into an extracorporeal blood circuit, exposed to an atmosphere of oxygen, and then returned to the patient by way of a systemic artery in a central direction. Thus, some of the patient’s cardiorespiratory functions might be temporarily performed by the extracorporeal blood circuit while the massive embolism was surgically removed.\textsuperscript{K3}

The first successful pulmonary embolectomies performed with use of CPB were reported by Cooley and colleagues in 1961 and by Sharp in 1962.\textsuperscript{C11,S5} This remains the preferred technique for surgical treatment of acute massive pulmonary embolism.\textsuperscript{S3}

**MORPHOLOGY**

Detached venous thrombi pass through the right heart and enter the pulmonary arteries as a single thrombus or as fragmented smaller thrombi. The majority lodge in the lower lobes, slightly more often in the right than left lung.\textsuperscript{G8} Shortly after reaching the lungs, emboli become coated with a layer of platelets and thrombin.\textsuperscript{G8} Pulmonary arterial obstruction and release by platelets of vasoactive agents such as serotonin, adenosine diphosphate, platelet-derived growth factor, and thromboxane elevate pulmonary vascular resistance (Rp).\textsuperscript{M2} Alveolar dead space increases as a result of redistribution of blood flow, and gas exchange is impaired. As right ventricular (RV) afterload increases, RV pressure rises. This may result in RV dilatation, ischemia, and dysfunction. Increased Rp results in reduced RV stroke volume and left ventricular filling (preload). Reduction in preload and coronary blood flow associated with systemic hypotension markedly reduces left ventricular stroke volume. If a patent foramen ovale or atrial septal defect is present, right-to-left shunting of blood and severe hypoxemia may occur, as may paradoxical embolization.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Symptoms**

Acute massive pulmonary artery embolism can result in dyspnea, tachypnea, tachycardia, diaphoresis, cyanosis, and occasionally loss of consciousness.

**Signs**

The patient may be hypotensive, dyspneic, and cyanotic, and there may be evidence of pulsus paradoxus.\textsuperscript{H2} Evidence of low cardiac output is present, with weak peripheral pulses and oliguria. Jugular venous pressure is elevated, often with a prominent wave, and neck veins may be distended. Cardiac examination may demonstrate tachycardia, a prominent RV impulse, a loud pulmonary component of the second heart sound, and a gallop rhythm.\textsuperscript{H2} An ejection or pansystolic murmur is often present that may represent tricuspid valve regurgitation. Rarely is there evidence of airway obstruction.

**Diagnostic Studies**

In patients in cardiogenic shock, performing studies to establish the diagnosis of pulmonary embolism is often not possible, and diagnosis is made based on presenting symptoms and signs, recognizing that the diagnosis may be incorrect.\textsuperscript{G13} The electrocardiogram (ECG) may demonstrate T-wave inversion in the anterior leads, reflecting inferoposterior ischemia from pressure overload, a pseudoinfarction pattern, or an S1Q3T3 pattern.\textsuperscript{F4,K10} Transthoracic echocardiography (TTE) is particularly useful in patients suspected of having pulmonary emboli, because it can identify RV pressure overload (Fig. 27-1). Transesophageal echocardiography (TEE) can demonstrate pulmonary artery thrombi as well as RV overload.\textsuperscript{P2,W3} Computed tomography (CT) of the chest with contrast medium can also detect thromboemboli in the major pulmonary arteries (Fig. 27-2). Gadolinium-enhanced magnetic resonance imaging (MRI) can identify pulmonary thromboemboli and RV wall motion abnormalities.\textsuperscript{M7} Contrast pulmonary angiography is a definitive diagnostic study but is infrequently performed in hemodynamically unstable patients.\textsuperscript{G3,G10,R1}

**Figure 27-1** Transthoracic echocardiogram of acute massive pulmonary embolism (parasternal short axis views of right and left ventricles in diastole [A] and systole [B]). There is diastolic and systolic bowing of interventricular septum (arrows) into left ventricle (LV)—a finding compatible with presence of right ventricular volume and pressure overload, respectively. Right ventricle (RV) is appreciably dilated and hypokinetic, with little change in apparent right ventricular area from diastole to systole. There is a small pericardial effusion (PE). (From Come.\textsuperscript{K3})
NATURAL HISTORY

In the United States, approximately 100,000 patients are diagnosed with acute pulmonary embolism each year, resulting in thousands of recognized deaths. Many additional deaths occur each year as a result of undiagnosed massive pulmonary embolus that is mistaken for acute myocardial infarction or ventricular arrhythmia. In the International Cooperative Pulmonary Embolism Registry of 2454 consecutive patients with acute pulmonary embolism from 7 countries, 4.2% had massive embolization.

Untreated massive pulmonary artery embolism, when accompanied by hypoxemia and hemodynamic instability, is nearly always fatal. Most deaths occur before effective treatment can be initiated. It is estimated that mortality for an obstruction of more than 50% of the pulmonary vasculature approaches 50%, and that it increases to 70% if the patient requires vasopressor therapy. If clinical deterioration continues, mortality approaches 100%.

TECHNIQUE OF OPERATION

Preoperative Preparation

As soon as massive pulmonary embolism is suspected, high-dose unfractionated heparin should be administered. Most patients should receive a 10,000-unit bolus followed by a continuous infusion of at least 1250 units/h, with a targeted activated partial thromboplastin time (APTT) of at least 80 seconds.

Maintaining adequate oxygenation and cardiac output before establishing CPB is essential. Endotracheal intubation should be established if hypoxemia is present. If adequate cardiac output cannot be maintained with vasopressors, phosphodiesterase inhibitors, and sodium bicarbonate, or if external cardiac massage is required, CPB should be established by peripheral cannulation (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2). Heparin (300 units · kg⁻¹), if not already given, should be administered as soon as it is determined that operative intervention is indicated. If the patient’s condition permits, the usual preparations for establishing CPB are made (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). If diagnosis of pulmonary embolism has not been made with certainty before the patient is transported to the operating room, TEE should be performed to establish the diagnosis before the chest is opened.

Pulmonary Embolectomy

A midline sternotomy is performed. If peripheral cannulation has not been established, cannulae are placed in the aorta and both venae cavae. If the femoral vein has been cannulated, a second venous cannula is positioned in the superior vena cava, and the femoral vein cannula is withdrawn from the right atrium into the inferior vena cava. Alternatively, a long, two-stage cannula can be used. CPB is established with mild hypothermia, and tapes are placed around the superior and inferior venae cavae and secured. The aorta is clamped and cardioplegic solution infused into the aortic root (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). Alternatively, the heart can be kept beating or fibrillating. The left atrium and left ventricle can be decompressed with a venting catheter inserted into the right superior pulmonary vein.

The pulmonary trunk is incised longitudinally several centimeters from the pulmonary valve. Using forceps and suction, the thrombus is removed. If necessary, the incision can be extended into the left pulmonary artery, and a separate incision can be made in the right pulmonary artery between the superior vena cava and ascending aorta. A sterile fiberoptic bronchoscope can be used to visualize and remove thrombus from secondary and tertiary branches of the pulmonary arteries. The pleural spaces can be incised, and the lungs gently massaged to dislodge smaller thrombi. Alternatively, retrograde perfusion of the pulmonary veins through the opened left atrium can remove additional thromboembolic material from smaller pulmonary arterial branches (along with entrapped air). The right atrial and RV cavities are explored through a right atriotomy to search for and remove residual thrombi.
After removing the thrombus, incisions in the pulmonary arteries and right atrium are closed with continuous 5-0 polypropylene suture. After completion of rewarming and evacuation of air from the cardiac chambers, CPB is discontinued. The procedure is completed in the standard manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Placing an inferior vena caval clip or filter is advisable in the majority of patients. A clip can be placed after completing the embolectomy by extending the median sternotomy to the level of the umbilicus and exposing the inferior vena cava using the Kocher maneuver. Alternatively, under fluoroscopic guidance, a vena caval filter can be positioned through the femoral vein at the end of the operative procedure.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Postoperative circulatory support with an RV assist device and intraaortic balloon counterpulsation or extracorporeal life support can be beneficial for patients with persisting severe RV failure after embolectomy.1,4,51

Anticoagulation with warfarin is recommended for a minimum of 6 months if there is no contraindication. If not already in place, an inferior vena caval filter should be inserted into patients for whom anticoagulant therapy cannot be used.

**RESULTS**

Hospital mortality is variable and depends largely on the patient’s hemodynamic state at the time of embolectomy.2,2,3,5,5,12 Among patients who require cardiopulmonary resuscitation or institution of CPB before operation, mortality has ranged from 45% to 75%.3,7,5,3,5,12 Mortality is substantially less (3% to 36%) for patients who are more hemodynamically stable.3,7,5,3,5,14 Although satisfactory results were obtained by Clarke and Abrams without CPB, review of a multicenter study by Del Campo demonstrated 40% early mortality for 651 patients operated on with CPB, and 51% for patients in whom CPB was not used.3,7,34 A more recent review by Stein and colleagues of patients operated on after 1985 reported an early mortality of 20%.5,12 Two individual series of patients operated on since 1999 have reported 30-day mortality of 6% (3 of 47 patients) and 8% (4 of 25 patients).5,1,12 Instituting CPB in patients who are in shock permits salvage of some who cannot be saved by alternative techniques. Principal modes of death following embolectomy are cardiac failure, brain injury, and sepsis.4,1,5,5

Recurrent embolism is uncommon among hospital survivors.3 The majority maintain normal exercise tolerance and pulmonary artery pressures.1,5,9

**INDICATIONS FOR OPERATION**

Surgical pulmonary embolectomy is indicated in patients who do not respond to aggressive resuscitative measures or require instituting CPB for cardiogenic shock, and in whom thrombolytic or percutaneous catheter-based interventions are contraindicated or unsuccessful. It should also be considered in selected patients who are at substantial risk for thrombolysis, or when there is insufficient time for thrombolysis to be effective.6,6

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Thrombolytic Therapy**

Thrombolysis, which dissolves fibrin, can be life saving in patients with massive pulmonary embolism, overt hemodynamic instability, and cardiogenic shock.6,6,7,15 However, the potential benefit of this form of treatment must be weighed against risk of major hemorrhage, which increases with increasing age and body mass index.6,3,8 In a report by Gulba and colleagues comparing medical and surgical treatment of massive pulmonary embolism and shock, 10 of 13 patients (77%; CL 59%-90%) treated surgically survived.6,12 Twenty-four patients were given alteplase (tissue plasminogen activator [tPA]) until systemic and pulmonary artery pressures stabilized; heparin was given thereafter. Sixteen of these patients (67%; CL 54%-78%) survived (P = .5). However, major nonfatal hemorrhage occurred in 28% of the alteplase-treated patients, and 20% had recurrent embolization.

Current thrombolytic therapy most commonly involves use of recombinant human tissue plasminogen activator (tPA). One hundred milligrams is given via continuous intravenous infusion over 2 hours with or without concomitant intravenous heparin.6,6 This therapy elevates the risk of major catastrophic bleeding, and despite its use for patients with massive pulmonary embolism, no survival benefit over embolectomy has been demonstrated in large clinical trials.6,6

**Transvenous Catheter Pulmonary Embolectomy**

Several catheter-based techniques have been evaluated for treating pulmonary embolism. The objective is to reduce RP resistance and RV afterload and increase cardiac output. Techniques include (1) transvenous catheter embolectomy, which uses a steerable cup catheter to which suction is applied, (2) use of a catheter that delivers high-velocity jets of saline that draw thrombus toward the catheter and subsequently pulverize the clot, and (3) mechanical fragmentation using various devices combined with pharmacologic thrombolysis.6,12,87 The largest experience in the absence of thrombolytics is with the aspiration technique. Among 89 patients treated with this technique, 30-day mortality was 25% (n = 22; CL 20%-29%). Clinical success, defined as immediate hemodynamic improvement, occurred in 72 patients (81%; CL 77%-85%).5,12 Catheter intervention is currently indicated in patients with acute massive pulmonary embolism in whom an increased bleeding risk precludes administering systemic standard-dose fibrinolysis, and in patients not considered candidates for surgical embolectomy.6,6,88

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**Section II Chronic Pulmonary Thromboembolic Disease**

**DEFINITION**

Chronic pulmonary thromboembolic disease is entrapment of thrombi in pulmonary arteries from a single episode or repeated embolic episodes that subsequently organize, or thrombi that develop in situ in the pulmonary arteries into firm, fibrous tissue that becomes incorporated into the vessel...
wall. These processes result in variable degrees of pulmonary artery obstruction and consequent pulmonary hypertension when obstruction becomes severe. It is estimated that chronic pulmonary thromboembolic disease develops in 1% to 5% of all cases of acute pulmonary embolism.

**HISTORICAL NOTE**

Chronic pulmonary embolism was suspected by Hart in 1916 and by Molle in 1920, but it was not until 1928 that Ljungdahl described two symptomatic patients with chronic obstruction of the pulmonary arteries who ultimately died of right heart failure. The first successful embolectomies for recurrent pulmonary embolism were reported by Allison and colleagues in 1958 and by Snyder and colleagues in 1962. The technique was refined by Cabrol and colleagues, who used a lateral thoracotomy approach to obtain access to distal branches of the pulmonary arteries. Subsequently, several small series of patients were reported by Sabiston, Daily, and Dor and their colleagues, who used the lateral thoracotomy approach or CPB with a midline sternotomy. In 1980, Daily and colleagues reported use of hypothermic circulatory arrest in combination with CPB. This technique was used to eliminate severe back-bleeding and improve visualization of the pulmonary arteries during endarterectomy. It is currently the preferred method of management.

**MORPHOLOGY**

The chronic thromboembolic process typically involves the proximal pulmonary arteries from trunk to sublobar levels. The distal arterial vasculature remains patent. This forms the basis for surgical treatment of this disorder. The disease can result from a single embolic episode with nonresolution of large thromboemboli or from repeated embolic episodes. Pulmonary arteries remaining unobstructed are chronically exposed to high flow and eventually high pressure. As a result, the proximal patent pulmonary arteries become greatly enlarged, and the distal arterial vasculature develops characteristic changes of pulmonary hypertension (i.e., intimal proliferation and medial hypertrophy as described in Chapter 35, Box 35-3). Plexiform lesions in adult lungs that are diagnostic of primary pulmonary hypertension have been observed in chronic thromboembolic pulmonary hypertension.

The occlusive process is commonly discrete and central. When the thrombi become fibrotic and endothelialized, they no longer respond to thrombolytic or anticoagulant therapy. Occasionally, fresh thrombus is attached to the organized thrombus. Microscopically, thrombotic material demonstrates well-organized fibrous tissue, penetrating blood vessels, elastic fibers, and absence of endothelial cells. There is intimal and medial hyperplasia. Infarction of lung tissue infrequently occurs.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Symptoms**

In general, symptoms do not develop until months or years after the embolic event. They occur as a result of pulmonary hypertension and RV failure. Dyspnea with exertion is the most frequent presenting symptom. Other symptoms include fatigue, substernal chest pain with exercise, pleuritic pain, and hemoptysis.

**Signs**

Pertinent physical findings are related to right heart failure: jugular venous distention, hepatomegaly, ascites, and peripheral edema. The RV may be palpable near the lower left sternal border, and the pulmonic second sound accentuated and split. If right heart failure is severe, a murmur of tricuspid regurgitation is often present.

**Diagnostic Studies**

The chest radiograph may demonstrate RV enlargement and prominence of central pulmonary arteries. The ECG commonly shows RV hypertrophy with strain, right axis deviation, ST depression, T-wave inversion in the anterior precordial leads, and (less frequently) right bundle branch block. Pulmonary function studies are necessary to exclude restrictive or obstructive pulmonary parenchymal disease as the cause of the pulmonary hypertension.

A lung perfusion scan showing at least one segmental or larger defect is suggestive of chronic vascular obstruction. Often, however, the scan underestimates the severity of obstructive disease. CT scanning (Fig. 27-3) and MRI (Fig. 27-4) of the chest are important diagnostic studies and are being used with increasing frequency. Right heart catheterization is performed to measure RV and pulmonary artery pressures and document presence of shunting at the atrial or ventricular level. Pulmonary angiography is often performed as a part of right heart catheterization. It can generally be safely accomplished in patients with chronic pulmonary hypertension. A single injection of contrast material in each pulmonary artery is usually sufficient. Characteristic findings include dilated proximal pulmonary arteries, with obstruction of one or more lobar arteries and appearance of organized thrombi as filling defects, webs, or bands or completely thrombosed vessels. Angioscopy may be a useful adjunct to angiography, CT, or MRI when the diagnosis cannot be clearly established with those studies.

Coronary angiography should be performed in patients older than 40 to 45 years or in younger patients with risk factors for coronary artery disease if surgical treatment is contemplated, so that obstructive coronary lesions, if present, can be bypassed at the time of pulmonary endarterectomy.

**NATURAL HISTORY**

Patients with chronic pulmonary thromboembolic disease may remain asymptomatic for months or years. Hemodynamic progression may be the result of recurrent thromboembolism or in situ pulmonary artery thrombosis. Without intervention, survival is low and proportional to degree of pulmonary hypertension at time of diagnosis. In the study of Riedel and colleagues, survival at 5 years was 30% among patients with a mean pulmonary artery pressure exceeding 40 mmHg at time of diagnosis, and only 10% among those with a mean pressure above 50 mmHg. In the study of Lewczuk and colleagues, a mean pulmonary artery pressure of 30 mmHg was the threshold for poor prognosis. Among the 13 patients evaluated by Riedel and colleagues,
Figure 27-3  Computed tomographic image of chest in chronic pulmonary thromboembolic disease.  A, Eccentric endothelialized thrombi are present in both pulmonary arteries (arrows). B, Image at level of aortic arch shows disparity in pulmonary vasculature, with more visible branches of pulmonary artery in left lung (arrows) than in right. C, Image obtained at same level as B with lung windows demonstrates a mosaic pattern of attenuation; areas of higher attenuation (arrows) are areas of lung that are normally perfused. (From Dixon and King.\textsuperscript{66})

Figure 27-4  Pulmonary embolism demonstrated by magnetic resonance angiography.  A, Oblique sagittal maximum-intensity projection image acquired with gadolinium-enhanced sequence shows right lower lobe clot (arrow).  B, Findings on corresponding conventional pulmonary angiogram confirm right lower lobe obstruction (arrow). (From Gefter and colleagues.\textsuperscript{64})
mobilized by retracting the vena cava laterally and the aorta medially using encircling tapes (Fig. 27-6). The pericardial reflection over the pulmonary artery is incised and the more distal portion circumferentially mobilized 1 to 2 cm beyond the origin of the right upper lobe branch.

The general technique for establishing hypothermic circulatory arrest in adults is described in detail under “Aortic Arch Replacement” in Chapter 26. During cooling, methylprednisolone (7 mg · kg\(^{-1}\)) and thiopental (10-15 mg · kg\(^{-1}\)) are administered to enhance the neuroprotective effect of hypothermia. Mannitol (0.3-0.4 g · kg\(^{-1}\)) and furosemide (100 mg) are infused to preserve renal function. Hematocrit is maintained in the range of 18% to 22%. When the nasopharyngeal temperature reaches 12°C to 14°C, bladder temperature reaches 15°C to 18°C, and the electroencephalogram becomes isoelectric, circulatory arrest is established.
The patient is placed in a moderate Trendelenburg position, and the head is packed in ice. Then 20% to 25% of the patient’s calculated blood volume is withdrawn through the venous tubing into the reservoir of the oxygenator.

After circulatory arrest is established, the right pulmonary artery is incised between aorta and superior vena cava (Fig. 27-7, A), extending the incision below the orifice of the right upper lobe branch and into the anterior surface of the artery distally (Fig. 27-7, B). An endarterectomy plane is established with a sharp dissector (see Fig. 27-7, B), and the intima and a portion of media are removed. Establishing the correct plane is important; a plane that is too deep will result in perforation of the vessel, and a plane that is too superficial will result in an inadequate endarterectomy.  

The core of thrombus is isolated circumferentially (Fig. 27-7, C) and removed from the upper lobe and from the remaining portion of the pulmonary artery (Fig. 27-7, D). Applying gentle traction with forceps on the endarterectomy specimen while sweeping the wall of the pulmonary artery away will result in progressive removal of the thrombus. The thrombotic core is separated from the proximal portion of the right pulmonary artery and removed (Fig. 27-7, E). The arteriotomy is closed with a continuous 5-0 or 6-0 polypropylene suture (Fig. 27-7, F). Alternatively, a patch of autologous pericardium can be used that is sutured into place with a continuous 6-0 polypropylene suture.

Periods of circulatory arrest are limited to 20 to 25 minutes. Cold blood (18°C-20°C) is reperfused for 7 to 10 minutes between these intervals. During a reperfusion interval, the left pulmonary artery is circumferentially mobilized and the pericardium incised to permit exposure of the left upper lobe branch (Fig. 27-8). The incision begins in the pulmonary trunk and extends onto the left pulmonary artery to the level of the pericardial reflection or just beyond (see Fig. 27-8). Endarterectomy is performed as described for the right pulmonary artery. The thrombus is removed first from the upper lobe and lingular branches and then from more distal branches of the artery. The artery is closed directly or with a patch of autologous pericardium. CPB is reestablished and rewarming is begun as closure of the artery is completed.

The atrial septum is examined through a small incision in the right atrium. If a patent foramen ovale or an atrial septal defect is present, it is closed to prevent right-to-left shunting and hypoxemia in the postoperative period. If additional procedures such as valve replacement or repair or coronary artery bypass grafting are required, they are performed during rewarming. Repair or replacement of the tricuspid valve is rarely necessary.  

When rewarming is completed, air is evacuated from the cardiac chambers, CPB is discontinued, and the procedure is completed in the standard manner (see “Completing Cardio-pulmonary Bypass” in Section III of Chapter 2).

### SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is conducted as described in Chapter 5. Mechanical ventilation is used with an FiO2 sufficient to maintain SaO2 greater than 95%. PaCO2 is maintained at or below 35 mmHg. Reperfusion pulmonary edema is commonly encountered postoperatively and is an important problem in approximately 10% of patients. Lung injury usually develops within the first 48 hours and is characterized by hypoxemia and radiographic infiltrates in the areas that have been endarterectomized and reperfused. Treatment is generally supportive, using the lowest FiO2 to maintain SaO2 greater than 90% and positive end-expiratory pressures of 5 to 10 cm. Infusion of prostaglandin E1 at 0.01 to 0.1 mg · min"1 and inhaled nitric oxide (20-40 parts per million) may be indicated. Aggressive diuresis is often necessary to remove fluid and reduce incidence of pulmonary edema. 

Reperfusion pulmonary edema has been demonstrated to be neutrophil mediated, and treatment with agents that block selectin-mediated adhesion of leukocytes to the endothelium has reduced the prevalence of this complication.

Heparin is administered subcutaneously (5000-7500 units every 12 hours). Permanent anticoagulation with warfarin is initiated on the second postoperative day. Aspirin (80 mg daily) may be added.

### RESULTS

In experienced centers, early mortality has ranged from 4.4% to 21%. Important risk factors for early death include reperfusion lung injury, RV failure related to residual pulmonary hypertension, and duration of CPB. Addition of other procedures to pulmonary thromboendarterectomy has not been associated with increased early mortality. In a follow-up study of 532 patients from the University of California–San Diego (UCSD), which has accumulated the largest series of patients undergoing pulmonary thromboendarterectomy, 6-year survival was 75% (Fig. 27-9). Predominant modes of late death were persistent pulmonary hypertension and recurrent pulmonary embolism.

Dramatic reduction and, at times, normalization of pulmonary artery pressure and Rp can be achieved with a mean reduction in Rp of approximately 65%. In the follow-up study from the UCSD, 56% of the 306 patients whose functional status could be assessed were in New York Heart Association functional class I, 37% class II, 6% class III, and 1% class IV. Similar findings were reported by Saoudi and colleagues. A relationship was demonstrated between Rp and cardiac output and the distance patients could walk and flights of stairs they could climb. Of 133 patients not employed before pulmonary thromboendarterectomy, 62% returned to work. Ten percent required supplemental oxygen. Disease-related hospitalizations and emergency services requirement over the duration of follow-up were minimal.

### INDICATIONS FOR OPERATION

Pulmonary thromboendarterectomy should be considered in symptomatic patients who have hemodynamic or ventilatory impairment at rest or with exercise. Potential candidates for operation who are at the lower end of the range of elevated Rp (300-2000 dyn · s · cm"−5") include those with involvement limited to one pulmonary artery, those accustomed to vigorous activity, and those who live at high altitudes. Operation should also be considered in patients who have normal or nearly normal hemodynamics at rest, but in whom marked pulmonary hypertension develops during exercise.

A critical determinant of operability is the location and extent of thromboembolic obstruction. Occlusive thrombi must involve the branch pulmonary artery, lobar, or proximal segmental arteries. More distal thrombi are not currently amenable to thromboendarterectomy.
Figure 27-7 Endarterectomy of right pulmonary artery in chronic pulmonary thromboembolic disease. A, Approach to pulmonary artery. View is from left side of operating table. Superior vena cava is fully mobilized and retracted laterally, and aorta is retracted medially; the pulmonary artery is incised between these vessels. B, Endarterectomy plane is established with sharp dissector. C-D, Core of thrombus is isolated circumferentially and removed from upper lobe and distal pulmonary artery. E, Core is separated from proximal pulmonary artery and removed. F, Arteriotomy is closed with a continuous 5-0 or 6-0 polypropylene suture.
PART V  Diseases of the Thoracic Arteries and Veins

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Pulmonary artery aneurysms (that are amenable to surgical treatment) are discussed.

HISTORICAL NOTE

The first description of a pulmonary artery aneurysm was by Bristowe in 1860. He reported an arteriosclerotic fusiform aneurysm of the pulmonary artery observed at autopsy. In a review of 109,571 autopsies by Deterling and Clagett in 1947, only 8 proximal pulmonary artery aneurysms were identified. The first successful repair of an aneurysm of the pulmonary trunk was reported by Williams and colleagues in 1971. It was resected and replaced with a woven polyester graft. Aneurysmorrhaphy and patch repair were subsequently used as alternative methods of treatment.

MORPHOLOGY

Structural abnormalities, pulmonary hypertension, cardiac malformations, and infection, existing alone or in combination, appear to be predisposing factors to developing pulmonary artery aneurysms. A classification of aneurysms not associated with arteriovenous communications is shown in Box 27-1. Cystic medial degeneration and arteriosclerosis may contribute to formation of pulmonary artery aneurysms. Patients with Marfan syndrome may develop them, and these are prone to dissection. Congenital cardiac abnormalities are commonly associated with aneurysms of the pulmonary arteries; these include patent ductus arteriosus (the most common), ventricular septal defect, tetralogy of Fallot, pulmonary valve stenosis, and transposition of the great arteries. Aneurysms have also been observed in association with acquired cardiac conditions such as mitral stenosis and tricuspid regurgitation. Infection can also contribute to development of pulmonary artery aneurysms. In the preantibiotic era, tuberculosis and syphilis were commonly associated with aneurysms. Bacteria, including staphylococcal, streptococcal, and gram-negative species, and fungi have

Section III  Pulmonary Artery Aneurysm

DEFINITION

Pulmonary artery aneurysm is a localized vascular dilatation with deterioration of one or more layers of the pulmonary arterial wall. In this section, only aneurysms of the pulmonary trunk and branch pulmonary arteries (proximal pulmonary artery aneurysms) that are amenable to surgical treatment are discussed.

Box 27-1  Classification of Pulmonary Artery Aneurysms without Associated Arteriovenous Communications

<table>
<thead>
<tr>
<th>Structural Vascular Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital</td>
</tr>
<tr>
<td>Cystic medial degeneration/arteriosclerosis</td>
</tr>
<tr>
<td>Acquired</td>
</tr>
<tr>
<td>Marfan syndrome</td>
</tr>
<tr>
<td>Vasculitis</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Structural Cardiac Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital heart disease</td>
</tr>
<tr>
<td>Acquired heart disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial and fungal</td>
</tr>
<tr>
<td>Tuberculosis</td>
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<tr>
<td>Syphilis</td>
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<table>
<thead>
<tr>
<th>Trauma</th>
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<table>
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<tr>
<th>Idiopathic Syndromes</th>
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Modified from Bartter and colleagues. F3

The only absolute contraindication to operation is presence of severe underlying obstructive or restrictive lung disease. The greatest risk factor for operation is presence of high Rp without gross abnormalities visible in the major pulmonary arteries by angiography. Advanced age, severe RV failure, and comorbid conditions are associated with increased risk and are relative contraindications to operation.
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27-12), MRI, and pulmonary angiography can document the presence of proximal pulmonary artery aneurysms.\textsuperscript{[32]}

**NATURAL HISTORY**

Because pulmonary artery aneurysms are rare and coexisting conditions are common, natural history remains largely unknown. It is known, however, that rupture and dissection of such aneurysms occur.\textsuperscript{[52,6,3,9,5,11,1,3,5,4,57]} Death following rupture or dissection is common and often sudden.

**TECHNIQUE OF OPERATION**

Usual preparations for establishing CPB are made (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). After inserting appropriate monitoring devices and placing ECG electrodes, a median sternotomy is made. Cannulae are inserted into the ascending aorta and both venae cavae, venae cavae are encircled with tapes, CPB is established, and a venting catheter is inserted into the left atrium through a purse-string suture in the right superior pulmonary vein. The procedure can be performed with the heart beating and mild (34°C) hypothermia or with cardioplegia. In the latter situation, a cannula is inserted into the ascending aorta for delivery of antegrade cardioplegia and for later aspiration of air. A cannula is inserted into the coronary sinus through a purse-string suture in the right atrial wall. Cardioplegic solution is infused every 15 minutes either through the aortic root or retrogradely through the coronary sinus (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3).

The pulmonary artery is examined to determine the location and extent of the aneurysm (Fig. 27-13, \textit{A}). If the aneurysm is confined to the pulmonary trunk, excising a portion of the anterior wall to establish a normal diameter and closing the defect with a continuous 4-0 or 5-0 polypropylene suture can be performed.\textsuperscript{[55,52]} Alternatively, the aneurysmal segment can be excised and replaced with a woven polyester graft or pulmonary allograft.\textsuperscript{[52]} If the aneurysmal changes involve right and left pulmonary arteries as well, the aneurysmal segments are excised and pulmonary trunk, right, and left pulmonary arteries are replaced with a woven polyester bifurcation graft or pulmonary allograft (Fig. 27-13, \textit{B}).

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Patients with proximal pulmonary artery aneurysms may present with cough, hemoptysis, chest pain, and dyspnea, although many are asymptomatic. Symptoms, if present, may be related to associated cardiac or pulmonary conditions. There can be compression of the left main coronary artery resulting in myocardial ischemia.\textsuperscript{[56]} There are no characteristic physical findings. The chest radiograph may be normal, but if the aneurysm is large, it demonstrates a prominence along the left heart border (Fig. 27-10). CT (Figs. 27-11 and

**Figure 27-10** Chest radiograph of pulmonary artery aneurysm. There is marked enlargement of pulmonary trunk.

**Figure 27-11** Computed tomographic study of chest of patient shown in Fig. 27-10, demonstrating a 6-cm aneurysm of pulmonary trunk.
If the pulmonary valve is abnormal, it can be replaced using a pulmonary valve allograft or a composite valved conduit (see Technique of Operation in Chapter 38). Other cardiac malformations, if present, are corrected.

When rewarming is completed, air is evacuated from the cardiac chambers, CPB is discontinued, and the procedure is completed in the standard manner (see Completing Cardiopulmonary Bypass in Section III of Chapter 2).

An alternative procedure, bilateral lung transplantation and reconstruction of the pulmonary arteries using the donor pulmonary artery, has been successfully accomplished by Wekerle and colleagues in an 18-year-old patient with pulmonary hypertension and massive dilatation of the proximal pulmonary arteries.\(^\text{W1}\)

**Special Features of Postoperative Care**

Postoperative care is conducted as described in Chapter 5.

**Results**

Results of operative repair are primarily contained in isolated case reports.\(^{C5,C6,C7,C8,C9,C10,C11}\) Among patients undergoing elective operation, early results have been excellent. Little information regarding long-term outcomes is available.

**Indications for Operation**

Because of the excellent results that have been achieved with elective resection of proximal pulmonary artery aneurysms, operation should be considered in patients with isolated and substantial (>5-6 cm) dilatation of the pulmonary trunk and of the right and left pulmonary arteries. Presence of pulmonary hypertension strengthens the indication for operation. Patients who have other indications for operation, such as congenital or acquired cardiac lesions, should have repair of large coexisting pulmonary artery aneurysms. Although conservative management of large aneurysms has been reported, documentation of rupture and dissection would make this strategy inadvisable for patients who would otherwise be considered suitable for operation.\(^{C4}\)

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**Section IV  Pulmonary Artery Dissection**

**Definition**

Pulmonary artery dissection is separation of vessel layers of pulmonary arteries, most commonly of the pulmonary trunk, although it can extend into the major branches. It is a rare condition.

**Historical Note**

According to Shilkin and colleagues, the first reported case of pulmonary artery dissection was by Helmbrecht in 1842.\(^{S6}\) Fewer than 100 cases have been reported in the English literature.\(^{I1}\) Diagnosis has been established after death in the majority of cases. Few patients have been treated surgically.\(^{I1,L5,S4}\)

**Morphology**

Pulmonary artery dissection originates most commonly in the pulmonary trunk (71% of the 52 patients reviewed by Inayama et al.)\(^{I1}\) and in the major branches of the pulmonary arteries. It is frequently associated with pulmonary hypertension. Among patients who have pulmonary hypertension, only a small percentage have primary pulmonary hypertension. In the review of Inayama and colleagues, 28 patients had secondary pulmonary hypertension, and congenital cardiac malformations were present in 23; patent ductus arteriosus was the most common.\(^{I1}\) Marfan syndrome was present in only 1 of the 52 patients, although cystic medial degeneration was observed in the pulmonary arteries of 23 of 29 patients with detailed histologic studies. Pulmonary hypertension was present in 20 of these 23 patients.\(^{I1}\)

In the majority of reported cases (86%), diagnosis of pulmonary artery dissection was made at autopsy.\(^{I1}\) Rupture of
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valvotomy for valvar pulmonary stenosis at age 21. MRI demonstrated a 6-cm aneurysm of the pulmonary trunk. At operation, an intimal flap was noted in the left lateral wall of the pulmonary trunk. The pulmonary valve, pulmonary trunk, and proximal portions of right and left pulmonary arteries were excised and replaced with a pulmonary allograft.

A second patient, a 34-year-old woman, had primary pulmonary hypertension diagnosed 10 years previously and presented with chest pain, shortness of breath, and a large pericardial effusion. CT demonstrated an aneurysm of the pulmonary trunk and an intimal flap (see Fig. 27-15). At operation, there was evidence for rupture with a large hemothorax.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presenting symptoms are identical to those observed with acute aortic dissection and include severe chest pain, dyspnea, central cyanosis, and shock. Several days may elapse between onset of pain and rupture. Diagnosis was established by echocardiography, pulmonary angiography, or MRI in only 6 of 52 patients reported by Inayama and colleagues (Fig. 27-14). In a subsequent report, diagnosis was established by CT (Fig. 27-15). A new left hilar mass may occasionally be seen on chest radiograph.

NATURAL HISTORY

Prognosis of untreated pulmonary artery dissection is extremely poor. Diagnosis has been infrequently made before death, and only a few patients have been successfully managed by surgical intervention.

TECHNIQUE OF OPERATION

Technique of operation is identical to that described for treatment of pulmonary artery aneurysm (see Technique of Operation in the preceding section and Fig. 27-13). Heart and lung transplantation is an alternative and has been successfully performed in several patients (see Chapter 21).

RESULTS

Few patients have been successfully treated by direct repair. One developed dissection in an aneurysmal pulmonary trunk at age 56 and presented with chest pain and shortness of breath of 2 weeks’ duration. He had undergone pulmonary

the pulmonary artery into the pericardial cavity or mediastinum or into a pleural space was a frequent finding.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presenting symptoms are identical to those observed with acute aortic dissection and include severe chest pain, dyspnea, central cyanosis, and shock. Several days may elapse between onset of pain and rupture. Diagnosis was established by echocardiography, pulmonary angiography, or MRI in only 6 of 52 patients reported by Inayama and colleagues (Fig. 27-14). In a subsequent report, diagnosis was established by CT (Fig. 27-15). A new left hilar mass may occasionally be seen on chest radiograph.
and competent. The pulmonary trunk was replaced with a 32-mm polyester tube graft and a second 32-mm polyester graft was interposed between right and left pulmonary arteries. The two grafts were then joined in a T configuration. Several patients with severe pulmonary hypertension and extensive dissection or Eisenmenger syndrome have been successfully treated by heart and lung transplantation.\textsuperscript{2,4}

**INDICATIONS FOR OPERATION**

Because of the extremely poor prognosis associated with pulmonary artery dissection, operative treatment should be considered for any patient in whom the diagnosis is established.

---

**Section V  Pulmonary Artery Tumors**

**DEFINITION**

Primary tumors of the pulmonary artery are malignant tumors, most commonly sarcomas, usually arising in the pulmonary trunk and extending into right and left pulmonary arteries. They commonly involve the pulmonary valve and may extend into the RV.\textsuperscript{1,6} These tumors, although rare, are being reported with increasing frequency.\textsuperscript{2,4,8}

**HISTORICAL NOTE**

The first report of a sarcoma of the pulmonary trunk was by Mandelstamm in 1923.\textsuperscript{3,3} Early surgical treatment consisted of resecting the segment of pulmonary trunk containing tumor, pneumonectomy, or both.\textsuperscript{1,6} More recently, resecting and reconstructing the pulmonary arteries using CPB has been used.\textsuperscript{2,6,0}

**MORPHOLOGY**

Sarcomatous tumors arise from the intima of the pulmonary artery, most frequently from the dorsal surface of the pulmonary trunk.\textsuperscript{4,4} They rarely extend through the adventitia or invade surrounding structures. Pulmonary metastases are present in up to 60% of patients. Metastases to lymph nodes and other organs are less common.\textsuperscript{2,6} Microscopic features are highly variable. In a review of 99 pulmonary sarcomas by Lyerly and colleagues, many cell types were represented, including leiomyosarcoma, myxosarcoma, fibrosarcoma, chondrosarcoma, angiosarcoma, osteogenic sarcoma, and liposarcoma.\textsuperscript{1,6}

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Clinical presentation resembles that of more commonly occurring conditions such as chronic pulmonary thromboembolic disease. Symptoms include dyspnea, chest pain, cough, and hemoptysis. There are no characteristic physical findings. Diagnostic studies such as ventilation/perfusion scans, CT, echocardiography, and pulmonary angiography have only infrequently established the diagnosis preoperatively.\textsuperscript{4,5,6}

(Fig. 27-16). MRI with gadolinium contrast may be a useful diagnostic tool because tumor enhances more than bland thrombus.\textsuperscript{2,8} Fluorodeoxyglucose positron emission tomography (FDG-PET) may demonstrate increased uptake within the tumor.\textsuperscript{2,8,1} In the review of Lyerly and colleagues, correct diagnosis was made at postmortem examination in 59% of cases and after surgical exploration in 31%.\textsuperscript{4,1}

**NATURAL HISTORY**

Median duration of survival from diagnosis is approximately 1.5 months without surgical resection. Survival has not been affected by addition of adjuvant therapy.\textsuperscript{2,6} In a review by Blackmon and colleagues of 66 patients reported since 1990 who received some form of therapy (chemotherapy, irradiation, or surgery), 5-year survival was 18.5%.\textsuperscript{8,5}

**TECHNIQUE OF OPERATION**

Technique of operation in most instances is identical to that described for treatment of pulmonary artery aneurysm (see **Technique of Operation** in Section III of this chapter and Fig. 27-13). All visible tumor should be removed. Pulmonary thromboendarterectomy and pneumonectomy may be added to pulmonary artery resection if indicated.\textsuperscript{2,6,0}

**RESULTS**

Among 39 patients in the report of Lyerly and colleagues in whom diagnosis of pulmonary sarcoma was made before death, only 11 survived more than 1 year after diagnosis or initiation of therapy.\textsuperscript{1,6} Isolated instances of longer survival following complete resection with reconstruction of the pulmonary valve and pulmonary arteries have been reported.\textsuperscript{2,6,0} The role of adjuvant radiotherapy and chemotherapy is inconclusive.\textsuperscript{2,8,6} Resection of pulmonary metastases in the absence of distant disease may be beneficial.\textsuperscript{2,8,5}
INDICATIONS FOR OPERATION

Because radical surgical resection likely represents the only chance for cure, operation should be considered in patients who have no comorbid conditions that would preclude the use of CPB and who have no evidence of distant metastases. Adequate pulmonary reserve should be documented for patients who may require pneumonectomy.

REFERENCES

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ings at CT and radiography. AJR Am J Roentgenol 2007;188:W126-34.

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Acquired Diseases of the Systemic Veins

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**DEFINITION**

Acquired disease of the systemic veins entails obstruction—partial or complete—of the major veins of the thorax. Veins of surgical importance are the superior and inferior venae cavae (SVC and IVC). Left and right brachiocephalic veins, including the jugular-subclavian vein confluence, are major tributaries of the SVC and may be considered collectively with conditions of the SVC. Congenital anomalies of the venae cavae and axillary vein conditions such as effort thrombosis are not considered in this chapter. Obstruction results from extrinsic compression, direct invasion by disease processes, or thrombosis. **SVC syndrome** is the result of venous hypertension in the head, neck, and arms caused by SVC obstruction.

**HISTORICAL NOTE**

William Hunter described the first recorded case of SVC syndrome in 1757 in a patient with syphilitic aneurysm of the aorta. SVC obstruction was due to compression by the aneurysm. William Osler described SVC compression in his classic text of 1892: “Along the convex border of the ascending part [of the aorta], aneurism frequently develops, and may grow to a large size.... In this situation the sac is liable indeed to compress the superior vena cava, causing engorge-ment of the vessels of the head and arm.” William Stokes’ text of 1853 described SVC obstruction and noted the more frequent occurrence with cancer: “As an indication of intra-thoracic tumour, an extensively varicose state of the superficial veins of the neck and thorax is probably less frequent in aneurismal than in cancerous disease.... The superior cava may be adherent to the tumour, and become narrowed, not only by pressure, but by adhesion of its internal surfaces.”

Gomes and Hufnagel reviewed cases of SVC obstruction reported before 1975. Data from more than 90 publications, including 1980 cases reported in the literature since 1934, were reviewed by Ahmann in 1984. The clinical problem was reviewed by Nieto and Doty in 1986.

The first successful bypass operations for SVC obstruction by Klassen and colleagues in 1951 and Bricker and McAfee in 1952 were performed using autologous femoral vein grafts. In 1965, Hanlon and Danis used other large veins to replace or bypass the SVC, employing variously the femoral, subclavian, and jugular veins. In 1962, Benvenuto and colleagues constructed a composite panel graft from pieces of saphenous vein for replacing the SVC. The operative approach to relieve venous obstruction up to 1970 was reviewed by Haimovici and colleagues. They concluded that autologous veins are preferable for venous replacement. All
reported experimental and clinical experiences with vena cava replacement or bypass up to 1974 were reviewed by Scherck and colleagues. A number of conduits had been tried, including autologous, homologous, and heterologous vein, aorta, and various synthetic materials. These authors concluded that autologous vein grafts of nearly the same size as the SVC were most likely to remain patent. To obtain such a large autologous vein usually requires a large vein from elsewhere in the body, with resultant venous drainage problems, or constructing a composite graft from a smaller vein.

Synthetic grafts are attractive because of their convenience and availability and because of the variety of sizes available. In 1973, Effeney and colleagues reported successful bypass of the SVC using polyester grafts. In 1977, Avasthi and Moghissi used a polyester graft interposed between the brachiocephalic vein on the left side and right atrial appendage to bypass the obstructed SVC. Thrombosis of polyester grafts limited success of the procedure. Expanded polytetrafluoroethylene (PTFE) was used successfully as a venous replacement conduit in experimental venous operations in dogs. Hiratzka and colleagues showed that PTFE and polyester were equally poor venous substitute conduits in the experimental setting, and that they did not approach the effective patency of autologous vein grafts. Reichle and colleagues suggested that this was because autologous vein grafts have a living endothelial surface even after initial endothelial desquamation, whereas prosthetic graft inner surfaces are composed of collagen matrix. Nevertheless, success using PTFE grafts has been reported. Antiplatelet-adhesive drugs may be of benefit in maintaining patency of PTFE grafts. Dartevelle and colleagues reported that 12 of 13 PTFE grafts used to replace the SVC were patent an average of 24 months after operation.

Composite vein grafts constructed from the saphenous or external jugular veins, in paneled or longitudinal fashion, have been used clinically for SVC bypass or replacement (both techniques are discussed in detail later in this chapter). In 1974, Chiu and colleagues reported constructing a composite vein graft from the external jugular vein, which was matched to the size of the SVC. The donor vein was opened longitudinally and wrapped in spiral fashion around a tubular stent of approximately the same size as the SVC. Vein edges were then sutured together to form the conduit. The graft occluded in the initial three experiments in dogs. After that, however, 10 consecutive grafts remained patent for up to 15 months. This report prompted successful application of this technique in humans by Doty and Baker in 1976. Successful percutaneous balloon dilatation of the SVC in a child was reported by Rocchini and colleagues in 1982. In 1986, Sherry and colleagues reported successful dilatation of an SVC stricture caused by pacemaker electrodes in an adult. In 1987, Rosch and colleagues used an expandable wire stent to treat SVC obstruction caused by malignant disease that recurred after extensive radiation therapy.

**MORPHOLOGY AND PATHOGENESIS**

**Morphology**

**Superior Vena Cava**
The SVC is located in the middle mediastinum and is surrounded by relatively rigid structures including the trachea, right bronchus, aorta, pulmonary trunk, and perihilar and paratracheal lymph nodes. It is thin walled, compliant, and easily compressible. Pressure within it is low. The SVC originates as the confluence of right and left brachiocephalic veins and extends for a distance of 6 to 8 cm to the right atrium. It is inside the pericardial sac for the distal several cm of its course. The azygos vein is the only major venous channel that enters the SVC; it enters posteriorly just above the pericardial reflection and is an important venous collateral pathway.

**Collateral Circulation**

SVC obstruction stimulates formation of extensive venous collateral circulation (Fig. 28-1). The azygos vein is the only major venous channel that enters the SVC and is the most important collateral pathway. When SVC obstruction is located caudad to a patent azygos vein, there is retrograde flow through the azygos and hemiazygos veins to the lumbar veins below the diaphragm and to the IVC. When obstruction is cephalad to the patent azygos vein, collateral veins in the neck allow blood flow to enter the azygos system and continue directly into the distal SVC below the obstruction. When connection of the azygos vein to the SVC is involved in the obstruction, more complex and varied pathways must develop to drain the upper body. One prominent system consists of the internal thoracic veins, which connect to superior and inferior epigastric veins and subsequently to the IVC by way of the external iliac veins. Lateral thoracic veins drain to thoracoepigastric veins; eventually, blood may enter the femoral veins. Paraspinal veins form a collateral network that connects to the IVC via lumbar veins. The esophageal venous network also can decompress the thorax via the left gastric vein to the portal system. This pathway is not very important unless esophageal varicosities develop, and only rarely are these associated with bleeding into the gastrointestinal tract. Subcutaneous veins are a particularly important means of bringing blood flow from the upper body to below the diaphragm via the IVC.

Despite extensive collateral circulation that may develop, venous pressure in the SVC as high as 200 to 500 cm of water has been recorded. Cerebral venous decompression may be provided through a single internal jugular vein, because the veins of the right and left sides of the brain are in continuity through midline venous sinuses. Superior and inferior sagittal sinuses drain the cerebral hemispheres to the confluence of sinuses that communicate through transverse and sigmoid sinuses to either internal jugular vein. The cavernous sinus also connect both sides of the brain to either internal jugular vein. Cerebral venous drainage, therefore, may remain adequate.

**Pathogenesis**

SVC obstruction may be caused by a spectrum of malignant (Table 28-1) and benign (Box 28-1) conditions. Disease in any adjacent anatomic structures may contribute to SVC syndrome. The common causes of SVC obstruction have changed over the past 50 years. In 1949, the most common were thoracic malignancy (33%), aortic aneurysm (30%), and chronic granulomatous mediastinitis (19%). Up until 1962, approximately 25% were due to benign disease; between 1969 and 1979, that proportion decreased to 3%. Currently, malignancies account for the majority of cases. Iatrogenic causes such as indwelling catheters are becoming more frequent, and an increasing number of
infectious causes are being reported in immunosuppressed patients. E3,R2

**Benign Causes**

Reviews from Mayo Clinic and Cleveland Clinic reported mediastinal granulomatous disease resulting in fibrosing mediastinitis as a prominent cause of benign SVC obstruction. M1,P1 The most common etiologic agent is histoplasmosis, which causes a caseating granulomatous process in mediastinal lymph nodes that compresses, fibroses, and contracts around the SVC and may result in secondary thrombosis. Fibrosing mediastinitis resulting from radiation therapy can be progressive and involve the SVC years after radiation treatment has been completed.

Iatrogenic causes have been increasing in importance because of increased use of invasive intravenous procedures such as cardiac pacemaker electrodes, central venous and pulmonary artery catheters, hyperalimentation and chemotherapy catheters, and extracorporeal membrane oxygenation. Mazzetti and colleagues reviewed pacemaker electrodes as a cause and found four cases of SVC obstruction among 2600 patients followed in a pacemaker clinic. M6 They also reviewed 37 cases reported in the literature and concluded that prevalence of this complication is likely lower than 1 in 1000. A more recent publication identified 104 patients from a review of 74 different publications. Williard and colleagues reported the Memorial Sloan-Kettering Cancer Center experience with thrombosis of long-term vascular access. W1 Occurrence of thrombosis of access catheters placed through the SVC was 7%, compared with 19% for catheters placed through the IVC. About half the thromboses involved just the catheter; the other half involved the blood vessel through which the catheter was introduced.

In infants, substantial morbidity is associated with chronic central venous access catheters. S16 In the series of Swaniker and Fonkalsrud, IVC occlusion occurred in 4.5% and SVC occlusion in 11% of 510 infants having 756 central venous catheters placed for parenteral nutrition. S16 Head and neck swelling developed in all with SVC occlusion, pleural effusions developed in 50%, and two infants died. Thrombosis of
the SVC around these catheters is especially troublesome when they are required for permanent life support and cannot be conveniently removed. In addition, thrombosis frequently follows the entire intravascular course of the catheter and thus is extensive, involving the major SVC venous tributaries. SVC thrombosis can be an important complication after extracorporeal membrane oxygenation. Zreik and colleagues reported 7 of 60 neonates (12%; CL 7%-18%) had either complete or partial SVC obstruction. Other benign causes include benign tumor, vascular aneurysm, a variety of cardiac and pulmonary diseases, and mediastinal hematomas.

**Malignant Causes**

Intrathoracic malignancy now accounts for more than 90% of SVC obstructions, with bronchogenic carcinoma responsible for 67% to 82%. SVC syndrome develops in 3% to 15% of patients with bronchogenic carcinoma. Bronchogenic carcinoma cell type associated with SVC obstruction appears to be somewhat variable, which may in part be related to difference in tumor classification schemes used by different investigators. Squamous (epidermoid) carcinoma accounts for 22% to 27% of cases and appears to be relatively consistent across reports. Small-cell carcinoma is the most variable (18%-46%), although its etiologic role appears to be increasing. Lymphoma is the second most frequent cause of SVC obstruction, accounting for 5% to 15% of cases. These malignancies are located in the anterior mediastinum and produce obstruction by external compression from the front. Thoracic metastasis from extrathoracic malignancies, particularly breast and testicle, accounts for a small number of SVC obstructions.

Malignancy is also the most common cause of SVC obstruction in children. In contrast to adults, however, non-Hodgkin lymphoma is the leading etiology.

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

#### Superior Vena Cava Syndrome

Because extrinsic compression usually produces obstruction gradually, collateral circulation develops, the obstruction is usually well tolerated, and the patient has few if any signs and symptoms. If obstruction develops rapidly, as in malignant tumor invasion and in infants and children with central venous catheters, collateral circulation may not have time to develop and adequately decompress upper body veins. The most severe syndrome develops in cases of SVC thrombosis in which obstruction is sudden and collateral venous channels have no time to develop. Thrombosis may involve major caval tributaries as well and thus eliminate major collateral pathways. Thrombosis often accompanies SVC obstruction from any cause and compounds the problem because (1) subsequent fibrotic organization of the clot results in permanent SVC stenosis or closure, and (2) thrombosis does not respond to treatment directed at the primary disease process that resulted in the SVC obstruction.

Thoracic lymphatic ducts drain into the subclavian veins and are affected by venous hypertension associated with SVC obstruction. Pulmonary lymphatics may also be secondarily affected, leading to increased lung water and dyspnea. Respiratory insufficiency is frequently associated with acute SVC obstruction and may be difficult to manage. Chyloous pleural effusion may result from thoracic lymphatic obstruction.

#### Symptoms

Patients with SVC obstruction usually present with a well-established syndrome that is easily recognized and unmistakable. Only rarely does complete SVC obstruction occur without noticeable signs or symptoms. The typical syndrome consists of swelling of face, neck, and arms; shortness of breath; orthopnea; and cough. Patients may notice tightness of a shirt collar and that their face is flushed and swollen, especially around the eyes. Other symptoms include hoarseness, stridor, tongue swelling, nasal congestion, epistaxis, dysphagia, headache, dizziness, syncope, lethargy, and

---

**Table 28-1 Malignant Causes of Superior Vena Cava Syndrome**

<table>
<thead>
<tr>
<th>Malignant Cause</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchogenic Carcinoma</td>
<td>170</td>
<td>83</td>
</tr>
<tr>
<td>Undifferentiated</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Epidermoid</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Small cell</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Large cell</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>22</td>
<td>11</td>
</tr>
<tr>
<td>Lymphoblastic</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Lymphocytic</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Histiocytic</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Hodgkin disease</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Unclassified</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Metastatic</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Thymic</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

*Data from Parish,18 Lochridge,19 and Perez.20

**Box 28-1 Benign Causes of Superior Vena Cava Syndrome**

- Mediastinitis (60%-70%)
- Idiopathic
- Histoplasmosis
- Postradiation therapy
- Other:
  - Tuberculosis
  - Actinomycosis
  - Syphilis
  - Sarcoidosis
  - Pyogenesis
  - Silicosis
- Benign tumor:
  - Thymoma
  - Teratoma (benign)
  - Substernal thyroid goiter
  - Cystic hygroma

*Data from Mahajan.21

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chest pain. Symptoms are aggravated by bending forward, stooping, or lying down. Many patients become dyspneic when recumbent and must sleep in a chair.

**Signs**

The most common signs are dilatation and tortuosity of upper body veins, plethora or cyanosis of the face, and swelling of face, neck, or arms. Other signs include proptosis, glossal edema, rhinorrhea, laryngeal edema, mentation changes, elevated venous and cerebrospinal fluid pressures, and chylous pleural effusion. Signs and symptoms suggesting cerebral or laryngeal edema were shown to be of prognostic importance by Lochridge and colleagues.18 Headache, vertigo, visual disturbances, decreased mentation, stupor, somnolence, and convulsions indicate cerebral edema12,14, hoarseness and stridor suggest laryngeal edema.

**Diagnosis**

Clinical diagnosis is usually obvious. Location, degree, and cause of SVC obstruction should be characterized in every case. There is some controversy about how specific this characterization should be, because more than 90% of cases are due to malignancy. Some believe that palliation of the intrathoracic malignancy should proceed without delay. Others argue that SVC syndrome is seldom a medical emergency and should be characterized as completely as possible in an orderly fashion so that treatment can be specific. Although tissue diagnosis by biopsy can usually be obtained, in some cases it may be difficult and even hazardous to do so. Patients seek relief of symptoms of SVC syndrome and seldom complain of symptoms related to the etiologic cause of the obstruction. Treatment of SVC syndrome should be accompanied by diagnostic measures and therapy directed at the causative primary disease.

**Chest Radiography**

Chest radiography is helpful but not specific in diagnosing SVC obstruction. Because bronchogenic carcinoma is the most common cause of SVC syndrome, the chest radiograph often shows a right-sided hilar mass. An anterior mediastinal mass suggests lymphoma.

**Venography**

The most useful diagnostic procedure is bilateral arm contrast venography10,13 (Fig. 28-2). It establishes:

- Location of SVC obstruction
- Degree of obstruction
- Degree of involvement of caval tributaries
- Extent of collateral venous pathways
- Extrinsic compression vs. intrinsic SVC obstruction

Identifying retrograde propagation of thrombosis that involves caval tributaries may indicate that caval obstructive symptoms are not likely to respond to nonoperative therapy.

Using venography in 36 patients, Stanford and Doty defined four patterns of venous circulation useful in planning therapy13 (Box 28-2).

**Box 28-2** Type of Superior Vena Cava Obstruction According to Venographic Pattern

| Type I | Partial obstruction (up to 90% stenosis) of the superior vena cava (SVC) with patency of the azygos–right atrial pathway |
| Type II | Near-complete to complete obstruction (90%-100%) of the SVC with patency and antegrade flow in the azygos–right atrial pathway |
| Type III | Near-complete to complete obstruction (90%-100%) of the SVC with reversal of azygos blood flow |
| Type IV | Complete obstruction of the SVC and one or more of the major caval tributaries, including the azygos systems |

**Two-Dimensional Echocardiography**

Masses in the SVC are imaged with great clarity by two-dimensional echocardiography (Fig. 28-4). The image is dynamic, so movement of obstructing lesions may be detected. It is useful in evaluating clot formation on central venous catheters and other devices.

**Computed Tomography**

Computed tomography (CT) provides an effective noninvasive means of analyzing the SVC and its tributaries. It has increasing importance in evaluating SVC syndrome and masses in the right atrium and IVC (Fig. 28-5). Its advantages are outlined by Moncada and colleagues11:

- Caval anatomy can be related to surrounding mediastinal structures.
- Mediastinal masses or lymph node pathology relative to the SVC can be located.
- Directed needle biopsy of mediastinal masses is facilitated.
- Patency of the internal jugular veins in the neck can be assessed despite extensive occlusion of tributaries of the SVC.

**Magnetic Resonance Imaging**

Magnetic resonance imaging is useful in assessing graft patency after operation for SVC syndrome15.

**Other Diagnostic Methods**

Other diagnostic methods including ultrasonography, positron emission tomography (PET), cytology, isotope venography, bronchoscopy, lymph node biopsy, mediastinal biopsy, mediastinoscopy with biopsy, and exploratory thoracotomy are indicated for individual cases. However, risks of interventional studies—patient discomfort, bleeding, and interruption of venous collaterals—should be weighed against the probability of a successful diagnosis. Invasive diagnostic tests may worsen SVC syndrome and should be avoided whenever possible.
Figure 28-2  Bilateral arm venogram showing obstruction of superior vena cava (SVC). A, Contrast injected via right basilic vein shows complete occlusion of SVC at right brachiocephalic vein junction. Collateral veins have formed in cervical region. There is reflux into right internal jugular vein, suggesting venous pressure is elevated enough to cause regurgitation of the valve at the jugular–subclavian vein confluence. B, Contrast injected via left cephalic vein shows left brachiocephalic vein occlusion back nearly to left jugular-subclavian confluence. A stump of brachiocephalic vein is accessible for attaching a bypass graft. Collateral veins formed in the cervical region communicate with paravertebral veins.

NATURAL HISTORY

The natural history of SVC obstruction and accompanying SVC syndrome is variable and depends on etiology of the obstruction, rapidity of onset, extent of the obstructive process, and extent of collateral venous circulation. Collateral venous circulation usually develops rapidly in response to SVC obstruction and is often sufficient to relieve SVC syndrome. The relationship of SVC obstruction to location and patency of the azygos vein has an important effect on natural history. When the azygos vein is closed, central thoracic collateral circulation is eliminated and SVC syndrome is worse because venous drainage from the upper body is dependent on smaller, less reliable venous channels in the chest wall and skin.

Even minimal tumor invasion of the SVC or compression by benign tumor may stimulate formation and propagation of blood clot within the vena cava. Malignant diseases resulting in acute SVC obstruction and thrombosis may not resolve with thrombolytic and radiation therapy. Acute SVC obstruction associated with signs of cerebral or laryngeal edema results in death within 6 weeks, apparently related to SVC syndrome rather than the primary etiology of the caval obstruction. The malignant process responds to therapy in
PART V Diseases of the Thoracic Arteries and Veins

Figure 28-3  Digital angiography in superior vena cava obstruction, venous phase. A, Anteroposterior projection shows extensive collateral venous network communicating with azygos system of veins in thorax and extending to a venous plexus below diaphragm. B, Oblique projection demonstrating extensive venous collateralization bringing systemic venous return from upper body to venous circulation below diaphragm.

a variable manner depending in part on cell type, ultimately determining the patient’s fate. Surgical intervention may be beneficial if the SVC syndrome is life threatening. It allows treatment of the malignancy to proceed in an orderly fashion and provides patient comfort.

Fibrosis associated with clot resolution and late clot propagation may be accompanied by worsening of symptoms and signs of SVC syndrome, despite adequate venous collateralization. Thus, SVC obstruction may persist even though there appears to be good response to treatment of the tumor. Some benign causes of SVC obstruction lead to severe and relentless inflammation and fibrosis, resulting in recurrent extending obstruction.

Clot propagation within the venous system proximal to the primary site of SVC obstruction may lead to progression of SVC syndrome in patients with benign etiology. Clot formation around indwelling catheters is especially prone to extensive thrombosis of the SVC and major thoracic and cervical venous tributaries. Some patients with SVC obstruction may never develop adequate collateral circulation even though the causative process is stabilized or eliminated.

TECHNIQUE OF OPERATION

Restoring thoracic venous drainage usually requires bypass of obstructed native venous channels using, when available, autologous tissue conduits to provide optimum long-term patency. Venous conduits include spiral saphenous vein, femoral vein, simple saphenous vein, and composite autologous vein grafts. In unusual situations, other venous conduits, such as composite azygos vein-IVC or jugular vein-femoral vein grafts, can be used. If autologous venous tissue is not available, aortic allografts, venous allografts, and autologous or homologous pericardial tubes can be used as conduit. Prosthetic grafts are generally inferior to autologous tissue grafts.

Successful bypass grafting depends on (1) adequate size of the conduit and (2) proper orientation. Graft diameter should closely match that of the native inflow vein to prevent residual obstructive flow gradients. To prevent graft kinking and obstruction, graft length should be measured so that it is not redundant. Both graft inflow and outflow sites should be free of intraluminal obstructions such as atrial trabeculations, adherent venous thrombus, or abnormal vascular intima.

Spiral Saphenous Vein Graft

The most extensive experience has been with the spiral saphenous vein graft conduit, a concept developed experimentally by Chiu and colleagues and applied clinically by Doty and Baker. Operation is performed through a median sternotomy or via a smaller incision using a partial upper half sternotomy (Fig. 28-6). A simultaneous incision is made in the thigh
over the course of the saphenous vein. The left brachioce-
phalic vein is mobilized to the left internal jugular–left sub-
clavian vein confluence. When the brachiocephalic vein and
subclavian-jugular confluence are thrombosed, it is necessary
to mobilize either the left or right internal jugular vein, which
then becomes the inflow point of the upper body venous
compartment. In this situation the midline incision may be
extended superiorly to the left or right and the strap muscles
divided to provide an unrestricted passageway for the bypass
conduit. The largest of the two jugular veins may also be
exposed and mobilized through a secondary cervical incision.
The two incisions are joined in a tunnel beneath the sterno-
cleidomastoid muscle. Biopsy samples of abnormal tissue sur-
rounding the SVC are obtained.

Diameter of the inflow vein (usually left brachiocephalic
or jugular) and distance from vein to right atrial appendage
are measured. After mobilizing the saphenous vein, its average
diameter is measured. Length of saphenous vein to be
removed is determined from (1) the ratio of the desired graft
diameter to the average diameter of the saphenous vein (SV),

Figure 28-4  Two-dimensional echocardiogram of partial obstruc-
tion of superior vena cava (SVC). Upper panel, (Before) shows image
of SVC before operation. Mass in SVC is an organized clot infected
with Candida albicans. Lower panel, (After) shows SVC cleared of
mass and patent.

Figure 28-5  Computed tomography of thorax showing heart with mass in right atrium. Inset shows
organized thrombus removed at operation.

Figure 28-6  Spiral vein bypass of obstructed superior vena cava
through a ministernotomy. Midline incision about 10 cm in length
is made over upper sternum. The sternum is divided in the midline
to the third intercostal space, where it is divided transversely.
Ascending aorta and right atrial appendage are exposed. Simultane-
ous incision is made in the thigh over greater saphenous vein.
graft diameter to less than that of the inflow vein, which could produce stasis.

After administering heparin (100 units · kg$^{-1}$) intravenously, a vascular clamp is applied at the internal jugular–subclavian vein junction and the brachiocephalic vein divided, retaining as much length as possible. The distal end of the brachiocephalic vein is oversewn for secure closure (Fig. 28-8). Thrombus or any other abnormal tissue is removed from the inside of the brachiocephalic vein. The vein graft is pushed slightly off the end of the stent to allow construction of an end-to-end anastomosis to the brachiocephalic vein using continuous 7-0 polypropylene suture (Fig. 28-8, B). If the internal jugular vein is selected as the site for anastomosis, a partial occlusion clamp is applied at the intended outflow point and an end-to-side anastomosis performed. The stent is then removed from the graft.

When the graft must cross the thoracic inlet, an external stent is employed to prevent graft compression. A short segment of an externally reinforced PTFE graft somewhat larger than the spiral vein graft is placed around the vein graft as it crosses the thoracic inlet. A curved vascular clamp is placed across the right atrial appendage, and the tip is excised. The opening in the appendage is cleared of trabeculae to ensure unrestricted blood flow. The graft is anastomosed to the appendage, using continuous 5-0 polypropylene suture

and (2) distance to the right atrial (RA) appendage according to the following formula (Eq. 28-1):

\[
\text{Inflow vein to SV length} = \frac{\text{Inflow vein diameter (mm)}}{\text{SV diameter (average)}} \cdot \text{Inflow vein to RA appendage length (cm)}
\]

For example, if the brachiocephalic vein diameter is 12 mm, saphenous vein diameter is 4 mm, and distance to right atrial appendage is 10 cm, then 30 cm of saphenous vein is required ([12/4] · 10 = 30 cm).

The required length of saphenous vein is removed and its side branches ligated. The vein is incised longitudinally through its entire length (Fig. 28-7, A). A thoracostomy tube of the same diameter as the brachiocephalic or jugular vein is selected as a stent. The opened vein graft is flattened and wrapped around the stent in spiral fashion (Fig. 28-7, B), with the endothelial surface of the vein against the stent. Continuous sutures of 7-0 polypropylene are used to join the edges of the graft (Fig. 28-7, C), forming a large conduit with the same internal diameter as the stent. There is no advantage of a larger or smaller conduit. A smaller conduit could, in theory, have a hemodynamic advantage by increasing flow velocity in the graft. However, because the graft diameter is always smaller than that of the SVC, velocity of flow through the graft is substantial, obviating need to reduce...
Figure 28-8 Insertion of spiral vein graft between brachiocephalic vein and right atrium to bypass obstructed superior vena cava. A, Left brachiocephalic vein is occluded with a soft-jaw clamp. Vein is divided and distal (caval) end oversewn. B, End-to-end anastomosis of spiral vein graft to brachiocephalic vein. C, Right atrial appendage is isolated by vascular clamp. Tip of appendage is excised and all trabeculae removed, and spiral vein graft is anastomosed to it. D, Completed repair.
(Fig. 28-8, C). If the atrial appendage is not present, the graft is anastomosed to the lateral wall of the right atrium. The completed bypass graft must be oriented correctly and be the right length (Fig. 28-8, D). Extra length serves no advantage and runs a risk of kinking the graft or impeding blood flow.

Direct Operation on Superior or Inferior Vena Cava

Direct operation on the SVC or IVC is performed when there is blood clot or tumor partially obstructing the lumen. Indications include removal of thrombus surrounding intraluminal catheters used for parenteral feeding, chemotherapy, or cardiac pacing. In these cases, the thrombus may adhere to the catheter or the intima of the SVC, making nonoperative removal of the mass hazardous or impossible. There may be infection associated with the foreign body or invading the thrombus. Procedures on the IVC are usually performed for renal cell carcinoma when there is a long mobile or adherent tumor mass in the IVC or right atrium extending from the renal vein that cannot be safely removed from the right atrium.

For procedures involving the SVC, a median sternotomy is made. Strategy for inserting the venous cannulae for venous return is based on location of the mass that is to be removed (see Figs. 28-4 and 28-5). If the mass is located completely within the SVC, a two-stage venous cannula is inserted through the right atrial wall and passed into the IVC. Masses that completely fill the right atrium require peripheral cannulation (femoral vein, internal jugular vein) (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2).

CPB is established, and the patient’s body temperature is lowered to 16°C to 20°C (see “Aortic Arch Replacement” under Technique of Operation in Chapter 26). Cardioplegic solution can be administered to arrest the heart after placement of an aortic occlusion clamp. Alternatively, the procedure can be performed using hypothermic fibrillation. When the target temperature is reached, CPB is discontinued. Venous cannulae may be removed to enhance exposure.

The SVC is incised to expose the mass. Endarterectomy technique using a Freer septum elevator may be necessary to remove adherent thrombus (see Fig. 27-7 in Chapter 27). The mass is removed completely, even if a secondary incision is required, and the access incision closed. If a portion of the wall of the vena cava has been excised, the defect can be repaired using a patch of autologous or bovine pericardium to prevent caval stenosis. Air is evacuated from the right heart, CPB is resumed, and rewarming commenced (see “Rewarming” in Section IV of Chapter 2).

Masses in the IVC adjacent to the right atrium are exposed through incision in the right atrium after establishing hypothermic circulatory arrest. It is sometimes necessary to extend the incision into the IVC. The orifices of the hepatic veins should be thoroughly inspected to ensure that no residual tumor or thrombus remains.

Retroperitoneal tumors, especially renal cell carcinoma, have a tendency to spread into the venous system and in advanced stages can involve the suprahepatic IVC and right atrium. Hypothermic CPB with an interval of circulatory arrest permits safe removal of tumor and thrombus from the retrohepatic segment of the IVC as well as from the right atrium and pulmonary artery. Alternative strategies include beating-heart CPB and veno-venous bypass.

RESULTS

Long-term follow-up of a small number of patients receiving spiral saphenous vein grafts for SVC obstruction has demonstrated excellent results. SVC syndrome is immediately relieved. When operation is performed in patients with malignancies, natural history of the tumor determines outcome. Lochridge and colleagues reported that of six patients undergoing operation for malignant disease, all were relieved of SVC syndrome with no recurrence, although all died within 1 year from their malignancy. Smith and Brantigan also reported successful use of a spiral vein bypass graft in the setting of bronchogenic carcinoma, and Anderson and Li have used it as an interposition graft to reconstruct the SVC after resecting a leiomyosarcoma; the graft was patent on computed axial tomography 10 months postoperatively.

Long-term results are known when operation is performed for SVC obstruction from benign causes. Doty and colleagues reported on outcome of 16 such patients with mean follow-up of 10.9 years (range 1 month to 23.7 years). All patients survived the operation and were discharged from the hospital. Anticoagulation with warfarin was not used after operation in any patient, but all received aspirin. Patient outcome is summarized in Table 28-2. Grant patency was confirmed by Doppler ultrasound, which showed increased flow velocity over the jugular vein on the side of the bypass graft. In some cases, venography documented patency (Fig. 28-9). Patency was inferred in most cases by freedom from symptoms of SVC syndrome.

Table 28-2  Outcome after Spiral Vein Bypass Graft

<table>
<thead>
<tr>
<th>Case</th>
<th>Years of Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23.7</td>
<td>Asymptomatic; farming</td>
</tr>
<tr>
<td>2</td>
<td>21.3</td>
<td>Asymptomatic; graft patent when divided during reentry sternotomy</td>
</tr>
<tr>
<td>3</td>
<td>20.3</td>
<td>Asymptomatic; runs 3-4 miles, tennis</td>
</tr>
<tr>
<td>4</td>
<td>17.0</td>
<td>Died; 3 reoperations for graft occlusion</td>
</tr>
<tr>
<td>5</td>
<td>14.9</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>6</td>
<td>13.8</td>
<td>Asymptomatic; exercises regularly; graft occlusion, revised at 4 days</td>
</tr>
<tr>
<td>7</td>
<td>12.4</td>
<td>Occasional swelling; graft occlusion at 5 months</td>
</tr>
<tr>
<td>8</td>
<td>9.6</td>
<td>Asymptomatic; runs regularly</td>
</tr>
<tr>
<td>9</td>
<td>10.2</td>
<td>Asymptomatic; skiing, scuba diving</td>
</tr>
<tr>
<td>10</td>
<td>7.1</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>11</td>
<td>7.8</td>
<td>Asymptomatic; scuba diving</td>
</tr>
<tr>
<td>12</td>
<td>3.7</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>13</td>
<td>1.0</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>14</td>
<td>1.1</td>
<td>Asymptomatic; runs 5K races, bicycles</td>
</tr>
<tr>
<td>15</td>
<td>0.2</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>16</td>
<td>0.1</td>
<td>Asymptomatic</td>
</tr>
</tbody>
</table>

Data from Doty and colleagues.
Figure 28-9  Venography after bypass of superior vena cava (SVC) with composite spiral saphenous vein graft. A, Bypass graft anastomosed to left brachiocephalic vein at left jugular–subclavian vein confluence, which courses anterior to aorta to the right atrial appendage. Contrast media from bilateral arm venography opacifies right atrium and pulmonary trunk. B, Closer view shows bypass graft between left brachiocephalic vein and right atrial appendage. There is streaming of unopacified blood from left internal jugular vein flowing into bypass graft. Continued

For patients in whom graft closure was documented, SVC syndrome promptly recurred and venography showed graft closure. Three patients had graft closure within the first year after operation. One had thrombosis of the proximal brachiocephalic vein–graft anastomosis 4 days after operation, with recurrence of face and neck swelling and other signs of SVC obstruction. Graft revision was performed, and the patient remained asymptomatic nearly 13 years later. Another had recurrence of symptoms 5 months after operation for spontaneous thrombosis of the SVC; she had not been given anticoagulants and, in retrospect, probably should have been treated with warfarin after operation. Symptoms of SVC syndrome recurred, and graft closure was documented by CT scan; no further operative treatment was given. In a third patient, graft closure developed 1 year after initial operation. This patient had fibrosing mediastinitis and retroperitonitis, which subsequently obliterated both internal jugular veins, the original bypass graft, three subsequent bypass grafts, and the IVC. SVC syndrome recurred promptly each time a bypass graft occluded.

At a second operation in another institution, bilateral straight saphenous vein grafts were placed from the right and
left external jugular veins to the right atrium. These grafts provided partial symptom relief for 8 years before they also occluded. At that point a 10-mm PTFE graft was placed from the left internal jugular vein to the right atrial appendage. It occluded 3 years later, and a composite graft was constructed from common iliac vein and IVC allograft tissue. This composite graft was placed from the left internal jugular vein near the angle of the mandible and a side branch to the left external jugular vein, to the right atrium; the graft was enclosed in a 12-mm PTFE graft. Four years later, SVC syndrome recurred and the patient died shortly thereafter.

Thus, 14 of 16 patients had patent spiral saphenous vein bypass grafts for the duration of follow-up (88%; CL 73%-96%). Once established, the spiral saphenous vein graft appears to be a permanent conduit unless invaded by continuing aggressive mediastinal or intrinsic thrombotic vascular disease. Gloviczki and colleagues\(^{18}\) reported similar excellent patency of spiral grafts at 5 years for nonmalignant venous occlusive disease, noting that bifurcated conduits tended to have occlusion of one limb. In their expanded series, cumulative 4-year patency for 20 spiral grafts was 67%.\(^{18}\)

Spiral vein grafts are useful in children as well as adults, as demonstrated by successful treatment of SVC obstruction secondary to intraatrial baffle obstruction for transposition of the great arteries using a bypass graft from the brachiocephalic vein to the left atrial appendage.\(^{18}\) Results of direct operations to remove obstructing masses from the SVC or IVC are difficult to assess because of small individual institutional experiences. Results should be good in adult patients, with nearly all surviving operation and most relieved of SVC obstruction. In infants and children in whom venous channels are small, results will be less favorable. Berman and colleagues reported 37 patients aged 4 days to 17 years with thrombus in the SVC or right atrium from central venous catheters over a 6-year period.\(^{18}\) Operations to remove the clot were performed in only 4 patients, 2 of whom died (50%; CL 18%-82%).

### INDICATIONS FOR OPERATION

Current recommendations for operative intervention in SVC obstruction are as follows:

- Persistent severe SVC syndrome caused by chronic SVC obstruction from benign process
- Acute SVC obstruction caused by benign or malignant processes with signs of cerebral or laryngeal edema
- Relief of life-threatening SVC syndrome during palliation of malignant process
- Failure of nonoperative treatment to resolve SVC syndrome (see “Nonoperative Treatment” later)
- Tumor or blood clot partially obstructing the SVC or IVC that is hazardous or impossible to remove without operation

Reconstruction is contraindicated in patients with:

- Adequate collateral circulation to provide upper-body venous decompression
- Extensive thrombosis of the SVC and its tributaries such that there is no suitable vein large enough to provide outflow from the upper body sufficient to decompress venous hypertension
- Large, bulky tumors of the anterior mediastinum
- Limited life expectancy because of advanced malignancy or associated medical disorders

### SPECIAL SITUATIONS AND CONTROVERSIES

**Femoral Vein Graft**

Since the original successful bypass operations were performed in the 1950s, the femoral vein has been used as a bypass graft.\(^{18,11,14,15}\) Gladstone and colleagues revived the concept of using autologous femoral vein to construct a
bypass graft in two patients, one with mediastinal fibrosis and the other with poorly differentiated carcinoma. \(^{62}\)

After median sternotomy to confirm feasibility of the bypass operation, the femoral vein is exposed from its junction with the greater saphenous vein as far distally as the adductor hiatus if necessary. Minor branches are ligated and the appropriate length of vein removed distal to the femoral-saphenous junction. Following heparinization, the femoral vein graft is interposed between the brachiocephalic vein and right atrial appendage, as described for spiral vein graft bypass. Femoral vein grafts have remained patent up to 18 months after operation, as reported by Marshall and Kououchoukov\(^{35}\) and Kalra and colleagues.\(^{K1}\) Addition of a ringed PTFE tube around the graft provided external support to prevent recurrent fibrosis in a patient who had previously undergone spiral vein bypass.\(^{35}\) There has been some concern about leg edema after femoral vein removal, but published reports indicate that this is not a major problem. A potential problem with femoral bypass grafts is their fixed diameter, which may not match the inflow vein or may be too small to relieve obstruction.

**Autologous Paneled Saphenous Vein Graft**

Large-caliber venous bypass conduits can be constructed using saphenous vein in a composite or paneled manner as first reported by Benvenuto and colleagues in 1962.\(^{53}\) The saphenous vein is divided into several segments, each of which is incised longitudinally. The segments are flattened, placed on a stent in a paneled or tiled manner, and sewn together to create the conduit. Both the initial report and a subsequent study by Miller and Sullivan demonstrated graft patency at 1 year.\(^{53,54}\) Scherck and colleagues reviewed 11 case reports in which autologous vein grafts were used in various configurations to bypass or reconstruct the SVC.\(^{55}\) Follow-up ranged from 8 days to 5 years, and overall graft patency was 70%.

**Saphenous Vein Grafts**

Intact saphenous veins can be used as bypass conduits. Their small caliber typically dictates constructing more than one graft to provide adequate venous flow. Mitchell and colleagues described two patients with mediastinal fibrosis in whom saphenous vein was used to create a double bypass graft to the proximal SVC.\(^{56}\) One patient was asymptomatic 11 years postoperatively; both grafts thrombosed 2 weeks after operation in the other. Larsson and Lepore reported three patients with thymoma in whom saphenous vein was used for bypass grafting.\(^{1,2}\) Two had double bypass graft construction to the right atrium and the third had single bypass graft construction to the proximal SVC. All patients had patent grafts at follow-up from 8 to 10 months.

Unmodified saphenous vein grafts may be too small to relieve venous obstruction unless two or more grafts are constructed from veins above the caval obstruction to the right atrium. Although patency is good, relief of symptoms may not be as predictable as when a single large-diameter graft is used.

**Alternative Venous Anastomoses**

Occasionally, patients with SVC obstruction can be surgically treated without constructing a venous bypass graft in the thorax. Schramel and Olinde were the first to describe subcutaneous tunneling of a long saphenous vein bypass conduit to the jugular vein.\(^{54}\) Taylor and colleagues later used a similar approach.\(^{71}\) Vincze and colleagues described seven cases of patients treated with saphenous-jugular bypass for SVC obstruction caused by lung carcinoma; all were free of obstructive symptoms at the time of death, ranging from 2 to 14 months.\(^{52}\) Graham and colleagues reported a series of three patients undergoing subcutaneous jugular vein–to–femoral vein bypass;\(^{63}\) all had relief of SVC syndrome at follow-up, ranging from 6 weeks to 13 months.

Cooley and Hallman reported a case of SVC obstruction in which contrast venography demonstrated retrograde flow through theazygos system.\(^{14}\) The patient was treated with side-to-side anastomosis of the azygos vein to the IVC, which resolved the SVC obstruction. Shimokawa and colleagues\(^{410}\) described extracorporeal axillofemoral venous bypass as a useful temporizing measure to reduce venous pressure in the upper thorax.

The extensive length of bypass grafts taken from the upper-body veins to the femoral vein in the groin presents enough resistance to flow to render long-term patency of such conduits unpredictable. Simple anastomoses between veins in a high-pressure system to venous channels with normal low pressure within the thorax are unusual opportunities, but they should be sought in all cases.

**Allografts and Pericardial Conduits**

In some cases, autologous venous bypass grafting cannot be accomplished. Alternative tissue conduits in this setting include aortic, SVC, or femoral vein allografts and autologous pericardial tube grafts. Aortic allografts have excellent handling characteristics and perform well when used for arterial system replacements. Scherck and colleagues\(^{53}\) demonstrated overall graft patency of nearly 90% on review of 17 patients (CL 74%-96%) who received aortic allografts to reconstruct the SVC. In 1997, Ohri and colleagues\(^{52}\) reported a case of SVC obstruction caused by drug-resistant tuberculosis and treated with aortic allograft reconstruction; the graft was patent at 6 months. Moore and colleagues examined the potential application of SVC allografts as a possible conduit\(^{511}\); graft patency was approximately 70% in their experimental model. Clinical use of an SVC allograft has been reported only once to date; the graft was patent 1 year after operation.

Initial experience with tube grafts constructed from autologous pericardium has been disappointing in the experimental setting. Scherck and colleagues reviewed three series of experimental pericardial tube grafts; none were patent.\(^{53}\) Clinical use of autologous pericardial tubes, however, has been more encouraging. Zembala and colleagues created a pericardial tube graft between the brachiocephalic vein and right atrial appendage that remained patent for 11 months in a patient with malignant teratoma.\(^{22}\) Piccione and colleagues successfully used autologous pericardial tube grafts in six patients to reconstruct portions of the SVC after resection for carcinoma, and all were relieved of obstructive symptoms.\(^{73}\) Lemmer and colleagues created composite conduits in two pediatric patients from pedicled right atrium and pericardium to reconstruct the SVC; the conduits were patent 24 and 43 months after operation.\(^{1,5}\)

Aortic or venous allografts have high patency in many applications within the thorax. Long-term patency depends
on methods of graft preparation and complex immune factors. Allografts should be viewed as palliative, and the graft should be expected to deteriorate with time. Pericardial venous conduits are probably no better than (and perhaps not as good as) prosthetic conduits. On the other hand, composite pericardial conduits consisting of pericardium and pedicled atrium should have a high probability of remaining patent for a long time because they include normal endocardium.

Prosthetic Grafts

Prosthetic grafts, principally externally supported (ringed) polytetrafluoroethylene (ePTFE), have been used to bypass or replace the SVC for both benign and malignant disease. Kalra and colleagues used ePTFE to bypass nonmalignant obstructed SVCs in 6 patients. Cumulative patency at 1 and 4 years was 50% and 17%, respectively, and was significantly lower than for 20 patients who received spiral saphenous vein grafts (67% and 67%, respectively; \( P = .02 \)).

Dartevelle and colleagues interposed ePTFE grafts between the proximal and cardiac ends of the SVC in eight patients, and between one or both brachiocephalic veins in 14 patients with malignant lung or mediastinal tumors. One graft occluded early postoperatively and one at 14 months. Patency of all remaining grafts was demonstrated from 1 to 98 months (mean 23 months) postoperatively.

Leo and colleagues used ePTFE grafts to bypass the SVC in 28 patients with malignant lung or mediastinal tumors who had total SVC resection. Early graft occlusion was observed in one patient. At 4 months, all grafts in surviving patients were patent.

Nonoperative Treatment

Medical Therapy

Medical measures may be beneficial in temporarily relieving symptoms of SVC syndrome, especially in hospitalized patients. Bed rest with the head elevated gradually brings improvement in most cases. Diuretics and reduced sodium intake usually reduce upper-body edema. Corticosteroids may be useful in reducing cerebral edema.

Anticoagulants have been frequently employed, but effectiveness has not been demonstrated by controlled trial. They may be effective in preventing propagation of clot into caval tributaries, thereby retarding progression of the syndrome. Anticoagulants most frequently used include heparin during hospitalization and warfarin for long-term therapy. Long-acting heparin-like medications (enoxaparin) may prove beneficial for preventing clot propagation. Patients best suited for anticoagulant therapy are those with quiescent benign disease (e.g., dormant granulomatous mediastinitis) or catheter placement in the SVC.

Thrombolytic therapy may be valuable in patients with acute thrombosis of the SVC if the cause of thrombosis can be eliminated, such as by removing an indwelling catheter. Gray and colleagues reported the Cleveland Clinic experience using urokinase or streptokinase for treating SVC syndrome in 16 patients, 11 of whom had indwelling central venous catheters; 56% (CI 40%-71%) had complete clot lysis and relief of symptoms. Success was most often achieved when thrombolytic medication was infused through the central venous catheters and when thrombus had been present less than 5 days. Reports of other cases from the literature indicate greatest success of clot lysis when the thrombosis is treated within 72 hours.

Radiation Therapy

Radiation therapy is the primary treatment modality for thoracic malignancies causing SVC syndrome, and nearly all patients receive radiation at some point in their clinical course. This treatment should be administered only after establishing a tissue diagnosis of the cause of SVC obstruction, because a few patients may develop life-threatening cerebral or laryngeal edema that requires urgent intervention.

Radiation is directed to the tumor mass, to a 2-cm margin surrounding it, and to mediastinal, hilar, and supraclavicular lymph nodes. Radiation is fractionated with an initial midplane dose of 4 Gy for 3 days and then 1.5 Gy per day until an accumulated 30 to 50 Gy is achieved. Total dose depends on the patient’s condition, extent of disease, response of disease to treatment, and tumor histology.

Rodrigues and colleagues used hypofractionated radiation therapy to treat 39 patients with primary lung cancer and SVC syndrome. The most successful regimen was administration of a high dose of 8 Gy weekly for 3 weeks, for a total dose of 24 Gy. Using this protocol, 96% of patients received some relief of SVC syndrome, and 56% had complete relief. Recurrence occurred within 6 months in 20% of patients.

Most patients respond to radiation treatment. Reports from the literature suggest only 10% to 20% of patients fail to obtain relief of SVC syndrome, but up to 50% relapse. Improved survival has been reported with radiation therapy for patients with SVC syndrome resulting from malignancy. Mean survival time for untreated persons is 6 to 7 months, whereas it is at least double that with radiation therapy, and some long-term cures have been reported. Perez and colleagues found that 10% of patients with bronchogenic carcinoma as a cause of SVC syndrome were alive at 30 months, and 45% of patients with lymphoma as a cause were alive late after treatment. Emergency radiation therapy may be indicated for treating critically ill children presenting with SVC syndrome, most commonly due to non-Hodgkin lymphoma.

Chemotherapy

Cancer chemotherapy can be effective as primary therapy or as an adjunct to radiotherapy or surgery in selected cases. Random use of chemotherapy has not been shown to be effective. Combined chemotherapy and radiotherapy is beneficial for relieving SVC syndrome caused by mediastinal lymphoma. Chemotherapy alone, using a combination of agents, may be the treatment of choice for small-cell anaplastic bronchogenic carcinoma, with symptom relief within 7 days. Best results occur with incomplete SVC obstruction and with extrinsic compression from large tumors at the thoracic inlet.

Transluminal Balloon Angioplasty and Stents

Successful transluminal balloon angioplasty and stenting require that the SVC not be completely obstructed, because a vascular passageway is needed to guide the device. Endovascular therapy initially involved balloon angioplasty, which was successful for benign causes of SVC obstruction but rarely for malignant causes. However, the SVC is unable to resist external compression by tumor or inflammation. These led to the use of intravascular stents.
Gaines and colleagues used the Gianturco Z self-expanding metallic device (consisting of a stainless steel wire bent in a Z configuration) as a single or double stent in 20 patients with malignant SVC obstruction; 13 (65%; CL 51%-77%) were free of SVC obstruction until death, and 3 required a second intervention.1,6 Oudkerk and colleagues treated 22 patients with malignant obstructions with Gianturco Z stents, with 68% (CL 55%-79%) free of symptoms of SVC syndrome and without recurrence until death from tumor progression. Another 4 (18%) showed improvement, and 3 (14%) had reocclusion.8,9 Dyet and colleagues achieved similar results using the Wallstent endovascular prosthesis in 17 patients.10 This device is a tube of woven stainless steel mesh, which is more secure for short-segment stenoses.

Stents have also been successfully used to treat benign causes of SVC obstruction, including stenosis caused by pacemaker electrodes.11,12 Subsequent series have confirmed the effectiveness of endovascular stenting for both benign and malignant SVC obstruction.2,13,14 It is now considered the first line of treatment in many institutions.1,13,21

Because of clot formation in patients with SVC obstruction, concomitant thrombolytic therapy has been recommended to remove the clot and establish a channel through which the stent can be deployed.15 Anticoagulation is recommended after stent implantation to avoid thrombosis, but optimal duration and methods of anticoagulation have not been completely defined.16

In addition to early thrombosis, complications of endovascular stenting include acute pulmonary edema, hemorrhage, perforation, cardiac tamponade, stent migration, infection, cardiac dysrythmias, and pulmonary embolism.17,22

Comparison of Operation with Catheter Intervention

Wisselink and colleagues compared operative vs. percutaneous catheter intervention for treating patients with central venous obstruction.23 Their study included patients with obstruction of not only the SVC but also its major tributaries. Of 27 patients, 12 underwent operation, 14 had angioplasty, and 1 had both. Stents were used in three patients. Primary symptom relief at 1 year was achieved in 88% of the surgical group vs. 36% of the angioplasty group (P < .05). When repeat angioplasty was performed, success in that group increased to 66%. Thus, surgical success exceeded that of single catheter intervention, but repeated angioplasty achieved comparable results.

A nonrandomized trial comparing open surgical repair with endovascular stenting has demonstrated equivalent midterm effectiveness in terms of symptom relief.24 Reinterventions were required more frequently in the stented patients. Assisted primary and secondary patency was significantly higher in the stented patients (P = .02). The authors concluded that open surgical repair remains an excellent option for patients who are unsuitable for endovascular stents.

Injury to Left Brachiocephalic Vein during Sternotomy

Laceration of the left brachiocephalic vein is a hazard of sternotomy. It occurs rarely during primary sternotomy, but is a common threat during repeat sternotomy. The hazard is reduced during reentry by dividing the sternum with an oscillating saw rather than using the standard blade. Once the sternum is divided, tissues adherent to the posterior table of the sternum superiorly are separated sharply or with the electrocautery. Mobilizing the tissues surrounding the brachiocephalic vein will reduce the role of disruption. Wide separation of the sternal edges should be avoided to reduce tension on the vein.

The most common method of managing major injuries is ligation. Usually, left arm or neck swelling is not observed, although later thrombosis of the tributaries of the vein may occur. The consequences of uncontrolled hemorrhage and difficulties in repairing the vein without creating stenosis appear to outweigh the risks of ligation. Repair of the vein is feasible if the disruption is not complete, and can be accomplished using autologous or bovine pericardium. If the vein is disrupted at its junction with the SVC such that ligation will compromise flow into the SVC or cause stenosis of the right brachiocephalic vein, repair or SVC bypass should be performed to avoid SVC syndrome.

Budd-Chiari Syndrome

In 1845, Budd described three cases of hepatic vein thrombosis caused by abscess-induced phlebitis.20 In 1899, Chiari reported another three cases of obliterative phlebitis of large hepatic veins.21 Budd-Chiari syndrome was thus initially defined as symptomatic occlusion of hepatic veins, but subsequent inclusion of various obliterative changes in the hepatic portion of the IVC and hepatic vein orifices broadened the definition. Membranous obstruction of the IVC is generally regarded as a congenital vascular malformation, yet it results in impaired hepatic venous outflow blockage and hence is included with the syndrome. However, obliterative disease of this type and primary hepatic vein thrombosis (classic Budd-Chiari), are different clinical entities.30

Hepatic vein thrombosis is more common in western than eastern countries and presents as severe, sometimes acute, hepatic failure. It is associated with a hypercoagulable state, the factor V Leiden mutation.31,32,33 Mahmoud and Elias recommend screening all patients with Budd-Chiari syndrome for activated protein C resistance and factor V Leiden mutation.32 Vasculitis accompanying Behçet disease is also associated with hepatic vein thrombosis.22 When there is associated thrombosis of the portal venous system, treatment options are limited and prognosis is poor, with 70% of patients dying before any treatment can be given or after operation.34

Treatment of classic Budd-Chiari syndrome is primarily by orthotopic liver transplantation when liver failure is fulminant or chronic.35 For acute and subacute forms when hepatic injury is reversible, a surgical or percutaneous portasystemic shunt is effective.33,34,35,36 A transjugular intrahepatic portosystemic shunt (TIPS) may also be effective while awaiting liver transplantation.

Obliterative disease of the hepatic portion of the IVC is often a membranous obstruction of the vena cava or of the hepatic vein orifices. It is primarily a condition found in Nepal, South Africa, China, and India.37 It is usually idiopathic, although many consider it to be a congenital anomaly. Complex congenital venous anomalies may cause hepatic venous congestion in rare instances.38 Clinical presentation is milder than with primary hepatic vein thrombosis, and time of onset is frequently unknown. Enlarged subcutaneous veins over the body trunk are characteristic, similar to those seen in obstruction of the SVC. Hepatocellular carcinoma is a frequent complication.
Treatment is generally by transvenous balloon angioplasty or stent placement, possibly in combination with a portasystemic shunt. Despite these less invasive treatment methods, operative intervention has a role in this condition. Transtrial membranotomy, reconstruction of the IVC, and bypass from the IVC to the right atrium are alternatives when catheter interventions are not possible.

Koja and colleagues describe direct exposure of the retrohepatic IVC via thoracoabdominal incision on the right. The vena cava is occluded above and below the liver while the patient is on femorofemoral bypass with an oxygenator. Hepatoma occurred 3 to 9 years after operation in 5 patients. Survival at 1, 5, and 10 years after operation was 100%, 94%, and 67%, respectively. Esophageal varices gradually resolve, and hepatic fibrosis improves histologically after this operation. Rarely, hepatic trauma with intraparenchymal or subcapsular hematoma may cause compression of the intrahepatic IVC, resulting in Budd-Chiari syndrome. Technical problems related to closure of atrial septal defect may also cause obstruction of the IVC and hepatic veins.

The authors reported a remarkable series of 29 patients treated between 1979 and 1997. All patients survived operation and had documented IVC patency at 1 to 2 months after surgery. Restenosis of the IVC developed in 2 patients 2 and 6 years after operation; both were successfully treated by either reoperation or balloon angioplasty. Hepatoma occurred 3 to 9 years after operation in 5 patients. Survival at 1, 5, and 10 years after operation was 100%, 94%, and 67%, respectively. Esophageal varices gradually resolve, and hepatic fibrosis improves histologically after this operation.

REFERENCES

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DEFINITION

Congenital heart disease in the adult is presence of unrepaired or repaired congenital heart disease in patients aged 21 years or older. A more practical working definition is not straightforward. Because physical and emotional maturity is variable, the distinction between an adult and non-adult is unclear. The designation “adult” implies provision of specific methods of caregiving best delivered in an adult care environment. The patient age at which this approach is advisable varies, ranging from mid-teens to mid-20s, depending on the individual.

It has been recommended that the process of transitioning young patients successfully to an adult healthcare environment should begin by age 12 years. Several models of care fit the definition of “adult healthcare environment,” including adult congenital heart disease programs based in pediatric hospitals and clinics, those based in adult hospitals and clinics, and hybrid arrangements. None has proven superior.

SURVIVAL VERSUS CURE

Survival does not necessarily, and usually does not, mean cure. Cure is best defined as a state that results when survival and quality of life are indistinguishable from normal.

PREVALENCE

Survival of patients with congenital heart disease (CHD) has steadily improved over the past 4 decades since reoperative surgery has become commonplace. Since the 1970s, more than 80% of patients have survived into adult life. The 32nd Bethesda Conference report (Bethesda Report) in 2000 contains an estimate that approximately 800,000 adults in the United States have CHD. With current surgical mortality less than 10%, it is expected that in the next decade almost 1 in 150 young adults will have some form of CHD.9,12

The level of development of health care in a particular environment will strongly influence the prevalence and profile of adult congenital heart patients. In countries with underdeveloped healthcare systems, fewer congenital heart disease patients will survive to adulthood, and a preponderance of these will have unrepaired anomalies. Consequently, many of these patients will have advanced sequelae consistent with the natural history of the particular anomaly. In this chapter, we emphasize adult congenital heart disease as it presents in environments with state-of-the-art pediatric congenital heart disease management.
CATEGORIES OF ADULT CONGENITAL HEART DISEASE

Primary Congenital Heart Disease

Primary CHD in the adult refers to previously untreated anomalies. These anomalies tend to cause relatively benign pathophysiologic perturbations, allowing survival into adulthood without treatment. Primary CHD is less common than secondary CHD.

Newly Diagnosed Anomalies

Newly diagnosed anomalies fall into two categories. The first consists of patients with anomalies that not only allow survival to adulthood, but are sufficiently benign to escape detection even in environments with well-organized healthcare systems. Typical anomalies include those causing left-to-right shunt (atrial septal defect [ASD], partial atrioventricular septal defect [AVSD], restrictive ventricular septal defect [VSD], and restrictive patent ductus arteriosus [PDA]) and those causing minor valvar obstruction or regurgitation (bicuspid aortic valve). The second consists of patients with anomalies that allow survival to adulthood, but are sufficiently malignant to cause serious pathophysiologic changes; typically, these patients spend their childhood in environments without the capability of diagnosing or treating the anomaly, and only as adults enter an environment capable of detecting it. Typical anomalies include all of those listed in the first category, but they are attended by more serious pathophysiologic perturbations (larger, less restrictive VSDs), as well as selected cases of many forms of cyanotic congenital heart disease (tetralogy of Fallot, pulmonary stenosis, and even some forms of single ventricle).

Previously Diagnosed Anomalies with Benign Pathophysiology

Typical anomalies include those resulting in small or restrictive left-to-right shunts and minor valvar lesions. They are detected in infancy or childhood, but because of lack of important symptoms and pathophysiologic changes, are left untreated. These anomalies may progress in adulthood, causing symptoms (bicuspid aortic valve) or complications that result in symptoms (restrictive VSD with endocarditis).

Previously Diagnosed Anomalies Thought to Be Inoperable

Occasionally, adult patients are encountered who were diagnosed with complex congenital heart disease in infancy; however, because their pathophysiology was not life threatening and their structural heart disease was so complex as to be thought inoperable, they have been managed without surgical correction into adulthood. New surgical approaches may by then have become available. An example is the occasional patient with pulmonary atresia, VSD, or aortopulmonary collaterals, with mild cyanosis. This patient may be a candidate for unifocalization and intracardiac repair as an adult.

Secondary Congenital Heart Disease

Secondary congenital heart disease refers to patients with previously treated CHD, which is more common in the adult than primary CHD. It covers the entire spectrum of congenital anomalies. As illustrated in Fig. 29-1, some but by no means all patients who have undergone surgery for CHD as infants and children are cured and are not considered to have secondary CHD as adults.

MANAGEMENT AND ORGANIZATION OF HEALTH CARE

Currently, delivery of appropriate health care to adults with CHD is not fully met, even in the developed world. This is partly due to inadequately trained healthcare providers managing these patients after they transition from pediatric care, partly to poor organization, and partly to loss of health insurance when these patients become adults—up to 20% of adults with CHD may be uninsured. Lapse of care for adults with CHD is associated with adverse outcome. According to the Society of Thoracic Surgeons (STS) database, early mortality following cardiac surgery for CHD is higher in adults than in children, although neonates and infants have the highest mortality (Fig. 29-2). This higher mortality in adults may be caused partially by lack of healthcare organization and experience.
Table 29-1 Personnel and Services Recommended for Regional Adult Congenital Heart Disease Centers

<table>
<thead>
<tr>
<th>Type of Service</th>
<th>Personnel/Resources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiologist specializing in ACHD</td>
<td>One or several 24/7</td>
</tr>
<tr>
<td>Congenital cardiac surgeon</td>
<td>Two or several 24/7</td>
</tr>
<tr>
<td>Nurse/physician assistant/nurse practitioner</td>
<td>One or several</td>
</tr>
<tr>
<td>Cardiac anesthesiologist</td>
<td>Several 24/7</td>
</tr>
<tr>
<td>Echocardiography* (includes TEE, intraoperative TEE)</td>
<td>Two or several 24/7</td>
</tr>
<tr>
<td>Diagnostic catheterization*</td>
<td>Yes, 24/7</td>
</tr>
<tr>
<td>Noncoronary interventional catheterization</td>
<td>Yes, 24/7</td>
</tr>
<tr>
<td>Electrophysiology/pacing/AICD implantation*</td>
<td>One or several</td>
</tr>
<tr>
<td>Exercise testing</td>
<td>Echocardiography</td>
</tr>
<tr>
<td></td>
<td>Radionuclide</td>
</tr>
<tr>
<td></td>
<td>Cardiopulmonary</td>
</tr>
<tr>
<td></td>
<td>Metabolic</td>
</tr>
<tr>
<td>Cardiac imaging/radiology*</td>
<td>Cardiac MRI</td>
</tr>
<tr>
<td></td>
<td>CT scanning</td>
</tr>
<tr>
<td></td>
<td>Nuclear medicine</td>
</tr>
<tr>
<td>Multidisciplinary teams</td>
<td>High-risk obstetrics</td>
</tr>
<tr>
<td></td>
<td>Pulmonary hypertension</td>
</tr>
<tr>
<td></td>
<td>Heart failure/transplant</td>
</tr>
<tr>
<td></td>
<td>Genetics</td>
</tr>
<tr>
<td></td>
<td>Neurology</td>
</tr>
<tr>
<td></td>
<td>Nephrology</td>
</tr>
<tr>
<td></td>
<td>Cardiac pathology</td>
</tr>
<tr>
<td></td>
<td>Rehabilitation services</td>
</tr>
<tr>
<td></td>
<td>Social services</td>
</tr>
<tr>
<td></td>
<td>Vocational services</td>
</tr>
<tr>
<td></td>
<td>Financial counselors</td>
</tr>
<tr>
<td>Information technology</td>
<td>Data collection</td>
</tr>
<tr>
<td></td>
<td>Database support</td>
</tr>
<tr>
<td></td>
<td>Quality assessment review/protocols</td>
</tr>
</tbody>
</table>

Modified from Warnes and colleagues. Modified from Warnes and colleagues. Modified from Warnes and colleagues.

*These modalities must be supervised/performe and interpreted by physicians with expertise and training in congenital heart disease. Key: 24/7, Available 24 hours a day, 7 days a week; ACHD, adult congenital heart disease; AICD, automatic implantable cardioverter defibrillator; CT, computed tomography; MRI, magnetic resonance imaging; TEE, transesophageal echocardiography.

The Bethesda Report recommends organizing care of adults with CHD within a regionalized system of specialized adult CHD units, with each unit providing education, care, and research for its designated region. The Bethesda Report describes three levels of training for adult cardiovascular specialists managing adults with CHD. These training levels emphasize cardiology training, but do not focus on specifics of training for surgeons who care for these patients. It is recommended that cardiothoracic surgeons caring for adults with CHD have formal fellowship training in pediatric heart surgery. There is evidence obtained from an analysis of national practice patterns involving more than 40,000 patients that mortality following CHD surgery in adults is lower if the surgeon performing the operation is an experienced pediatric heart surgeon. The cardiothoracic surgeon managing adults with CHD should be fully integrated into the adult CHD unit and may take a leadership role in the functioning of the unit.

The combined American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines Committee for the Management of Adults with CHD recognizes three levels of complexity of congenital heart disease in adults (Boxes 29-1 to 29-3) and makes specific recommendations for the Management of Adults with CHD.
for the management protocols based on these levels (Box 29-4).  

SPECIAL CIRCUMSTANCES

Pregnancy and Contraception

Overview

The most common cardiac cause of morbidity and mortality in pregnant women in North America is congenital malformations. Ideally, women with CHD should receive counseling by an adult CHD expert before becoming pregnant. Both fetal and maternal risks should be discussed. If pregnancy occurs, fetal echocardiography should be obtained and the consequences of pregnancy discussed.  

If functional class and systemic ventricular function are good, the outcome of pregnancy is favorable in most women with CHD. Even in women with well-compensated cardiac status, however, specific risks are present. In those with intracardiac shunts, air entry into intravenous lines may cause paradoxical embolism. Any degree of immobilization of the pregnant woman should be attended by prophylaxis for deep vein thrombosis, particularly if there is the potential for right-to-left intracardiac shunting.  

Pulmonary hypertension, especially when above 70% systemic, presents a serious risk during pregnancy. Pulmonary hypertensive events may occur after delivery. If Eisenmenger physiology is present, maternal mortality is up to 50% fetal loss at a similar level. Even after a successful pregnancy, maternal mortality may increase in the first several days after delivery. Anticoagulation during pregnancy, even to a level required for mechanical valves, is not a strict contraindication to pregnancy; however, it poses an increased risk to both mother and fetus.  

In a small group of women with complex CHD or with decompensated cardiac status, pregnancy is either dangerous or contraindicated. These women should be managed and delivered in specialized centers with expertise in adult CHD, obstetrics, anesthesiology, and neonatology. Vaginal delivery is preferable for most women with CHD; cesarean section and delivery is recommended for obstetric reasons and for women fully anticoagulated with warfarin at the time of delivery, because of the risk of fetal intracranial hemorrhage. Although pregnancy is not contraindicated in women with repaired congenital anomalies, increased complications may occur. An excess of miscarriages, preterm delivery, and maternal mortality is found after successful coarctation repair and repair of congenital aortic stenosis.  

Certain medications are contraindicated during pregnancy. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) cause congenital and renal disorders in the fetus. Warfarin should be used only after full discussion with the patient about its risks during pregnancy. Endocarditis is a recognized risk for maternal morbidity; however, endocarditis prophylaxis at the time of delivery is not universally recommended. Some believe that risk of bacteremia is low; others routinely

<table>
<thead>
<tr>
<th>Box 29-3</th>
<th>Diagnoses in Adult Patients with Congenital Heart Disease of Great Complexity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conduits, valved or nonvalved</td>
<td>Cyanotic congenital heart (all forms)</td>
</tr>
<tr>
<td>Double-outlet ventricle</td>
<td>Eisenmenger syndrome</td>
</tr>
<tr>
<td>Fontan procedure</td>
<td>Mitral atresia</td>
</tr>
<tr>
<td>Single ventricle (also called double inlet or outlet, common, or primitive)</td>
<td>Pulmonary atresia (all forms)</td>
</tr>
<tr>
<td>Pulmonary vascular obstructive disease</td>
<td>Transposition of the great arteries</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td>Truncus arteriosus/hemitruncus</td>
</tr>
<tr>
<td>Other abnormalities of atrioventricular or ventriculoarterial connection not included above (e.g., crisscross heart, isomerism, heterotaxy syndromes, ventricular inversion)</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Warnes and colleagues.  

*These patients should be seen regularly at adult congenital heart disease centers.

<table>
<thead>
<tr>
<th>Box 29-4</th>
<th>American College of Cardiology/American Heart Association Recommendations for Access to Care for Adults with Congenital Heart Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>An individual primary caregiver or cardiologist without specific training and expertise in ACHD should manage the care of adults with complex and moderate CHD only in collaboration with level 2 or level 3 ACHD specialists.</td>
</tr>
<tr>
<td>2.</td>
<td>For ACHD patients in the lowest-risk group, cardiac follow-up at a regional ACHD center is recommended at least once to formulate future needs for follow-up.</td>
</tr>
<tr>
<td>3.</td>
<td>Frequent follow-up (generally every 12 to 24 months) at a regional ACHD center is recommended for the larger group of adults with complex and moderate CHD. A smaller group of adults with very complex CHD will require follow-up at a regional ACHD center at a minimum of every 6 to 12 months.</td>
</tr>
<tr>
<td>4.</td>
<td>Stabilized adult patients with CHD who require admission for urgent or acute care should be transferred to a regional ACHD center, except in some circumstances after consultation with the patient’s primary level 2 or level 3 ACHD specialist.</td>
</tr>
<tr>
<td>5.</td>
<td>Diagnostic and interventional procedures, including imaging (i.e., echocardiography, MRI, CT), advanced cardiac catheterization, and electrophysiology procedures for adults with complex and moderate CHD should be performed in a regional ACHD center with appropriate experience in CHD and in a laboratory with appropriate personnel and equipment. Personnel performing such procedures should work as part of a team with expertise in the surgical and transcatheter management of patients with CHD.</td>
</tr>
<tr>
<td>6.</td>
<td>Surgical procedures that require general anesthesia or conscious sedation in adults with moderate or complex CHD should be performed in a regional ACHD center with an anesthesiologist familiar with ACHD patients.</td>
</tr>
<tr>
<td>7.</td>
<td>ACHD patients should be transferred to an ACHD center for urgent or acute care of cardiac problems.</td>
</tr>
<tr>
<td>8.</td>
<td>Adult patients with complex or high-risk CHD should be transferred to an ACHD center for urgent or acute noncardiac problems.</td>
</tr>
<tr>
<td>9.</td>
<td>An ACHD specialist should be notified or consulted when a patient with simple or low-risk CHD is admitted to a non-ACHD center.</td>
</tr>
</tbody>
</table>

Modified from Warnes and colleagues.  

Key: ACHD, Adults with congenital heart disease; CHD, congenital heart disease; CT, computed tomography; MRI, magnetic resonance imaging.
administer antibiotics. Intravenous amoxicillin and gentamicin should be considered for women with high-risk anatomy or previous history of endocarditis.

Estrogen-containing oral contraceptives are generally contraindicated in women at risk of thromboembolism. Those containing progesterone are contraindicated in women with heart failure because of their tendency to cause fluid retention. The risk of endocarditis with intrauterine devices is controversial, and recommendations should be individualized on the basis of discussions between the adult CHD specialist and gynecologist. 

Maternal Cardiac Surgery during Pregnancy
Cardiac surgery during pregnancy is rarely necessary. About 1% to 4% of pregnancies are complicated by cardiac disease. Occasionally, owing to progression of cardiac disease during pregnancy or to cardiovascular changes induced by pregnancy, cardiac surgical intervention is indicated. Although about 20% of adverse cardiac events during pregnancy will require surgery or an invasive interventional procedure, the majority of these can be managed medically. Maximal interdisciplinary efforts and proper assessment of maternal and fetal risks are mandatory in managing these patients. The maternal-fetal conflict of interest, nonelective presentation for surgery, and vulnerability during the postpartum period contribute to a higher risk of cardiovascular operations during pregnancy and postpartum than in the nonpregnant population.

Mortality risk of cardiac surgery is high, 2% to 9% for the mother and 20% to 30% for the fetus. Thus, the risk of maternal death during pregnancy increases 500- to 3000-fold if cardiac surgery is required. On the other hand, the 2% to 9% maternal mortality risk is probably onefold to twofold higher than the risk of the same cardiac operation in a nonpregnant woman of the same age. Several recent reports suggest that maternal mortality is not increased relative to the risk in nonpregnant women. Maternal risk will vary depending on the cardiac lesion. From a literature review of 161 cardiac operations during pregnancy, the greatest maternal risk was found to be associated with cardiac operations for pulmonary embolism (22%) and aortic dissection (22%), followed by operations for either native (9%) or prosthetic valve disease (9%). The underlying etiology of the embolism, dissection, and valve disease was not given; however, from the age range of the pregnant women, it is reasonable to assume, at least for the native and prosthetic valve categories, that congenital anomalies represent the underlying cause for a substantial number of the cases. In this same review, a separate category of “congenital anomalies” accounted for 11 (7%) of the 161 cases. Of these 11, 6 required cardiopulmonary bypass (CPB) to accomplish the repair. None of these 11 patients died. The other common underlying etiology of heart disease in pregnant women requiring cardiac surgery is likely rheumatic disease.

Other risk factors for death in pregnant women undergoing cardiac surgery include moderate or severe obstruction of the aortic or mitral valve, left ventricular ejection fraction below 40%, higher preoperative New York Heart Association (NYHA) functional class, and a preoperative history of stroke from arrhythmias. Risk factors for fetal death are shown in Table 29-2. To minimize risk to the fetus, if surgery is being considered during the third trimester, controlled delivery before the mother’s cardiac operation should be considered. If cardiac surgery is required at an earlier stage of gestation, alterations in managing the operation are necessary. Fetal bradycardia is a common complication; thus, fetal heart rate monitoring, and ideally fetal echocardiographic monitoring, should be performed. CPB adjustments are important to maximize uterine circulation and maintain fetal heart rate. These adjustments include increasing perfusion flow rates, maintaining high perfusion pressure (60 mmHg), avoiding hypothermia, maintaining high hematocrit, avoiding vasoconstrictive agents, and using pulsatile perfusion. The latter can be achieved using an intracoronary balloon pump during CPB, and this has been shown to improve uterine and fetal perfusion. Uterine contractions occur in response to CPB, possibly as a response to the dilution of progesterone, which stabilizes the uterus; thus, tocolytic pharmacologic therapy may be beneficial during CPB.

Table 29-2 Incremental Risk Factors Associated with Fetal Death after Cardiac Surgery Requiring Cardiopulmonary Bypass in Pregnant Women

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Death</th>
<th></th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maternal Age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;35</td>
<td>27.3%</td>
<td>72.7%</td>
<td>.023</td>
</tr>
<tr>
<td>&lt;35</td>
<td>70.0%</td>
<td>30.0%</td>
<td></td>
</tr>
<tr>
<td><strong>Reoperation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>66.7%</td>
<td>33.3%</td>
<td>.016</td>
</tr>
<tr>
<td>No</td>
<td>26.2%</td>
<td>73.8%</td>
<td></td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Emergency</td>
<td>70.6%</td>
<td>29.4%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Planned</td>
<td>18.9%</td>
<td>81.1%</td>
<td></td>
</tr>
<tr>
<td><strong>Preoperative NYHA Class</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>66.7%</td>
<td>33.3%</td>
<td>.003</td>
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<tr>
<td>III</td>
<td>20.0%</td>
<td>80.0%</td>
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</tr>
<tr>
<td>II</td>
<td>16.7%</td>
<td>83.3%</td>
<td></td>
</tr>
<tr>
<td><strong>Myocardial Protection</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cardioplegic</td>
<td>66.7%</td>
<td>33.3%</td>
<td>.053</td>
</tr>
<tr>
<td>Anoxic</td>
<td>28.9%</td>
<td>71.1%</td>
<td></td>
</tr>
</tbody>
</table>

From Arnoni and colleagues. Key: NYHA, New York Heart Association.

Pulmonary Arterial Hypertension and Eisenmenger Physiology
Irreversible pulmonary arterial hypertension (PAH) associated with CHD usually results from anomalies that allow long-standing left-to-right shunts. All such shunts cause PAH from birth onward; however, initially the PAH is flow related, meaning pulmonary blood flow (Qp) is increased and pulmonary vascular resistance (Rp) is low. Over time, PAH may evolve from flow related to resistance related, meaning that Rp becomes elevated and Qp decreases. Flow-related PAH is reversible after eliminating the shunt with surgery or other intervention. Resistance-related PAH is generally irreversible.
The shunt's type, size, and duration influence the likelihood that, and rapidity with which, irreversible PAH will develop. Thus, these factors will be important in determining the age at which patients with irreversible PAH present. Type and size of the shunt determine the magnitude of shunt flow, which in turn determines the amount of shear stress on the endothelial surface of resistance-level pulmonary arteries. Shear stress induces vasoactive changes and ultimately permanent obstructive structural changes in these arteries. Pulmonary vascular histology in shunt-induced irreversible PAH resembles that described for idiopathic PAH, with medial thickening and plexiform lesions in severe cases.\textsuperscript{24}

Individuals with atrial-level left-to-right shunts are least likely to develop irreversible PAH, those with ventricular-level shunts are more vulnerable, and those with arterial-level shunts are at greatest risk. Whether the variation in risk among these different levels is solely related to shunt flow or to an underlying genetic predisposition is unknown. A number of specific congenital heart anomalies can lead to irreversible PAH. Unrepaired large ASD, VSD, AVSD, and PDA account for most cases, simply because these defects are common.\textsuperscript{W13} However, many less common complex lesions, such as partial or total anomalous pulmonary venous return, unrepaired or palliated conoventricular defects, including truncus arteriosus or transposition of the great arteries (TGA), and single-ventricle variants, can also result in development of irreversible PAH. Other congenital causes of PAH unrelated to shunting include pulmonary vein stenosis and pulmonary veno-occlusive disease.\textsuperscript{W13}

Over time, as severe vascular obstructive changes develop, Rp approaches and exceeds systemic vascular resistance (Rs), causing a bidirectional or predominantly right-to-left shunt accompanied by oxygen-unresponsive hypoxemia, identified as Eisenmenger physiology.\textsuperscript{W27} In patients with large ventricular- and arterial-level left-to-right shunts or unrepaired complex congenital heart defects, irreversible PAH can develop as early as the first year of life and Eisenmenger physiology within the first decade of life (see “Pulmonary Vascular Disease” under Natural History in Section I of Chapter 35); however, in patients with medium or larger ASDs, Eisenmenger physiology may not appear at all, but when it does, it typically appears in the second, third, or fourth decade. Pregnancy may unmask pending Eisenmenger physiology.

PAH and Eisenmenger physiology may develop late after surgical repair of left-to-right shunts. The most common explanation is that the repair was performed too late or was incomplete. However, additional factors such as left ventricular hypertrophy and diastolic dysfunction, valve abnormalities, pulmonary venous hypertension or obstruction, restrictive or hyperventilatory lung disease, chronic liver disease, and toxin use must be considered and, if present, addressed to the degree possible.\textsuperscript{W13}

Dyspnea on exertion is the most common presenting symptom of patients with severe PAH and Eisenmenger physiology, followed by palpitations, peripheral edema, volume retention, hemoptysis, syncope, and progressive cyanosis.\textsuperscript{W27} Morbidity is progressive and becomes substantial, typically by the third decade of life. Hypoxemia-related secondary erythrocytosis leads to increased blood viscosity and intravascular sludging. Organ damage may result in the brain from cerebrovascular changes brought about by sludging, with resultant stroke, and in the kidneys, with altered renal function. Right heart pressure and volume overload cause elevated systemic venous pressure leading to hepatic dysfunction. Hyperuricemia may result in gout. Hemoptysis is potentially life threatening. Chest pain due to right ventricular ischemia, coronary artery compression by a dilated pulmonary artery, or arteriosclerosis may occur with exertion or at rest. Ultimately, right heart failure is inevitable. Poor functional status is an important predictor of mortality, as are serologic evidence of low systemic organ perfusion, worsening hypoxemia, and left ventricular systemic dysfunction.\textsuperscript{C2}

Premature death is the rule. The immediate modes of death include right ventricular failure, severe hemoptysis from bronchial artery rupture or pulmonary infarction, complications during pregnancy, and cerebral vascular events, including occlusive strokes, systemic paradoxical embolization, and brain abscesses.\textsuperscript{S2,S17} Death during noncardiac surgery also occurs.

Changes that occur with left-to-right shunt-related PAH can be reversible after eliminating the shunt, provided that the surgery is performed during the vasoactive stage of PAH development, before irreversible obstructive pulmonary vascular changes occur. Catheterization-based calculations of \( Q_p \), individualized measurements of resistance in isolated lung segments, and direct measurement of pulmonary venous pressure are typically used to assess PAH reversibility and likelihood of surgical success. One hundred percent inspired oxygen, inhaled nitric oxide, and intravenously administered prostacyclin are frequently used in such investigations to determine the degree of pulmonary vascular reactivity and the potential to subsequently lower pulmonary artery pressure with surgical correction of the shunt. Increasingly, acute and chronic pharmacologic pulmonary vasodilatory and vascular remodeling therapy accompanies surgery in these cases. Specific data are not available that firmly establish the pressures, flows, and resistances that determine if operation to remove the shunt is indicated. Typically, Rp less than 10 to 14 Wood units and a \( Q_p/Q_s \) less than or equal to 2/3 are associated with better surgical outcomes.\textsuperscript{C32,S49} Even less clear is the predictive value of degree of vasodilatation achieved in the catheterization laboratory in response to vasodilatory agents. An additional confounding factor is that calculated Rp itself can vary with \( Q_p \) based on flow; Rp calculated under shunt conditions with high \( Q_p \) may actually be lower than that calculated after the high-flow condition is eliminated by surgical repair. Pulmonary vessels that were recruited because of high \( Q_p \) may be lost after flow is reduced to normal following surgery, resulting in higher postoperative Rp and pulmonary pressure than was anticipated using the catheterization data.

If evaluation determines that surgical closure of the shunt is indicated, a multidisciplinary team approach is mandatory, including an anesthesia team and intensive care team experienced in managing both PAH and the adult with CHD. The surgical procedure itself will often be technically simple; however, pre- and postoperative management will not. The optimal type and mode of anesthetic administration should be individualized (see Chapter 4). Risk of right-to-left embolization warrants avoiding bubbles following intravenous catheter placement. Use of inhaled nitric oxide both pre- and postoperatively should be considered.

Diagnosis of Eisenmenger physiology requires a detailed history, documenting all previous cardiac surgical and interventional procedures and medical treatments. Thorough
documentation of the current cardiac morphology and cardio-pulmonary physiology is mandatory using chest radiography, electrocardiography, echocardiography, cardiac catheterization, computed tomography (CT), pulmonary function studies, and assessment of all end-organ function. Once the diagnosis is made, the option of surgical treatment by repair of the anomaly causing the shunt is no longer an option because this approach will result in physiologic decompensation from severe PAH, right heart failure, and mortality. Proven treatment options are strictly medical, with the exception of lung or heart-lung transplantation (see Chapter 21). Transplantation offers a limited survival benefit, given the unpredictability of transplant-free survival and significantly higher perioperative mortality in this cohort of patients, although individual outcomes may warrant individual considerations. Medical treatment options are complex and must be tailored to the individual patient, as discussed in detail in the ACC/AHA 2008 guidelines. The evolving concept of treat and repair, meaning initially using advanced pharmacologic regimens to treat PAH followed by surgical repair of the structural anomaly, has the potential to change some patients from “inoperable” to “operable,” although long-term benefit is currently unknown.

Heart Failure and Transplantation

Heart Failure
Myocardial dysfunction resulting in depressed cardiac function (heart failure) is present more frequently in adults being considered for surgery to correct a structural heart anomaly than in neonates, infants, and children. Distinguishing between heart failure and existing structural heart disease as the cause of cardiopulmonary decompensation is critical to successful decision making and managing of adults with CHD. Recognizing heart failure may be difficult because the associated congenital cardiacl condition may mimic symptoms of heart failure. For example, dyspnea on exertion may be due to cyanosis and not heart failure. As a result, NYHA functional status may be inadequate in this patient population.

The blurring between heart failure and structural heart disease is further complicated because the underlying disease itself may lead to heart failure in the adult, and thus both may be present in the same patient. The ACC/AHA guidelines identify the most common underlying cardiac structural substrates leading to late heart failure:

- Severe aortic stenosis or regurgitation secondary to bicuspid aortic valve and variants
- Subvalvar or supravalvar left ventricular outflow tract pathology
- Coarctation of the aorta
- Severe congenital mitral stenosis or regurgitation
- Unoperated ASD or partial AVSD
- Congenitally corrected TGA
- TGA after Mustard or Senning atrial switch procedures in which the morphologic right ventricle is the systemic ventricle
- Tetralogy of Fallot with early-era surgery, long-standing shunt, or severe pulmonary regurgitation or stenosis after repair
- Single-ventricle mixed circulation and chronic cyanosis
- Single ventricle after a Fontan procedure

Heart failure can be accelerated further in this patient population by unrelated conditions and chronic degenerative processes common in all adults:

- Acquired valvular heart disease
- Coronary artery disease
- Systemic hypertension
- Diabetes mellitus
- Pregnancy
- Endocarditis
- Chronic pulmonary disease
- Cardiotoxic chemotherapy and mediastinal irradiation
- Illicit drug use
- Acquired renal or liver disease
- Obstructive sleep apnea
- Hyperthyroidism or hypothyroidism.

Arrhythmia and heart block therapy may play a role in heart failure. Rhythm disturbances are common sequelae of cardiac surgery for CHD, and progressively deteriorating hemodynamics and rhythm disturbances often coincide without a clear etiology. Nevertheless, the functional effect of combined heart failure and rhythm disturbance in the adult with CHD is additive. A surgically placed epicardial or transvenously placed endocardial right heart sequential atrioventricular pacing system may benefit the patient with heart block or sinus node disease and related bradycardia.

Patients with heart failure induced by abnormal activation sequences from right ventricular pacing, and selected patients with structurally abnormal hearts, heart failure, and normal sinus rhythm, may benefit from resynchronization therapy.

Resynchronization therapy is not of proven benefit in single-ventricle patients with heart failure.

Pharmacologic therapy is first-line therapy for many arrhythmias; however, transvenous or surgical ablation techniques may benefit selected patients with both atrial and ventricular tachyarrhythmias. The maze procedure may have therapeutic value in patients with atrial fibrillation or flutter, particularly when combined with reconstructive surgical procedures such as Fontan revision, repair of Ebstein anomaly, and right ventricular outflow tract surgery in tetralogy of Fallot.

Other factors, such as a history of early-era surgery with poor myocardial protection or prior surgery with prolonged CPB and myocardial ischemia, inadequate surgical reconstructive techniques, or other surgical sequelae can also contribute to heart failure. When heart failure and structural heart disease coexist with these chronic pressure or volume overload and cyanotic conditions, case-by-case judgment must be made with respect to specific management. Options include surgical correction of the structural defect and simultaneous medical management of the heart failure, medical management of both the heart failure and structural disease, and heart or heart-lung transplantation.

Transplantation
When irreversible heart failure is judged to be the predominant factor limiting survival, and it is due to an uncorrected structural anomaly or residual structural heart disease after surgery, reconstructive heart surgery should be considered. Otherwise, if reconstructive surgery is not possible, heart transplantation should be considered. If pulmonary vascular obstructive disease is present and limits survival, lung or
heart-lung transplantation should be considered. The decision between lung and heart-lung transplantation is made based on the complexity of the structural heart anomaly. If a PDA, ASD, or simple VSD is present, lung transplantation along with reconstructive surgery for the heart may be possible. If the CHD is more complex, or if heart failure accompanies one of these simple defects, heart-lung transplantation is most appropriate.

Pre-transplantation evaluation is multidisciplinary, similar to that for any other heart failure patient. Rp may be elevated in any patient with heart failure; however, it is more commonly encountered when there is a history of long-standing CHD in addition to heart failure, particularly if the CHD is associated with left-to-right shunting. If there is no evidence of intracardiac or arterial-level shunting, Rp-related contraindications to heart transplantation in the adult with CHD are similar to those for any patient and include Rp greater than or equal to 6 Wood units or a transpulmonary gradient above 15 mmHg that is unresponsive to pulmonary vasodilator therapy in the catheterization laboratory. Transpulmonary gradient alone is less helpful in the presence of either increased or decreased Qp, which is commonly encountered in many forms of uncorrected CHD. In addition, magnetic resonance imaging (MRI) or CT of the chest may be helpful in defining extracardiac morphology, such as systemic venous anomalies, arch anomalies, and the relationship of the aorta, pulmonary trunk, conduit (if present), or ventricular mass to the posterior table of the sternum.

Noncardiac contraindications to transplantation in CHD are similar to those for transplantation in acquired cardiac disease:

- Uncontrolled infection
- Positive serology for human immunodeficiency virus (HIV) or hepatitis C infection
- Uncontrolled metabolic disease
- Additional severe congenital anomalies
- Multisystem organ failure
- Uncontrolled malignancy
- Psychosocial disability affecting compliance

Additionally, previous thoracotomy, especially if multiple and associated with chronic cyanosis, is a relative contraindication, particularly for lung or heart-lung transplantation, because of the likelihood of fatal bleeding from collaterals.

Mortality risk is doubled in the first year after transplantation if the indication has been adult CHD. Outcomes after lung and heart-lung transplantation for PAH in adults with CHD are comparable with those reported for children, with actuarial survival at 10 years of 20%. There is increased risk of early death compared with transplantation for obstructive pulmonary disease or cystic fibrosis because of perioperative complications related to increased complexity of the operation. Outcomes for combined lung transplantation and cardiac repair are similar to those for heart-lung transplantation.

Endocarditis

As stated earlier in this chapter, most forms of CHD are not cured by surgery or other intervention. Residual defects or surgical and interventional remnants present in most adults with CHD often predispose to infective endocarditis (see Chapter 15). More than 10% of patients with endocarditis have a history of CHD, and endocarditis is the cause for 4% of hospital admissions for adults with CHD. Some anomalies carry a higher risk of endocarditis than others, including bicuspid aortic valve, unrepaired VSD, PDA, tetralogy of Fallot, TGA, single-ventricle anomalies with systemic to pulmonary artery shunts, and those whose repair includes a conduit or prosthetic valve. Surgical closure of a VSD reduces the risk of endocarditis, and when endocarditis develops at the site of a surgically repaired defect, a residual patch leak is frequently observed. In a series of adults with CHD admitted for a diagnosis of endocarditis, certain anomalies were underrepresented, including ASD, completely closed VSD, unrepaired Ebstein anomaly, and Mustard and Senning atrial switch repairs.

Definitive diagnosis of infectious endocarditis requires positive blood cultures with appropriate organisms and physical evidence of endocardial involvement (typically identified by echocardiography). Surface echocardiography may be adequate, but transesophageal echocardiography may be particularly helpful, especially when complex structural anomalies are present. Once the diagnosis is made or suspected, further management should occur at a center with an established adult CHD program. Consultation with a cardiac surgeon who has a focus on adult CHD should be undertaken early in the patient’s course, because rapid deterioration requiring surgery is common. Relative indications for surgery are:

- Development of hemodynamic decompensation
- Evidence of embolic complications
- Intractable infection despite appropriate antibiotic therapy
- Infection of prosthetic valves, conduits, or other material
- Abscess development
- Contained rupture
- Development of heart block

The indication to operate may be clear, or it may be ambiguous. Consultation among the cardiologist, infectious disease specialist, and surgeon should take place in all cases under consideration for surgery.

Recommendations for infectious endocarditis prophylaxis have changed in recent years. The 2007 AHA guidelines recommend selective use of preventive antibiotic therapy, but also emphasize behavioral elements. The latter include maintaining daily oral hygiene and skin hygiene, particularly with respect to acne, and avoiding nail biting. Prophylactic antibiotic therapy is confined to dental procedures (no longer gastrointestinal or genitourinary procedures) in patients with prior endocarditis, prosthetic heart valves, conduits, shunts, unrepaired cyanotic CHD, CHD repaired with prosthetic patches or other material within 6 months of surgery, residual defects after reparative surgery for CHD if the residual defect is in the proximity of prosthetic material, and valve lesions in transplant patients.

Niwa and colleagues reported 69 cases of endocarditis in adults with CHD. Prior cardiac surgery and a history of cyanosis were common. Involvement of the left and right sides of the heart was equally common. Dental procedures, cardiac surgery, and pneumonia commonly preceded
endocarditis. *Streptococcus* and *Staphylococcus* accounted for 87% of cases, with *Streptococcus* the most common organism. Surgical intervention was needed in 26% of cases, and the indication for surgery was large vegetations in 45% and heart failure in 29%. Endocarditis-related mortality was 8% in patients treated medically and 11% in those treated surgically. Di Filippo and colleagues note that adults increasingly account for cases of endocarditis in patients with CHD, and that complex cyanotic heart disease is also increasingly common.\(^{316}\) *Streptococcus* and *Staphylococcus* remain the most prevalent organisms. Again, dental procedures and cardiac surgery frequently preceded endocarditis, but these authors note an increasing frequency of cutaneous infections in recent years. A precipitating cause for endocarditis, however, is often not identified. Awadallah and colleagues identified a predisposing event in 56% of cases, but Gersony and colleagues in only 32%.\(^{32,612}\)

**Arrhythmias**

Both atrial and ventricular arrhythmias are a more important source of morbidity in adults with CHD than in infants and children. *Ventricular arrhythmias* in particular, uncommon in young patients, are frequent in adults. Arrhythmias can be observed in all adult clinical groups: surgically repaired anomalies,\(^{315}\) surgically palliated and single-ventricle anomalies,\(^{312}\) and unrepaired anomalies (Table 29-3). Cause of conduction system pathophysiologic is multifactorial, including cyanosis, volume and pressure overload, surgical incisions, suture lines, and patches with subsequent scarring; ischemic insults of any etiology, including coronary embolism in patients with left-to-right shunting; and inadequate myocardial protection during previous surgery. In general, the longer the inciting cause is present, such as cyanosis or volume overload, the more likely arrhythmias will occur. It is this cumulative effect that results in the higher prevalence of arrhythmias in the adult population.

Rhythm disturbances may come to the attention of the surgeon in several ways. Most commonly, a patient being evaluated for reconstructive surgery, such as repair of a large ASD or replacement of a right ventricle to pulmonary trunk conduit, will have an associated rhythm disturbance that may influence intraoperative and postoperative care. Antiarrhythmic therapy may be required, and existence of an arrhythogenic substrate may influence the choice or concentration of inotropic support used.

The arrhythmia may require surgical therapy concomitant with the reconstructive surgical procedure, such as an atrial maze procedure or placement of ventricular cryoablation lesions (see Chapter 16). In other circumstances the sole, or primary, indication for surgery may be the rhythm disturbance. The atrial maze procedure, an epicardial pacemaker system for heart block or bradyarrhythmia, a biventricular pacemaker system for resynchronization therapy,\(^{38}\) or placement of an implantable cardioverter-defibrillator (ICD) are examples of surgery that may be needed.

*Intraatrial reentrant tachycardia* (IART), or atrial flutter, is the most common rhythm disturbance in adults with CHD. It usually develops late postoperatively, most often in patients who have had a right atrial incision or some other right atrial suture line. The amount of right atrial surgery tends to correlate with prevalence of IART, the greatest being in patients who have had Mustard atrial switch intracardiac type Fontan procedures. It can, however, occur after ASD closure. Pharmacologic therapy and catheter ablation are the first- and second-line therapeutic choices. Pacemaker placement to increase baseline heart rate may suppress fibrillation episodes if sinus bradycardia coexists. If a pacemaker is indicated, a transvenous approach is preferred; however, numerous contraindications exist, including presence of any intracardiac shunt (even if trivial, such as a small patent foramen ovale), previous bidirectional Glenn or extracardiac-type Fontan procedure, single-ventricle physiology of any kind, and upper body central venous thrombosis. In these situations, surgical pacemaker placement is indicated. Surgical therapy with a concomitant right atrial maze procedure is indicated if reconstructive intracardiac surgery is planned. Isolated right atrial maze may be considered if IART is poorly controlled by other means. The right atrial maze procedure and its modifications have been shown to be effective in eliminating IART in Fontan patients undergoing concomitant conversion of an intracardiac-type Fontan to an extracardiac type (see Chapter 41).\(^{317}\)

*Atrial fibrillation* occurs most often in adults with congenital aortic stenosis, congenital mitral valve disease, or single ventricle.\(^{315}\) Medical therapy includes anticoagulation, pharmacologic ventricular rate control, and electrical cardioversion. There is no role for catheter ablation. Indications for pacemaker therapy if sinus bradycardia coexists are similar to

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**Table 29-3 Rhythm Disturbances in Adults with Congenital Heart Disease**

<table>
<thead>
<tr>
<th>Rhythm Disturbance</th>
<th>Associated Lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tachycardias</strong></td>
<td></td>
</tr>
<tr>
<td>Wolff-Parkinson-White syndrome</td>
<td>Ebstein anomaly</td>
</tr>
<tr>
<td></td>
<td>Congenitally corrected transposition</td>
</tr>
<tr>
<td>Intraatrial reentrant tachycardia (atrial flutter)</td>
<td>Postoperative Mustard</td>
</tr>
<tr>
<td></td>
<td>Postoperative Senning</td>
</tr>
<tr>
<td></td>
<td>Postoperative Fontan</td>
</tr>
<tr>
<td></td>
<td>Tetralogy of Fallot</td>
</tr>
<tr>
<td></td>
<td>Other</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Mitral valve disease</td>
</tr>
<tr>
<td></td>
<td>Aortic stenosis</td>
</tr>
<tr>
<td></td>
<td>Tetralogy of Fallot</td>
</tr>
<tr>
<td></td>
<td>Palliated single ventricle</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>Tetralogy of Fallot</td>
</tr>
<tr>
<td></td>
<td>Aortic stenosis</td>
</tr>
<tr>
<td></td>
<td>Other</td>
</tr>
<tr>
<td><strong>Bradycardias</strong></td>
<td></td>
</tr>
<tr>
<td>Sinus node dysfunction</td>
<td>Postoperative Mustard</td>
</tr>
<tr>
<td></td>
<td>Postoperative Senning</td>
</tr>
<tr>
<td></td>
<td>Postoperative Fontan</td>
</tr>
<tr>
<td></td>
<td>Sinus venous ASD</td>
</tr>
<tr>
<td></td>
<td>Heterotaxy syndrome</td>
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<tr>
<td>Spontaneous AV block</td>
<td>AV septal defects</td>
</tr>
<tr>
<td></td>
<td>ASD</td>
</tr>
<tr>
<td>Surgically induced AV block</td>
<td>Subaortic stenosis relief</td>
</tr>
<tr>
<td></td>
<td>AV valve replacement</td>
</tr>
</tbody>
</table>

Modified from Warnes and colleagues.\(^{311}\)

Key: ASD, Atrial septal defect; AV, atrioventricular; VSD, ventricular septal defect.
Ventricular arrhythmias may develop in the adult with CHD. Macroreentrant ventricular tachycardia can develop late after ventricular surgery, related to ventriculotomy or VSD patching. In repaired tetralogy of Fallot, reentry circuits typically form through narrow conduction pathways created by right ventricular outflow tract scarring. Prevalence of late ventricular tachycardia or sudden death for repaired tetralogy is 0.5% to 6.0%. Older age at repair, right ventricular dilatation, and QRS duration longer than 180 ms have been identified as risk factors for development of ventricular tachycardia and sudden death in tetralogy of Fallot patients. Palpitations, dizziness, or syncope warrant electrophysiologic testing in the adult with repaired tetralogy of Fallot. These symptoms may be elicited at the time of evaluation for surgical therapy for recurrent or residual right ventricular outflow tract disease. Electrophysiologic testing should be performed prior to surgery.

Ventricular tachycardia can develop in any form of CHD in the adult, even if there has never been a ventricular incision or suture line. The onset may coincide with deteriorating ventricular function.

Complete hemodynamic and electrophysiologic evaluation is required before therapy for ventricular tachycardia is undertaken. If sustained ventricular tachycardia is documented or the patient has a history of cardiac arrest, the next step is to determine whether there is a physiologically significant residual or recurrent structural anomaly. If there is no structural anomaly, the treatment option of choice is implanting an ICD. A surgically placed ICD is indicated for patients with single-ventricle physiology, obstructed upper body systemic veins, bidirectional cavopulmonary anastomosis, a Fontan procedure, residual intracardiac shunts, or other unusual or distorted intracardiac morphology; otherwise, transvenous systems are available. In selected cases, catheter-based ablation can also be performed to reduce the likelihood or frequency of ventricular tachycardia episodes. Catheter-based ablation is unreliable as sole therapy, with recurrence that may exceed 20%. Pharmacologic therapy alone is currently considered inadequate if sustained ventricular tachycardia or a history of cardiac arrest exists, but may be indicated if less serious ventricular arrhythmias are present.

If structural cardiac anomalies with important hemodynamic impairment are present in an adult with ventricular tachycardia, surgical repair of the anomaly combined with either concomitant surgical ablation or concomitant surgical ICD placement may be indicated. In such cases, it is necessary to map the ventricular tachycardia, either by preoperative electrophysiologic testing or intraoperative mapping. If a discrete focus of ventricular tachycardia is inducible and there is no clinical history of cardiac arrest, surgical ablation may be the best option. A typical situation appropriate for this form of therapy is the patient with tetralogy of Fallot originally repaired with a transanular patch who presents late with severe pulmonary regurgitation, a dilated right ventricle, and inducible ventricular tachycardia mapped to the right ventricular outflow tract. Surgical therapy includes placing a pulmonary valve prosthesis and creating cryoablation lesions from the outflow patch to the pulmonary trunk and from the outflow patch to the tricuspid anulus. Follow-up electrophysiologic evaluation is indicated in all such cases to determine if ventricular tachycardia is controlled. Placement of an ICD is indicated if ventricular tachycardia is inducible at follow-up. In the patient presenting with a history of cardiac arrest whose evaluation reveals structural disease as well as ventricular tachycardia, or the patient with structural disease and poorly localized ventricular tachycardia, the best choice of therapy is probably structural repair and concomitant surgical ICD placement.

Sinoatrial (SA) node dysfunction in adults with CHD typically is acquired, occurring as a result of localized trauma or ischemia following previous cardiac surgery. The most common procedures that result in SA node dysfunction are the Mustard, Senning, Glenn, and Fontan operations. Less frequently, SA node dysfunction is congenital, associated with some forms of heterotaxy syndrome. Patients with SA node dysfunction may be symptomatic as a result of chronotropic incompetence or of development of atrial fibrillation or flutter, which are more likely to occur when SA node dysfunction is present. Ventricular tachycardia can also develop as a result of prolonged sinus pauses. Placing a pacemaker system is indicated in several circumstances. Implantation of an atrial, or atrioventricular sequential, pacing system with activity responsiveness is indicated for symptoms related to chronotropic incompetence, tachy-bradycardia syndrome, recurrent atrial tachycardias, and pause-dependent ventricular tachycardia. It is also indicated for the asymptomatic adult patient with a resting heart rate of less than 40 beats per minute or atrial pauses greater than 3 seconds. Typically, atrioventricular conduction is normal when SA node dysfunction is present; therefore, atrial pacing alone is effective therapy. Nevertheless, atrioventricular sequential pacing systems are recommended in all cases, with appropriate programming of the system such that atrial pacing occurs along with natural atrioventricular conduction. Pacemaker systems can be placed transvenously or surgically. Surgical placement is indicated in the presence of single-ventricle physiology, bidirectional cavopulmonary anastomosis, Fontan surgery, distorted or thrombosed upper body central veins, and any intracardiac shunt; otherwise, transvenous placement is preferred.

Atrioventricular (AV) block in the adult with CHD may be acquired or congenital. Acquired block is more common and results from surgical trauma to the AV node or surrounding tissues during intracardiac repair. Block usually develops during surgery. Typical operations that may result in block include closure of perimembranous or inlet VSDs, resection of left ventricular outflow tract obstruction, and surgery to repair or replace the inlet valves. Transient heart block...
with full recovery of AV conduction is common after these operations, occurring in over half of all patients who suffer block at surgery. Recovery typically occurs within 10 days. Transvenous or surgical placement (see indications for each in the preceding text) of an AV sequential pacemaker system is indicated if postoperative second- or third-degree block has not recovered after 10 days of observation. A relative indication for pacemaker placement is presence of persistent bifascicular block.

The AV node and bundle of His may also be congenitally abnormal, associated with specific anomalies such as congenitally corrected TGA and AVSD. These patients are more likely to develop block with any form of intracardiac manipulation and to develop spontaneous block either before or after surgery. Spontaneous development of second- or third-degree heart block is an indication for either transvenous or surgical placement of an AV sequential pacemaker system.

Other Organ Systems

Other organ systems may be abnormal in the adult with CHD. These abnormalities may result from altered hemodynamics, chronic cyanosis, or associated syndromes (see “Syndromes Associated with Congenital Heart Disease” in text that follows), and may contribute important morbidity and mortality risks when cardiac surgery is performed in the adult with CHD.

*Altered hemodynamics* can lead to pulmonary vascular abnormalities. This subject is discussed under “Pulmonary Arterial Hypertension and Eisenmenger Physiology” earlier in this section. An altered hemodynamic state is well documented in patients with coarctation of the aorta, both repaired and un repaired. Systemic hypertension and decreased systemic vascular compliance contribute to, and may even play a causal role in, development of and morbidity related to intracranial aneurysms. All adults with a history of coarctation should undergo evaluation of the cerebral vasculature to rule out vascular aneurysms, particularly if repeat aortic surgery is being contemplated. Long-standing abnormal right-sided hemodynamics, particularly in patients with tetralogy of Fallot, single-ventricle morphology with Fontan surgery, and Ebstein anomaly, may result in chronic hepatic venous hypertension and hepatic congestion, leading to hepatic dysfunction and cirrhosis, gastroesophageal varices, and even hepatocellular carcinoma. Particularly in Fontan patients, additional problems may include protein-losing enteropathy, plastic bronchitis, and renal compromise.

*Chronic cyanosis* leads to erythrocytosis, iron deficiency, and clotting disorders. Blood viscosity is increased. Combined erythrocytosis and iron deficiency leading to microcytosis increases risk of thrombosis and stroke, which may be particularly relevant perioperatively. Additionally, cyanosis-related platelet dysfunction and deficiency of plasma and clotting factors due to erythrocytosis combine to increase the risk of hemorrhagic complications, again of particular relevance perioperatively. An additional complication of erythrocytosis is an increased rate of red cell turnover, leading to abnormal bilirubin metabolism and development of gall stones. The risk of cholecystitis and pancreatitis perioperatively is increased. Chronic cyanosis also leads to renal glomerulosclerosis. Glomerular filtration rate is decreased, resulting in creatinine elevation.

*Renal dysfunction* is found in adult patients with a wide spectrum of CHD.

*Scoliosis* is common in patients with chronic cyanosis. This may lead to deformity of the thorax, causing ventilatory compromise. Pulmonary function tests are required in all adult patients with CHD and scoliosis who are under consideration for cardiac surgery.

There is a risk of *stroke* after all cardiac procedures in patients of all ages. It was found to be 0.8% in 124 adults undergoing surgery for CHD. Interestingly, this is lower than the risk of stroke in adults undergoing different types of surgery for various acquired heart problems.

Syndromes Associated with Congenital Heart Disease

A number of syndromes are associated with CHD, many associated with neurologic, developmental, and cognitive deficits (Table 29-4). Many of these syndromes include other coexisting disease processes in other organ systems that represent specific risks during anesthesia and surgery (Table 29-5).

The deficits may be mild enough in many cases to allow these individuals to live somewhat independently. When the cardiac surgeon is asked to consult on the adult patient with CHD, he or she must keep in mind that the patient may have one of these syndromes. Additionally, many adults with CHD who do not have specific syndromes may be overprotected by caring family members and may not have the emotional or intellectual maturity expected for their age. Accordingly, these patients may have limited ability to fully appreciate the complexities, risks, complications, and alternatives to a proposed surgical procedure. Family members and primary care providers should be included in such consultations.

Table 29-4 Syndromes Associated with Congenital Heart Disease

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Typical Congenital Heart Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down</td>
<td>AVSD, TF</td>
</tr>
<tr>
<td>DiGeorge</td>
<td>TF, IAA, TA</td>
</tr>
<tr>
<td>Williams</td>
<td>Supravalvar AS, PS</td>
</tr>
<tr>
<td>Noonan</td>
<td>PS</td>
</tr>
<tr>
<td>Turner</td>
<td>CoA, AS</td>
</tr>
</tbody>
</table>

Key: AS, Aortic stenosis; AVSD, atrioventricular septal defect; CoA, aortic coarctation; IAA, interrupted aortic arch; PS, pulmonary stenosis; TA, truncus arteriosus; TF, tetralogy of Fallot.

Table 29-5 Syndromes and Associated Diseases

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Associated Diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Down</td>
<td>Hypothyroidism, obstructive airway disease</td>
</tr>
<tr>
<td>DiGeorge</td>
<td>Immune deficiency, endocrinopathies</td>
</tr>
<tr>
<td>Williams</td>
<td>Hypercalcemia, diabetes mellitus</td>
</tr>
<tr>
<td>Noonan</td>
<td>Clotting disorders, hydrocephalus</td>
</tr>
<tr>
<td>Turner</td>
<td>Hypothyroidism, osteoporosis, diabetes mellitus, renal abnormalities</td>
</tr>
</tbody>
</table>
Repeat Sternotomy

Overview
Many adults undergoing surgery for CHD have had at least one, and often several, previous cardiac operations via median sternotomy. Risk of life-threatening hemorrhage is present with any repeat sternotomy. Other risks include entry of air into the circulation and arrhythmias. Thus, special preparation is required when repeat sternotomy is planned. First, all previous operative notes should be obtained and reviewed. Along with the details of previous cardiac procedures, they may provide important information regarding whether a prosthetic barrier was placed between the sternum and cardiac structures, whether the native pericardium was reapproximated, and whether difficulty was encountered during the previous sternotomy. Also, comments warning about such things as conduit placement in proximity to the posterior sternal border may be given. Second, CT or MRI of the chest can be helpful in defining the position of the anterior border of the heart, ascending aorta, pulmonary trunk, brachiocephalic vein, and conduits relative to the posterior sternal table (Fig. 29-3).

Technical Considerations
Several options are available for patients at high risk of injury during repeat sternotomy. An attempt to open the sternum slowly under direct vision, beginning inferiorly at the xiphoid and progressing superiority, dissecting along the posterior table of the sternum, is the best initial approach in most cases. Using this approach, a segment of posterior sternal table is dissected, and only then is the oscillating saw used to split the freed portion of the sternum. This process proceeds in steps until the sternum is completely split. If, however, at any point the posterior sternal table dissection can no longer be performed under direct vision, or if even minimal bleeding is encountered, dissection is stopped. Peripheral cannulation for CPB is then performed by several means. The femoral artery and vein may be exposed and cannulated and CPB established. If the patient has a completely separated two-ventricle circulation and risk of injury is to any right-sided structures, including right ventricle to pulmonary trunk conduits, then sternotomy can be performed as soon as CPB is established. If the patient has single-ventricle physiology, Fontan physiology, any potential for intracardiac shunting, or two-ventricle physiology but the aorta is at risk of injury, then he or she must be cooled to deep hypothermic temperatures prior to further attempts to open the sternum.

Femoral vascular abnormalities may be present secondary to previous cardiac catheterization or operative procedures. Knowledge of the status of femoral vessels is critically important in all patients undergoing repeat sternotomy. Alternative methods of cannulation for CPB exist (see Chapter 2), and these may be preferable in some patients, including those with femoral vessel abnormalities. If sternotomy cannot be performed safely, the sternal skin incision can be extended superiorly, and the brachiocephalic artery superior to the brachiocephalic vein is exposed and cannulated. The inferior vena cava is also exposed and cannulated within the pericardial space by dissecting inferior to the xiphoid along the diaphragm surface. CPB can then be initiated, and the operation proceeds as described for femoral cannulation.

Outcomes
There are no large studies examining repeat sternotomy specifically in adults with CHD. Three studies examine repeat sternotomy in patients with CHD; however, the average age was 2.1, 3.6, and 4.7 years, although all involved some adults. Overall, the risk of life-threatening hemorrhage during repeat sternotomy in these three series was low—0.3%, 0.7%, and 5.2%—with no specific analysis of adults. Risk factors included presence of right ventricular to pulmonary trunk conduits and increasing number of previous sternotomies. In another series of 2555 adult patients with acquired heart disease undergoing repeat sternotomy, 3% suffered major injury at sternal opening. Mortality, if injury occurred, was 25%.

There are specific congenital anomalies and situations for which risk may be increased. Presence of PAH (regardless of the specific cardiac morphology) may be associated with an enlarged right ventricle and right atrium, both of which have elevated pressure and may be in close proximity to the sternum. Mustard and Senning patients will have markedly hypertrophied and often dilated right ventricles positioned directly behind the sternum. Additionally, the morphologic right atrium, which serves as the physiologic left atrium, may be markedly dilated, and its free wall or appendage may be positioned anteriorly behind the sternum. Injury to this structure during sternotomy, with blood loss and hypovolemia, may result in massive air embolism to the systemic circulation as attempts to control the hemorrhage are undertaken. All conotruncal anomalies, including tetralogy of Fallot, truncus arteriosus, TGA, and double outlet right ventricle, have an

Figure 29-3 Three-dimensional computed tomography reconstruction, lateral view, of adult with L-transposition of the great arteries, double inlet single left ventricle, and previous median sternotomy. Note proximity of ventricular mass to posterior aspect of sternum. Superiorly, the transposed aorta is separated from the sternum by interposed lung tissue. Both observations are important for planning sternal reentry.
Several studies provide an overview of the practice of adult congenital cardiac surgery. Putman and colleagues report a single-institution experience with 963 adult congenital cardiac surgical procedures in 830 patients (mean age 39 years, 50% male) between 1990 and 2007. Underlying diagnoses are shown in Table 29-6; 51% were primary operations and 49% reoperations. Underlying anomalies tended to be more complex in the reoperation group and simpler in the primary operation group. The most common operations were those involving aortic valve replacement (26%); ASD closure (18%); pulmonary valve replacement (13%); mitral valve operation (7.1%); pacemaker placement (6.4%); VSD closure (5.5%); and coarctation repair (4.6%) (Table 29-7). Concomitant coronary artery bypass grafting was performed in 3.4%. CPB was used in 90%. Overall early mortality was 1.5%, and actuarial survival at 17 years was 71% (Fig. 29-4). Risk factors for mortality are shown in Table 29-8. Functional status, estimated by NYHA functional classification, was improved in most survivors.

### Specific Anomalies

Definition, surgical history, morphology, and natural history, as well as general aspects of pathophysiology, clinical presentation, diagnosis, and treatment of specific anomalies discussed in the remainder of this chapter, are described elsewhere in this book in the specific chapters named for each anomaly. The following sections focus on preoperative, operative, and postoperative care issues that are specifically related to adults with these anomalies.

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**Table 29-6** Original Primary Anatomic Diagnoses, Classified According to European Association for Cardiothoracic Surgery Congenital Database

<table>
<thead>
<tr>
<th>Anatomic Diagnosis</th>
<th>Number (%) (N = 963)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Septal Defects</strong></td>
<td>332 (34.5%)</td>
</tr>
<tr>
<td>Atrial septal defect, secundum</td>
<td>196 (20.4%)</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>57 (5.9%)</td>
</tr>
<tr>
<td>Atrioventricular septal defect, partial</td>
<td>56 (5.8%)</td>
</tr>
<tr>
<td>Atrial septal defect, sinus venosus</td>
<td>12 (1.2%)</td>
</tr>
<tr>
<td>Ventricular septal defect + aortic coarctation</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Atrioventricular septal defect, complete</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td><strong>Left Heart Lesions</strong></td>
<td>242 (25.12%)</td>
</tr>
<tr>
<td>Aortic stenosis, valvar</td>
<td>162 (16.8%)</td>
</tr>
<tr>
<td>Aortic stenosis, subvalvar</td>
<td>28 (2.9%)</td>
</tr>
<tr>
<td>Aortic insufficiency</td>
<td>18 (1.9%)</td>
</tr>
<tr>
<td>Aortic insufficiency + stenosis</td>
<td>11 (1.1%)</td>
</tr>
<tr>
<td>Aortic stenosis, subvalvar + valvar</td>
<td>7 (0.7%)</td>
</tr>
<tr>
<td>Mitral valve stenosis</td>
<td>7 (0.7%)</td>
</tr>
<tr>
<td>Sinus of Valsalva aneurysm</td>
<td>5 (0.1%)</td>
</tr>
<tr>
<td>Mitral insufficiency</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td><strong>Right Heart Lesions</strong></td>
<td>194 (20.1%)</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>123 (12.8%)</td>
</tr>
<tr>
<td>Ebstein disease</td>
<td>31 (3.2%)</td>
</tr>
<tr>
<td>Pulmonary stenosis, valvar</td>
<td>18 (1.9%)</td>
</tr>
<tr>
<td>Pulmonary stenosis, valvar + subvalvar</td>
<td>8 (0.8%)</td>
</tr>
<tr>
<td>Pulmonary atresia, VSD including TOF/PA</td>
<td>8 (0.8%)</td>
</tr>
<tr>
<td>Pulmonary atresia, IVS</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Pulmonary stenosis, subvalvar</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Double-chambered right ventricle (DCRV)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Thoracic Arteries and Veins</td>
<td>98 (10.2%)</td>
</tr>
<tr>
<td>Aortic coarctation</td>
<td>43 (4.5%)</td>
</tr>
<tr>
<td>Aortic coarctation + aortic valve stenosis</td>
<td>34 (3.5%)</td>
</tr>
<tr>
<td>Aortic aneurysm</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Anomalous origin of left coronary artery from pulmonary artery</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Coronary fistula</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Coronary artery anomaly, origin</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>6 (0.6%)</td>
</tr>
<tr>
<td>Vascular ring</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td>Transposition of the Great Arteries (TGA)</td>
<td>37 (3.8%)</td>
</tr>
<tr>
<td>TGA, IVS, including LVOTO</td>
<td>17 (1.8%)</td>
</tr>
<tr>
<td>TGA, VSD, including LVOTO</td>
<td>12 (1.4%)</td>
</tr>
<tr>
<td>Congenitally corrected TGA (ccTGA)</td>
<td>4 (0.4%)</td>
</tr>
<tr>
<td>ccTGA, VSD, including LVOTO</td>
<td>4 (0.4%)</td>
</tr>
<tr>
<td>Single Ventricle</td>
<td>35 (3.6%)</td>
</tr>
<tr>
<td>Tricuspid atresia</td>
<td>18 (1.9%)</td>
</tr>
<tr>
<td>Double inlet left ventricle (DILV)</td>
<td>8 (0.8%)</td>
</tr>
<tr>
<td>Mitral atresia</td>
<td>4 (0.4%)</td>
</tr>
<tr>
<td>Double outlet right ventricle (DORV)</td>
<td>4 (0.4%)</td>
</tr>
<tr>
<td>DilV and DORV</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Electrophysiologic</td>
<td>16 (1.7%)</td>
</tr>
<tr>
<td>Arrhythmia, heart block, congenital</td>
<td>16 (1.7%)</td>
</tr>
<tr>
<td>Pulmonary Venous Anomalies</td>
<td>7 (0.7%)</td>
</tr>
<tr>
<td>Partial anomalous pulmonary venous connection</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td>Cor triatriatum</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Aneurysm, atrial</td>
<td>2 (0.2%)</td>
</tr>
</tbody>
</table>

From Putman and colleagues.²²³
Table 29-7  Actual Procedures Performed According to European Association for Cardiothoracic Surgery Congenital Database

<table>
<thead>
<tr>
<th>Main Procedures</th>
<th>Number (%) (N = 963)</th>
<th>Main Procedures</th>
<th>Number (%) (N = 963)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left Heart Lesions</strong></td>
<td></td>
<td>RVOT procedure: 2× ASD, 1× VSD, 1× LVOT, 1× DCRV</td>
<td>6 (0.6%)</td>
</tr>
<tr>
<td>Aortic valve replacement, mechanical: 10× LVOT, 3× VSD, 4× MVP, 3× MVR, 4× CABB, 3× ASD</td>
<td>77 (8.0%)</td>
<td>Pulmonary artery plasty</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Aortic valve replacement, homograft: 5× LVOT, 1× CABB, 1× PAA</td>
<td>67 (7.0%)</td>
<td>Double-chambered right ventricle (DCRV) repair</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Ross procedure: 2× PAA, 2× aortoplasty, 1× CABB, 2× LVOT</td>
<td>51 (5.5%)</td>
<td>Occlusion MAPCA(s)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Aortic root replacement, mechanical (Bentall): 1× ASD, 2× LVOT, 1× MVR, 2× pulmonary mechanical root, 3× PHG, 3× MVP, 1× CABB, 2× prosthetic aortic arch</td>
<td>46 (4.8%)</td>
<td>Electrophysiologic</td>
<td>62 (6.4%)</td>
</tr>
<tr>
<td>Mitral valvuloplasty: 15× ASD, 1× AHG, 5× CABB, 1× PDA, 1× MAZE</td>
<td>41 (4.0%)</td>
<td>Pacemaker procedure</td>
<td>62 (6.4%)</td>
</tr>
<tr>
<td>Mitral valve replacement: 7× ASD, 6× TVP, 1× AVSD, 2× aortic valve, 1× MAZE, 2× CABB, 1× PDA</td>
<td>31 (3.1%)</td>
<td><strong>Thoracic Arteries and Veins</strong></td>
<td>58 (6.0%)</td>
</tr>
<tr>
<td>Subvalvular aortic repair: 2× AVRM, 1× PHG, 1× VSD, 1× RVOT, 1× shunt takedown, 1× aortoplasty, 1× CABB</td>
<td>22 (2.3%)</td>
<td>Coarctation repair, end-to-end</td>
<td>25 (2.6%)</td>
</tr>
<tr>
<td>Aortic valve replacement, bioprosthetic: 2× MVP, 3× ASD, 1× CABB</td>
<td>17 (1.7%)</td>
<td>Coarctation repair, interposition graft</td>
<td>17 (1.8%)</td>
</tr>
<tr>
<td>Aortic valveoplasty: 1× PAA, 2× LVOT, 1× MVP</td>
<td>6 (0.6%)</td>
<td>Coronary artery fistula ligation</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Sinus of Valsalva, aneurysm repair</td>
<td>3 (0.3%)</td>
<td>ALCAPA: 1× coronary fistula#</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Transplant, heart</td>
<td>3 (0.3%)</td>
<td>PDA closure: 1× TVP</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Aortic root replacement, valve sparing: 1× MVP</td>
<td>3 (0.3%)</td>
<td>Vascular ring repair</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td><strong>Septal Defects</strong></td>
<td>255 (26.5%)</td>
<td>Aortic aneurysm repair</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Atrial septal defect repair: 7× MAZE, 15× CABB, 3× PAR, 15× MVP, 1× TVP, 1× PVP</td>
<td>176 (18.3%)</td>
<td>Coronary artery bypass for anomalous coronary artery</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Ventricular septal defect repair: 7× ASD, 7× PHG, 7× RVOT, 1× LVOT, 2× DCRV, 2× AVRM, 1× CABB</td>
<td>53 (5.5%)</td>
<td><strong>Single Ventricle</strong></td>
<td>14 (1.4%)</td>
</tr>
<tr>
<td>Partial atrioventricular septal defect repair: 1× LVOT, 4× TVP, 4× ASD, 1× AHG</td>
<td>26 (2.7%)</td>
<td>Fontan, revision or conversion (re-do Fontan)§</td>
<td>10 (1.0%)</td>
</tr>
<tr>
<td><strong>Right Heart Lesions</strong></td>
<td>180 (18.8%)</td>
<td>Fontan, TCPC, lateral tunnel: 1× MAZE, 1× PM</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Pulmonary valve replacement: 12× VSD, 30× RVOT, 7× PAP, 10× ASD, 2× AVRM, 2× TVR, 10× TVP, 4× Pm</td>
<td>121 (12.6%)</td>
<td><strong>Palliative Procedures</strong></td>
<td>8 (0.8%)</td>
</tr>
<tr>
<td>Ebstein repair: 2× Glenn, 1× ASD, 1× PM</td>
<td>17 (1.8%)</td>
<td>Glenn procedure: 1× PDA, 2× Blalock takedown, 1× PM, 1× PAP</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Tricuspid valve replacement</td>
<td>12 (1.2%)</td>
<td>Shunt, modified Blalock-Taussig</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td>Tetralogy of Fallot primary repair</td>
<td>11 (1.1%)</td>
<td>Shunt, central</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>Valvuloplasty tricuspid valve: 4× ASD, 1× MAZE, 2× MVR, 1× MVP</td>
<td>8 (0.9%)</td>
<td>Shunt, ligation and takedown</td>
<td>1 (0.1%)</td>
</tr>
</tbody>
</table>

*Data following colon after each procedure shows the concomitant procedures and their frequency ("×" is shorthand for a multiplier).

Includes two re-do procedures for sclerosed homografts and eight conversions (two extracardiac and six lateral tunnel).

Key: AHG, Aortic homograft procedure; ALCAPA, anomalous origin of the left coronary artery from the pulmonary artery; ASDL, atrial septal defect closure; AVRM, mechanical aortic valve replacement; AVSD, atrioventricular septal defect repair; LVOT, left ventricular outflow tract procedure; MVP, mitral valvuloplasty; MVR, mitral valve replacement; PAA, prosthetic ascending aorta; PAP, plasty of the pulmonary artery(ies); PDA, patent ductus arteriosus closure; PHG, pulmonary homograft procedure; PM, pacemaker procedure; PVP, pulmonary valvuloplasty; RVOT, right ventricular outflow tract procedure; TVR, tricuspid valve replacement; VSD, ventricular septal defect closure.

Modified from Putman and colleagues.212
In a multi-institutional (37 Child Health Corporation of America [CHCA] centers) study of 719 adult congenital cardiac operations performed between 2005 and 2007, Mahle and colleagues report that the most frequent principal procedures were pacemaker placement (29%), pulmonary valve replacement (17%), aortic valve replacement (8.3%), and Fontan revision (5.2%). Early mortality was 1.9%. Among the 37 freestanding children’s hospitals that make up this consortium, 0% to 11% of all cardiac operations were performed in adults.

Data from the CONCOR (CONgenital CORvitia) Dutch national registry of adults with CHD show several notable gender-specific outcomes in 7414 patients. Women had a 33% higher risk of pulmonary hypertension, a 33% lower risk of aortic events, a 47% lower risk of endocarditis, and a 55% lower risk of arrhythmias and ICD placement. There were no gender-related mortality differences.

### Section II Atrial Septal Defect

**Definition**

Definition, morphology, and basic physiology of atrial septal defect (ASD) are described in Chapter 30. ASD is one of the most common anomalies found in adults. It typically presents as newly diagnosed primary disease, or previously diagnosed primary disease with benign physiology. It constitutes 25% to

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**Table 29-8 Incremental Risk Factors for Early and Late Mortality Following 963 Adult Congenital Heart Operations**

<table>
<thead>
<tr>
<th></th>
<th>30-Day Univariate OR (95% CI)</th>
<th>30-Day Multivariate OR (95% CI)</th>
<th>1-Year Univariate OR (95% CI)</th>
<th>1-Year Multivariate OR (95% CI)</th>
<th>3-Year Univariate HR (95% CI)</th>
<th>3-Year Multivariate HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary HT</td>
<td>7.82 (2.08-29.38)</td>
<td>7.72 (1.99-29.86)</td>
<td>7.20 (2.54-20.38)</td>
<td>7.59 (2.55-22.59)</td>
<td>NS</td>
<td>—</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>2.02 (1.01-4.03)</td>
<td>1.92 (0.90-4.07)</td>
<td>1.79 (1.04-3.07)</td>
<td>NS</td>
<td>2.02 (1.44-2.82)</td>
<td>1.97 (1.34-2.91)</td>
</tr>
<tr>
<td>Age at surgery</td>
<td>1.03 (1.00-1.06)</td>
<td>1.03 (0.99-1.06)</td>
<td>1.03 (1.01-1.06)</td>
<td>1.03 (1.00-1.05)</td>
<td>1.05 (1.03-1.06)</td>
<td>1.04 (1.02-1.06)</td>
</tr>
<tr>
<td>Impaired VEF</td>
<td>NS</td>
<td>—</td>
<td>3.71 (1.69-8.15)</td>
<td>3.61 (1.60-8.15)</td>
<td>4.02 (2.52-6.62)</td>
<td>3.71 (2.27-6.07)</td>
</tr>
<tr>
<td>Active endocarditis</td>
<td>NS</td>
<td>—</td>
<td>6.30 (1.74-22.80)</td>
<td>NS</td>
<td>NS</td>
<td>—</td>
</tr>
<tr>
<td>Preoperative ventilation</td>
<td>NS</td>
<td>—</td>
<td>8.04 (2.21-29.23)</td>
<td>6.67 (1.66-26.86)</td>
<td>NS</td>
<td>—</td>
</tr>
<tr>
<td>Additive EuroSCORE*</td>
<td>NS</td>
<td>—</td>
<td>1.32 (1.14-1.54)</td>
<td>NS</td>
<td>1.29 (1.17-1.42)</td>
<td>NS</td>
</tr>
<tr>
<td>Logistic EuroSCORE*</td>
<td>NS</td>
<td>—</td>
<td>1.10 (1.04-1.16)</td>
<td>NS</td>
<td>1.08 (1.04-1.14)</td>
<td>NS</td>
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<td>NYHA III or IV</td>
<td>NS</td>
<td>—</td>
<td>3.28 (1.49-7.21)</td>
<td>NS</td>
<td>3.01 (1.89-4.82)</td>
<td>—</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>NS</td>
<td>—</td>
<td>NS</td>
<td>NS</td>
<td>1.90 (1.07-3.37)</td>
<td>2.37 (1.30-4.33)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>NS</td>
<td>—</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>COPD</td>
<td>NS</td>
<td>—</td>
<td>NS</td>
<td>NS</td>
<td>4.82 (2.39-9.74)</td>
<td>2.57 (1.19-5.52)</td>
</tr>
<tr>
<td>Creatinine</td>
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<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>NS</td>
<td>—</td>
<td>NS</td>
<td>NS</td>
<td>2.31 (1.18-4.55)</td>
<td>3.17 (1.58-6.36)</td>
</tr>
<tr>
<td>Extracardiac artery</td>
<td>NS</td>
<td>—</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>—</td>
</tr>
<tr>
<td>Male sex</td>
<td>NS</td>
<td>—</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

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Modified from Putman and colleagues. 

*See reference P24 for description of EuroSCORE.

**Note:** Thirty-day and one-year mortality were analyzed using logistic regression, long-term mortality was analyzed using Cox regression.

Key: CI, confidence interval; COPD, chronic obstructive pulmonary disease; HR, hazard ratio; HT, hypertension; NS, nonsignificant; —, not tested multivariate; NYHA, New York Heart Association; OR, odds ratio; VEF, ventricular ejection fraction.
30% of newly diagnosed congenital heart disease (CHD) cases in adults.\textsuperscript{20}

**MORPHOLOGY**

Each of the four morphologic forms of ASD is found in adults, with associated cardiac defects in up to a third (see Chapter 30). Most commonly, these are classic associations found with sinus venous and ostium primum defects. Mitral valve prolapse and valvar pulmonic stenosis may be seen with ostium secundum defects.\textsuperscript{3,13,515} Patent foramen ovale (PFO) is of particular interest.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Presentation**

The chronic right-sided volume and pressure overload found with large ASDs leads to reduced aerobic capacity, atrial arrhythmias, and respiratory infections. Dyspnea and palpitations are the most common presenting symptoms, typically in the third and fourth decades of life.\textsuperscript{37,22} Atrial fibrillation or flutter and paradoxical embolism may also lead to presentation. Pulmonary arterial hypertension (PAH) is usually mild and primarily flow related; however, severely elevated pulmonary vascular resistance (Rp) and obstructive pulmonary vascular disease leading to Eisenmenger physiology occur in a minority of patients.

Smaller ASDs—those less than 5 mm in diameter—and PFOs do not cause these changes, but can be the source (as can larger ASDs) of paradoxical emboli.\textsuperscript{11,29,99} Defects smaller than 1 cm may not cause symptoms for many decades, but the left-to-right atrial shunt may increase later in life as left ventricular compliance decreases because of acquired cardiac diseases such as coronary artery disease and hypertension, causing symptoms to develop late.\textsuperscript{37}

**Diagnosis**

The electrocardiographic and chest radiographic findings are the same in the adult as in the child (see Chapter 30). The mainstay of diagnosis is echocardiography. In adults, thoracic studies may produce inadequate images of the atrial septum. Transesophageal studies often produce more accurate atrial septal images and detail the dimensions and position of the defect.\textsuperscript{37,31,26,27,75} PAH is estimated by measuring velocity of tricuspid regurgitation flow, if present. Contrast echocardiography can be used to confirm atrial-level shunting if direct imaging and color Doppler evaluation are not definitive. Both magnetic resonance imaging (MRI) and computed tomography (CT) angiography may be helpful if echocardiography is not definitive, and are particularly helpful in defining the pulmonary venous anatomy in sinus venous ASD. MRI is preferred to CT, which requires substantial radiation exposure.\textsuperscript{27,31,18,32,73} Cardiac catheterization is reserved for three situations: to assess pulmonary vascular hemodynamics if PAH is suspected or confirmed; to assess presence of coronary artery disease, typically in patients over age 35 (male) and 40 (female); and as a therapeutic procedure if percutaneous device closure is planned.

**TECHNIQUE OF OPERATION**

Options for ASD closure include surgical and percutaneous device approaches. Surgical techniques used are the same as those used in children (see Chapter 30). Because most defects that come to surgery in the current era are large, patch closure should always be used in adults, even for secundum ASDs; primary closure should be avoided. Concomitant procedures such as tricuspid valve repair and the maze procedure, uncommonly used in children, may be required.

Percutaneous device closure of secundum ASDs can be performed in adults regardless of age.

**RESULTS**

Early mortality following surgery is less than 1%, and long-term survival approaches that of the general population for straightforward cases without associated anomalies or PAH. Closure effectively relieves shunt-related symptoms. New-onset late atrial arrhythmias can develop in patients after surgery. The maze procedure is effective in reducing, but not always eliminating, atrial fibrillation and flutter.

Percutaneous device closure of secundum ASDs can be performed in adults with less than 1% mortality and low morbidity, with demonstration of reduction in right ventricular size and pulmonary artery pressure in all age groups.\textsuperscript{122}

A recent study of 100 adults with secundum ASD revealed similar, but not identical, outcomes using closure by surgery or percutaneous device.\textsuperscript{53} The 52 surgical patients underwent treatment between 2001 and 2003, and the 48 device closure patients between 2003 and 2005. The procedure was successful in all surgical patients (100%; CL 96%-100%) and in 45 of the 48 (94%; CL 88%-97%) percutaneous device patients. There was no mortality in either group (CL 0%-3.6% for surgical closure and 0%-3.9% for device closure). The number of complications was similar, but the surgical group had more serious ones. Postprocedure length of stay was shorter in the percutaneous device group. At 1-year follow-up, there was no mortality and equal reduction in right ventricular size and pulmonary artery pressure.

In a series of 25 adults with surgical repair of sinus venous ASD and partial anomalous pulmonary venous return, there was no early mortality (CL 0%-7.3%) and one late death due to heart failure.\textsuperscript{15} One patient (4%; CL 0.6%-13%) had superior vena cava obstruction. In a series of 75 adult patients with either secundum or sinus venous ASD, there was one early death (1.3%; CL 0.2%-4.4%) in a patient with secundum ASD, recurrent pulmonary emboli, and severe PAH.\textsuperscript{51}

An ostium primum ASD repair was performed in 51 patients (mean age 27 years) with an early mortality of 2.0% (CL 0.3%-6.5%).\textsuperscript{34} Preoperative left atrioventricular (AV) valve regurgitation was moderate in 35% and severe in 4%. With respect to the left AV valve, cleft closure was performed in all patients, but anuloplasty in only two. At 36-month follow-up, 21% had moderate regurgitation and 8% severe regurgitation; one had mitral valve replacement. Postoperative regurgitation was progressive (Fig. 29-5). Risk factors for postoperative moderate or severe mitral regurgitation were female gender and preoperative PAH. Interestingly, moderate or severe preoperative left AV valve regurgitation was not a risk factor.

In another series, there was no early (CL 0%-12%) or late mortality in 15 patients (mean age 31 years).\textsuperscript{14} The left AV
adults with secundum ASD, 84% met criteria for device closure and 16% underwent surgical closure. Older age is generally not a contraindication to surgical ASD closure, although there is some controversy. Two older studies demonstrate symptom improvement and survival benefit in patients over age 60 undergoing surgical closure. A more recent randomized trial of surgical ASD closure in patients over age 40 showed symptom improvement but no survival benefit.

If percutaneous device closure is not contraindicated, this approach may provide a better risk/benefit ratio than surgery in older patients.

**Section III  Patent Foramen Ovale**

**DEFINITION**

Patent foramen ovale (PFO) is incomplete closure of the septum primum resulting in a valve-like flap closure. It allows intermittent interatrial shunting, which may occur in the left-to-right or right-to-left direction.

**MORPHOLOGY**

PFO appears as a small slit at the upper margin of the fossa ovale (see Chapter 1). It represents incomplete obliteration of the fetal foramen ovale.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Presentation**

Of the 280,000 individuals who suffer a cryptogenic stroke in the United States every year, a PFO is found twice as often as in the normal population, suggesting an association between PFO and stroke. Nevertheless, three prospective class 1 studies addressing cryptogenic stroke all suggest that when patients who suffer an initial cryptogenic stroke are
followed, recurrent cryptogenic stroke has no relationship to the size or presence of a PFO. A number of studies examining the effectiveness of different treatment options in preventing recurrent stroke in patients with PFO have suggested that recurrent strokes occur less often when the PFO is treated with a device or surgery closure rather than with antiplatelet or anticoagulation therapy. Larger PFO size has also been associated with increased risk of recurrent cryptogenic stroke following an initial event. Thus, PFO closure is influenced by multiple factors, including the presence of a PFO and its size. When flow occurs in the right-to-left direction, the potential for paradoxical embolism exists. There is probably an association between PFO and cerebrovascular events; however, the nature of the relationship is unclear and controversial, as described in previous text.

**TECHNIQUE OF OPERATION**

Percutaneous device closure is currently favored over surgical closure; however, surgical PFO closure is an option if a patient refuses device closure, there is another reason for open heart surgery, or there is a contraindication. In patients with atrial septal aneurysm without PFO, surgical resection with reconstruction of the atrial septum can be considered when anticoagulation therapy has failed.

Unfortunately, a surgical closure arm is not included in any of the ongoing randomized trials. This oversight may be pertinent because the preliminary report of the CLOSURE 1 trial noted that in some cases thrombus has been identified on the closure device at follow-up.

**RESULTS**

Antiplatelet therapy, anticoagulation therapy, percutaneous device closure, and surgical closure are all used to prevent recurrent stroke in patients with PFO. No consensus has been reached about whether one form of therapy is better than the others. A number of studies examining the effectiveness of these different treatment options in preventing recurrent stroke point to an advantage of closure over antiplatelet or anticoagulation therapy; however, the criticism of all these studies is that none of them randomized the treatment options. A science advisory published jointly by the American Heart Association, American Stroke Association, and American College of Cardiology in 2009 notes that five different prospective randomized trials addressing this question are currently in progress, but no evidence base can determine whether PFO closure is superior to antiplatelet and anticoagulation therapy for preventing recurrent stroke. A preliminary report from one of these randomized trials, the CLOSURE 1 trial, was presented at the American Heart Association 2010 Scientific Sessions. No difference in recurrent stroke was noted between anticoagulation therapy and the STARFlex PFO closure device. Certain design flaws in this study have been noted.

The association of PFO and migraine headache is even more controversial than the association between PFO and cryptogenic stroke. It appears, based on an extensive meta-analysis, that percutaneous device closure of PFO may cure or improve migraine headache symptoms in a subset of migraine patients who have a PFO and suffer from a cryptogenic stroke. In general, the cause of migraines is multifactorial, with not all migraines due to paradoxical embolism or paradoxical streaming of causative humoral factors. This may explain the findings in the Migraine Intervention with STARFlex Technology (MIST) trial, a randomized, double-blinded, sham procedure controlled study of PFO closure in patients with PFO and migraine. In this study population, there was no other indication (i.e., no cryptogenic stroke) for PFO closure other than migraine headache. The study showed no benefit to PFO closure in this broader group of migraine patients.

**INDICATIONS FOR OPERATION**

The joint advisory recommends antiplatelet therapy as the first-line treatment for patients with PFO and cryptogenic stroke, vitamin K antagonist anticoagulation if there is an associated hypercoagulable state or atrial fibrillation, and PFO device closure if recurrent stroke occurs on anticoagulation. PFO closure is also indicated in patients exposed to alterations in atmospheric pressure, increasing the risk of paradoxical air embolism.

At the present time, PFO closure is considered standard medical practice for treating migraine headache. There is substantial evidence, however, that patients with PFO who suffer a cryptogenic stroke and also suffer from migraines will have their migraines cured or improved about 80% of the time after PFO device closure performed to prevent recurrent paradoxical embolism.

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**Section IV Ventricular Septal Defect**

**DEFINITION**

Definition, morphology, and basic physiology of ventricular septal defect (VSD) are described in Chapter 35. In the adult, VSD presenting for surgical closure is rare. When it does occur, it is unusual for it to present as newly diagnosed primary disease. More commonly, VSD presents as previously diagnosed primary disease with benign physiology, such as a restrictive defect, with new development of a specific VSD-related complication requiring intervention. It may also present as a secondary disease, such as late after...
surgical VSD closure, in association with a new VSD-related complication.

MORPHOLOGY

Each of the morphologic forms of VSD is found in the adult (see Chapter 35).

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presentation

Adults with a history of VSD closure as an infant or child may present with infectious endocarditis in the presence of a small residual defect; distortion of the tricuspid valve septal leaflet due to previous VSD closure, resulting in clinically important tricuspid regurgitation or progressive aortic regurgitation due to surgical injury; distortion of the valve during VSD closure; or prolapse of the valve into the VSD prior to VSD closure that progresses after closure.

Diagnosis

Transthoracic echocardiography is usually diagnostic for patients with unrepaired or previously repaired VSD unless the surface windows do not provide adequate images. In that case, transesophageal echocardiography is usually diagnostic. It is important not only to focus on size and position of the native or residual VSD, but also to rule out aortic valve prolapse and regurgitation, tricuspid regurgitation, double-chamber right ventricle, subaortic membrane, membranous septal aneurysm, primary pulmonary arterial hypertension (PAH), and ventricular dysfunction.

If PAH is suggested by echocardiography, diagnostic cardiac catheterization is indicated to assess status of the pulmonary vascular bed (see “Pulmonary Arterial Hypertension and Eisenmenger Physiology” in Section I). Cardiac catheterization may also be indicated in the patient with a small to moderate VSD, either unrepaired or repaired with a residual defect, for whom the indications for surgical closure are equivocal. Specific data obtained at catheterization may assist in the decision to close the VSD, including magnitude of the shunt, left ventricular end-diastolic pressure, pulmonary artery pressure, and pulmonary vascular resistance (Rp). Catheterization and angiography may also be indicated to assess the coronary arteries if arteriosclerotic disease is suspected, if the patient is older than age 35 (male) or 40 (female), or to further characterize unusual structural problems, such as membranous septal aneurysms (Fig. 29-7).

Magnetic resonance imaging (MRI) and computed tomography (CT) may play a role in defining anatomic details if echocardiography is not definitive. These imaging modalities may help define multiple VSDs, unusually positioned muscular VSDs, and suspected associated pulmonary artery or vein anomalies.

NATURAL HISTORY

Unrepaired large (unrestrictive, > 50% aortic diameter) VSD first presenting in the adult is rare. When it occurs, there is likely to be PAH or Eisenmenger physiology. Occasionally, evaluation reveals a reactive pulmonary vascular bed. Unrepaired moderate (restrictive, 25%-50% aortic diameter) VSD presenting in the adult is also rare. When it does, there is pulmonary overcirculation and symptoms of high-output heart failure. Unrepaired small (highly restrictive, <25% aortic diameter) VSD may be newly diagnosed or, more likely, previously diagnosed. These patients are hemodynamically asymptomatic.

Secondary complications related to a small VSD may develop in the adult. These include aortic, mitral, and tricuspid regurgitation, double-chamber right ventricle, subaortic membrane, and endocarditis. Aneurysms of the membranous septum may develop and progress in long-standing unrepaired perimembranous VSD. In one large series of 254 adults with perimembranous VSD, aneurysms developed in 51 cases (20%). When aneurysms form, flow restriction occurs through the VSD, resulting in pulmonary to systemic flow ratio (Qp/Qs) of less than 2 : 1. Aneurysms may enlarge over time, causing important secondary hemodynamic changes, including right ventricular outflow tract obstruction, tricuspid regurgitation, and rupture of the aneurysm, resulting in an acute increase in Qp/Qs (see Fig. 29-7).

Prevalence of endocarditis and aortic valve prolapse and regurgitation may increase when a membranous septal aneurysm is present.

TECHNIQUE OF OPERATION

Surgical techniques used to close VSDs in adults are the same as those used in infants and children (see Chapter 35). Percutaneous device VSD closure may be used for selected muscular VSDs remote from ventricular inlet and outlet.

If aneurysm of the membranous septum is present, it should be completely excised via exposure through the right atrium, with standard patch closure of the anatomic borders of the perimembranous VSD. Closure of the shunt by approximating aneurysmal tissue should be avoided because recurrence of the aneurysm and residual leaks have been described. Associated tricuspid regurgitation or aortic regurgitation should be addressed concomitantly.
RESULTS

Early mortality for uncomplicated VSD closure in the adult is less than 1%. If complex associated problems or pulmonary vascular disease coexist, early mortality is 5% to 10%. In a series of 51 adults (mean age 22 years, age range 15-59 years) with perimembranous VSDs complicated by aneurysm of the membranous septum, there was no early mortality (CL 0%-3.7%). In another experience, there was no early mortality (CL 0%-4.0%) in 46 adult patients (mean age 34 years) with perimembranous and subarterial VSDs.

Late mortality in patients without associated comorbidity is low: 5% at a mean follow-up of 10 years, 5% at a mean follow-up of 15 years, and 0% at a mean follow-up of 5.6 years in three separate series.

Surgical complications associated with VSD closure in adults are similar to those seen in younger patients, including residual VSD requiring reoperation, complete heart block, and injury to aortic and tricuspid valves.

In a series of 220 patients with small perimembranous VSDs followed into adulthood, 7% required surgical closure over a 6-year observation period. In the remaining 93%, 4% had spontaneous closure, 1% died of cardiac disease, and 4% developed endocarditis. Prevalence of PAH increased from 3% to 9%. In this study the average Qp/Qs was 1.2. These data emphasize that a small VSD is not always benign. In another analysis of 125 adolescent and adult patients (mean age 23 years, age range 10-51 years) with unrepaired VSD, 41 were treated surgically, 70 were considered to have no indication for surgery (small VSD and no associated problems), and 14 were inoperable due to PAH. At 15-year follow-up, even though the group with no indication for surgery had less complex defects, mortality was twice that of the operated group, and there was a higher occurrence of endocarditis and new valvar lesions. New York Heart Association (NYHA) functional class deteriorated in the unoperated group and improved in the operated group. Pulmonary artery pressure rose in the unoperated group and fell in the operated group. In the small group of 14 patients in which surgery was contraindicated because of PAH, mortality at 15 years was 71%.

INDICATIONS FOR OPERATION

Indications for operation are the same whether the VSD is un repaired or a residual defect following attempted surgical or device closure.

Large VSDs should be closed if cardiac catheterization demonstrates reversible PAH. They should not be closed if fixed-resistance severe PAH or Eisenmenger physiology is present. Levels of Rp and PAH that contraindicate surgical closure are described under “Pulmonary Arterial Hypertension and Eisenmenger Physiology” in Section I. Moderate VSDs should be closed. They almost always cause pulmonary overcirculation and Qp/Qs of 1.5 or greater. They are some what restrictive and do not cause Eisenmenger physiology. There is evidence that surgical closure provides long-term benefit for these patients. Traditionally, surgical closure has not been recommended for small VSDs. Most will have a Qp/Qs of less than 1.5. However, considering the low morbidity and mortality of surgical closure of VSD in the current era and the morbidity and mortality in adults with small unrepaired VSDs, the traditional recommendation to not close a small VSD in the adult should be questioned.

Other indications for surgical intervention include development of important associated problems, usually in the setting of a small restrictive VSD: aortic regurgitation, tricuspid regurgitation, subaortic membrane, double-chamber right ventricle, large aneurysm of the membranous septum, and infectious endocarditis. Surgery may require addressing the VSD and the associated problem concomitantly, or the associated problem alone if the VSD has been previously closed. In one series of 20 patients (mean age 43 years) an associated problem was the indication for surgery in 35%; in another series of 42 patients (mean age 27 years) an associated problem was the indication for surgery in 52%.

Section V  Atrioventricular Septal Defect

DEFINITION

The definition, morphology, and basic physiology of atrioventricular septal defect (AVSD) are described in Chapter 34. Most adults presenting with AVSD fall into the category of secondary congenital heart disease, having undergone surgical repair in infancy or childhood.

MORPHOLOGY

AVSD may be partial or complete. Adults rarely present with complete unrepaired AVSD, and when they do, it is usually inoperable because of pulmonary arterial hypertension (PAH). This is because of the combination of unrestrictive ventricular- and atrial-level shunting and the high likelihood of Down syndrome. Partial AVSD may present unrepaired in the adult and is usually operable. Down syndrome is uncommon in partial AVSD.

The most common indications for surgery in the adult with repaired AVSD are left-sided atrioventricular (AV) valve stenosis or regurgitation, followed by left ventricular outflow tract obstruction.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presentation

The clinical presentation of repaired AVSD depends on the nature of residual or recurrent lesions after repair, and on development of new lesions. The most common residual or recurrent lesion is left-sided AV valve regurgitation, which presents with left ventricular volume overload and failure, left atrial dilatation, and atrial fibrillation. The next most common lesion is subaortic left ventricular outflow tract obstruction, which may be residual, recurrent, or new onset. Signs and symptoms are the same as for any patient with left ventricular outflow obstruction. Other presentations include signs and symptoms related to left or right AV valve stenosis, right AV valve regurgitation, residual ventricular septal defect (VSD), endocarditis related to any of these residual structural lesions, or PAH, particularly in patients with repaired complete AVSD.
Diagnosis

The electrocardiogram shows typical superior left-axis deviation, and this finding alone in a previously undiagnosed adult is highly suggestive of AVSD. In adults with residual or recurrent lesions, electrical findings of left atrial enlargement, left ventricular hypertrophy, and right ventricular hypertrophy may be present. Atrial fibrillation or flutter may also be present.

The chest radiograph will show a prominent pulmonary artery bulb and distal pulmonary artery pruning if PAH is present, cardiomegaly if valve regurgitation or left-to-right shunting exists, and pulmonary venous congestion if left-sided AV valve regurgitation is present. Echocardiography is diagnostic, just as it is in infants and children. In previously repaired patients, this study should focus on determining presence of residual atrial or ventricular shunts, right and left AV valve function, left ventricular outflow tract patency, and signs of PAH.

Cardiac catheterization is performed in all unrepaired adults under consideration for surgical repair to assess the pulmonary vasculature. Coronary angiography is indicated if the patient is over age 35 (male) or 40 (female) or if coronary insufficiency is suspected. Catheterization may also be indicated to assess PAH in repaired patients and general hemodynamics in patients with equivocal indications for surgical intervention. Magnetic resonance imaging can be helpful in assessing regurgitant fraction when AV valve regurgitation is present in patients with equivocal indications for surgical intervention.

NATURAL HISTORY

Presentation of partial AVSD in the adult has some similarities to that of a large atrial septal defect (ASD), with chronic right heart volume overload leading to right ventricular failure. Mild PAH is present, but Eisenmenger physiology is uncommon. Unlike a large ASD, however, regurgitation of the right-sided, left-sided, or both AV valves is common, causing earlier onset of ventricular failure and atrial fibrillation and flutter.

Presentation of the adult with unrepaired complete AVSD will be similar to that of a large or unrestricted VSD, with PAH and likely Eisenmenger physiology. Additionally, important AV valve regurgitation may be present, increasing the likelihood of ventricular failure and atrial fibrillation or flutter.

TECHNIQUE OF OPERATION

The surgical approach to unrepaired AVSD, whether partial or complete, is the same in the adult as in infants and children (see Chapter 34).

Postrepair residual or recurrent left AV valve regurgitation requires repeat surgery in 5% to 10% of patients. It may be due to an open cleft or breakdown of a previous cleft closure. Surgical closure of the cleft is performed. Reduction anuloplasty is almost always indicated. If the etiology of regurgitation is more complex, then standard techniques used for mitral valve repair are used (see Chapter 11). Rigid valve anuloplasty rings may be contraindicated because the shape of the anulus in repaired AVSD is different from that of the normal mitral valve. Mixed regurgitation and stenosis is particularly difficult to repair, and valve replacement may be required. The inferiorly displaced position of the AV node and bundle of His must be kept in mind to avoid causing heart block.

Left ventricular outflow tract obstruction is rarely due to a simple subaortic membrane. Typically, there is an elongated, narrow, muscular tunnel with or without the addition of AV valve chordal tissue. The chordal tissue is rarely functional. Most commonly these chords were previously normal components of the superior bridging leaflet of a Rastelli type A defect. They become nonfunctional as part of standard original AVSD repair. Surgical correction of late left ventricular outflow obstruction is best performed through the aortic valve, with extensive circumferential myectomy and resection of the obstructive AV valve and chordal tissue. Damage to the mitral valve can still occur during this procedure, as it can for any left ventricular outflow tract resection; however, injury to the conduction system is not of concern because the AV node is displaced inferiorly. Occasionally, myectomy will not be effective, and a Konno operation will be required (see Chapter 12).

RESULTS

Death

Early mortality for primary repair of partial AVSD in the adult can be less than 1%; however, some older series report early mortality as high as 6%. There was no (CL 0%-4.8%) early mortality in a series of 39 patients (mean age 36 years) in whom the indication for surgery was left-to-right shunt. One patient required concomitant left AV valve replacement and 37 underwent cleft closure, five of whom also underwent reduction anuloplasty. At a median follow-up of 7 years, there were six late deaths, five of which were cardiac in origin. In a series of 132 patients with partial AVSD, 10% of whom were older than age 20 years, early mortality was 4.5% (CL 2.7%-7.2%) and late mortality 3.2%. By univariable analysis, older age (more than 10 years at initial repair) was among the risk factors. By multivariable analysis, however, only preoperative PAH and a grossly deformed left AV valve were risk factors, suggesting that the association of death with older age is due to development of PAH and valve deformity over time. In a series of 31 patients with partial AVSD, all of whom were over age 40, early mortality was 6.4% (CL 2.2%-15%); however, some of the operations were performed as long ago as 1958, and the two deaths occurred in 1967 and 1981. There were nine additional deaths at late follow-up (Fig. 29-8). In a separate report from the same authors, an analysis of all patients with partial AVSD showed that age older than 20 years at repair was a risk factor for death. In a series of 29 adolescents and adults (mean age 28 years) undergoing repair of partial AVSD, early mortality was 3.4% (CL 0.6%-11%), and actuarial survival after 25 years was 79%. There was important left AV valve regurgitation in 68% of the long-term survivors and important arrhythmias in 20%. In a larger series of reoperations in 96 adults (median age 26 years) with prior repair of partial AVSD, early mortality was 5.2% (CL 2.9%-8.7%); however, three of the deaths occurred prior to 1983. Since 1983, 2 of 76 patients experienced early death (2.6%; CL 0.9%-6.1%) (Fig. 29-9).

Primary repair of complete AVSD in the adult is rare; however, there are isolated case reports of such repairs.
other in 6%. About half of the patients requiring reoperation for left AV valve regurgitation underwent valve repair, and the other half underwent valve replacement.

Reoperations following prior repair of complete AVSD have been reported in a series of 50 patients. As expected, the primary repair was performed early in life (median age 1 year), and the median interval between primary repair and reoperation was 15 months. Thus, most reoperations were performed in young children, although some were performed in adults as old as 38 years. Left AV valve regurgitation was the indication for reoperation in 41 patients. There were two early deaths, both in young patients; thus, there were no deaths in adults, although the specific number of adults treated is not designated. In two other series examining long-term outcomes after AVSD repair in infancy and childhood, freedom from reoperation was 80% at 25 years in one and 76% at 20 years in the other. In both studies the majority of first reoperations were for left AV valve problems, and these reoperations occurred relatively early. In one of these studies, mean age at first reoperation was 2 years. Thus, few patients present for their first left AV valve reoperation in adulthood. Second reoperations on the left AV valve are common, with freedom from reoperation after first reoperation of only 42% at 15 years.

INDICATIONS FOR OPERATION

Surgery is indicated for all unrepaired patients with partial AVSD unless important PAH is present. One analysis suggests that outcome after surgery is better than expected with medical management. Surgery is indicated only rarely for the adult with complete AVSD because of the high likelihood of advanced pulmonary vascular obstructive disease. Repaired patients with residual lesions should undergo surgery if these cause important symptoms. If residual lesions cause no or minimal symptoms, then standard physiologic criteria are used for residual shunts, AV valve regurgitation or stenosis, and left ventricular outflow tract obstruction. A maze procedure may be indicated concomitant with the structural repair if atrial fibrillation or flutter is present. Coronary artery bypass grafting is indicated as a concomitant procedure if standard criteria are met (see Chapter 7).

Left Atrioventricular Valve and Left Ventricular Outflow Tract Lesions

Early mortality after repair of residual or recurrent left AV valve lesions or left ventricular outflow tract lesions is similar to that after mitral valve or left ventricular outflow tract procedures performed in adults without AVSD. One report describes 11 patients with prior repair of partial AVSD in whom surgery as an adult was required. Indications were left AV valve regurgitation in six (two of whom required valve replacement), subaortic stenosis in three, left AV valve stenosis in one, and atrial shunt in one. There were no early deaths (CL 0%-16%), and at median follow-up of 7 years, there were two late deaths, one of which was cardiac in origin.

In a series of 96 reoperations in adults after partial AVSD repair, indications for reoperation were left AV valve regurgitation in 67%, subaortic stenosis in 25%, right AV valve regurgitation in 22%, residual atrial septal defect in 11%, and
CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presentation

Small PDA is asymptomatic, causing clinically unimportant left-to-right shunt. A continuous murmur may or may not be detectable, depending on size of the PDA. The patient may present with endocarditis or endarteritis.

Moderate PDA results in restrictive left-to-right shunting of variable magnitude, depending on its size. The larger the PDA, the more likely it will cause shortness of breath, fatigue, a wide pulse pressure, left atrial and ventricular enlargement, and some elevation of pulmonary artery pressure. In some cases, initial presentation is an incidental finding of ductal calcification or aneurysm on chest radiography or other imaging.

Large PDA is nonrestrictive and produces a large left-to-right shunt, pulmonary arterial hypertension (PAH), and almost always Eisenmenger physiology. Lower body cyanosis develops with advanced Eisenmenger physiology. Left and right ventricular failure may be present.

Diagnosis

The electrocardiogram is abnormal with large PDA, showing left atrial enlargement and left (volume-loaded) and right (pressure-loaded) ventricular hypertrophy. Chest radiography varies from normal to abnormal depending on shunt size. With larger shunts, cardiomegaly from left atrial, left ventricular, and right ventricular enlargement is seen. The pulmonary trunk is prominent. Calcification of the ductus may be detected.

Echocardiography confirms the diagnosis by using color Doppler to identify flow across the ductus. If PAH is present, pressure gradient and flow across the ductus are small, and echocardiography may fail to identify the PDA. Cardiac catheterization is performed in most cases of adult PDA, either as a diagnostic tool to assess the state of the pulmonary vasculature in large PDAs, or as a therapeutic tool to close small and some moderate PDAs. Magnetic resonance imaging or computed tomography may be useful if the PDA is complicated by aneurysm. Using these, the specific size and position of the aneurysm and its adjacency to other structures can be determined. Most reported aneurysms are patent at only one end, either aortic or pulmonary, but cases of true patency have been reported (Fig. 29-10).

TECHNIQUE OF OPERATION

Surgical closure can be performed either via median sternotomy or left thoracotomy. This is partially surgeon preference; however, other factors may influence the choice. A prior left thoracotomy or other left pleural space problem make a thoracotomy approach less advisable. Additional cardiac disease requiring surgery, such as associated ventricular septal defect or coronary artery occlusive disease, demands a median sternotomy approach. If cardiopulmonary bypass (CPB) is required or likely to be required to close the PDA, median sternotomy is preferred.

If the PDA is not complicated by calcification, aneurysm, or very short length, closure is performed using techniques similar to those described for children. When calcification is present, these techniques are contraindicated because simple ligation and division carries substantial risk of rupture.

Figure 29-10 Aneurysm of ductus arteriosus. A, Contrast-enhanced computed tomography image showing 50-mm aneurysm (arrows) of ductus arteriosus with mural thrombus and calcification. B, Magnetic resonance image showing aneurysm (arrows) arising from distal aortic arch. C, Angiography at catheterization also showing aneurysm (arrows) and its communication with both aorta and pulmonary artery. (From Tofukuji and colleagues.)
The same approach may be used for large PDA with little or no length. Another option for this anatomy, especially if there is no calcification of the ductus or aorta, does not use CPB and can be performed by either median sternotomy or left thoracotomy. The pulmonary artery and aorta at the ductal site are clamped, the ductus is divided, and the pulmonary artery and aorta are either sutured primarily or patched.

Aneurysm resection and repair is performed using median sternotomy and CPB, and the technique is similar to that used for arch aneurysm repair (see Chapter 26). Patching the aorta or pulmonary artery may be required.

RESULTS

Early mortality for surgical PDA closure in adults is low, but probably slightly higher than that in infants and children, which approaches zero. This is due to the increased technical demands of the procedure in adults. In a series of 55 adults (mean age 24 years) reported in 1971, there was no early mortality (CL 0%-3.5%). Currently, with alternative therapeutic options, series of this size no longer exist; however, it is reasonable to assume that mortality has decreased. In a series of nine adults (mean age 55 years) reported in 2000, there were no early deaths (CL 0%-19%). CPB with temporary balloon occlusion was used in this series, along with direct suture and patch closures from within the pulmonary artery. Pulmonary artery pressure decreased from 55 mmHg systolic prior to surgery to 35 mmHg at 6-month follow-up. In a series of 25 complex patients, many of whom had heavy calcification, aneurysm, heart failure, or PAH, early mortality was 4% (CL 0.7%-13%). In a series of 29 patients age 50 or older at surgery, early mortality was 3.4% (CL 0.6%-11%). In another series of 71 adults (mean age 24 years) with relatively uncomplicated PDA, there was no early or late mortality (CL 0%-2.6%). Many of the patients in this series (35%) were asymptomatic; 91.5% were treated with simple surgical ligation and 8.5% with surgical division.

Premature late death after PDA closure in adults is related to chronic changes in left ventricular function and in the pulmonary vascular bed resulting from long-standing left-to-right shunt.

Outcomes after repair of ductal aneurysm are not well documented because the lesion is so rare. There are case reports of successful surgical management.

INDICATIONS FOR OPERATION

Surgery is rarely indicated for PDA in adults. Most small and small to moderate PDAs are closed percutaneously at cardiac catheterization with coils or other occlusive devices. Most patients with large PDAs have Eisenmenger physiology and are not candidates for closure.

An emerging technology that can be applied to selected cases of PDA is endovascular stent-grafting. Stents are placed into the aorta and deployed to occlude the aortic opening of the ductus (Fig. 29-12). Hybrid approaches, with access to the aorta via surgical incision and deployment of an endovascular device, have been described and may be useful in selected cases.

Figure 29-11 Technique of closing patent ductus arteriosus (PDA) when calcium is present. A, After cardiopulmonary bypass is initiated, pulmonary trunk is incised to the left and right pulmonary arteries. B, An 8F Foley catheter is inserted into PDA through pulmonary trunk. Inset, Two or more pledgeted 4-0 polypropylene mattress sutures are placed around pulmonary artery orifice of PDA. Catheter is removed before sutures are tied. Pulmonary arteriotomy incision is closed. (From Kataoka and colleagues and Tekin and colleagues.)

CPB via median sternotomy, with internal patch or primary closure of the ductal orifice through the pulmonary trunk, is the preferred approach (see Chapter 37). It may be helpful to use a catheter device with a balloon, such as a Foley catheter, to temporarily occlude the ductus after it is exposed via the pulmonary arteriotomy and prior to definitive surgical closure. Cardioplegic arrest is not necessary (Fig. 29-11).
Surgery is indicated for any PDA that causes shunt-related symptoms, shunt-related cardiac enlargement, or PAH, or for a PDA that cannot be closed percutaneously because of endarteritis. Typical cases include those with a large lumen and short length, those complicated by aneurysm, and those with other unusual anatomic features.

In contrast to infants and children, adults requiring surgery for intracardiac problems who have a coexisting PDA should have the PDA closed percutaneously prior to the cardiac operation.

**DEFINITION**

The definition, morphology, and basic physiology of bicuspid aortic valve (BAV) are described in Chapter 12 and Chapter 47. Most commonly, BAV presents in the adult as primary congenital heart disease, either newly diagnosed or previously diagnosed with benign physiology. It may present as secondary congenital heart disease, because some patients may have undergone previous surgical or interventional procedures on the aortic valve.

**MORPHOLOGY**

Primary disease presenting in the adult is usually an isolated lesion, with the exception of associated aortic disease. Frequency of ascending aortic dilatation varies widely. It has been reported to be as low as 10% to 12% and as high as 83%. These variations are largely due to differences in patient population, length of follow-up, and definition of dilatation. Dilated aortas are at increased risk of developing complications (Fig. 29-13). BAV presenting in infants and children may be associated with other left-sided obstructive lesions, including coarctation (which is particularly common), subvalvar aortic stenosis, parachute mitral valve, and supramitral ring. When multiple lesions occur together, the term **Shone complex** is applied. Rarely, adults present with newly diagnosed Shone complex; however, secondary presentation occurs in adulthood essentially all survivors, because most of the cardiac lesions are palliated and not cured during childhood intervention. BAV may be a component of William and Turner syndromes.

Bicuspid aortic valve is a gross morphologic oversimplification. Two large and equally sized cusps are unusual, in

**Figure 29-12** Endovascular stent-grafting for selected cases of patent ductus arteriosus (PDA). **A**, Arteriography of thoracic aorta via left brachial artery showing large PDA with aneurysmal pulmonary artery. Placing an occlusion device via this access was considered contraindicated. **B**, Access to thoracic aorta via right femoral artery was obtained and a stent-graft placed distal to left subclavian artery with PDA closure. (From Munoz and colleagues.)

**Figure 29-13** Risk of aortic complications based on diameter of ascending aorta. Graph shows that all patients with abnormally increased diameters have increased risk of an aortic complication. For a given diameter, risk is higher for patients with either Marfan syndrome or bicuspid aortic valve relative to patients who do not manifest either of these. Blue dotted line represents patients without bicuspid aortic valve or Marfan syndrome; red line, patients with bicuspid aortic valve; and green line, patients with Marfan syndrome. Key: **MD**, Measured diameter of ascending aorta; **PD**, predicted normal diameter of ascending aorta; **R**, relative risk of aortic complication. (From Codecasa and colleagues.)
contrast to the bicuspid pulmonary valve seen in tetralogy of Fallot. Typically, BAV morphology has one large well-formed cusp, usually making up 40% to 50% of the anular circumference, and a second cusp consisting of a fusion of two cusps with a thick raphe representing the point of fusion. This abnormal cusp may prolapse, causing regurgitation, or it may calcify, particularly at the immobile raphe, leading to late stenosis. In cases of early stenosis, there is usually associated anular hypoplasia or variable degrees of fusion of the two other relatively normally formed commissures.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Presentation**

Patients with primary or secondary disease often present with gradual stenosis and/or regurgitation that eventually leads to symptoms or physiologic criteria for surgical intervention. Less often, the primary presentation is ascending aorta dilatation and, rarely, aortic dissection, aneurysm, or rupture. Occurrence of dissection may be tenfold higher than in the normal population. Associated coarctation appears to increase risk of dissection. Occasionally, BAV presents with signs and symptoms of infective endocarditis.

Adults with secondary disease may present with a failed aortic valve repair, failed bioprosthetic aortic valve, failed or outgrown mechanical aortic valve, or failed pulmonary autograft (Ross procedure) in the aortic position. Bioprosthetic valves tend to require earlier replacement in young adults compared with older adults. This is likely due to a combination of patient growth after original placement and more rapid calcific degeneration. Need for replacement of mechanical valves is mostly related to patient growth, but gradual encroachment of pannus may also play a role. After the Ross procedure, neoaortic regurgitation necessitates reoperation in up to 10% of patients within a decade. Neoaortic root dilatation occurs in about half of cases by 7 years and may or may not be associated with neoaortic regurgitation. Risk of dissection or aneurysm formation in the dilated neoaortic root is not clear. Coronary obstruction may also present late after the Ross procedure because of scarring and kinking of the translocated coronary arteries and from compression by the calcified right ventricle to pulmonary trunk conduit. One of the most common late developments after the Ross operation is right ventricular outflow tract conduit failure. Freedom from conduit reoperation is better following the Ross operation than for conduits placed for other congenital heart diseases, such as tetralogy of Fallot. Brown and colleagues demonstrated freedom from conduit reoperation of 96% at 10 years. Raanani and colleagues report one reoperation for conduit failure in 109 patients at a mean follow-up of 39 months, although moderate to severe stenosis was noted in 3.8% and moderate to severe regurgitation in 9.5%. 

**Diagnosis**

Electrocardiography and chest radiography show typical findings associated with aortic valve disease. Echocardiography is the mainstay of diagnosis. It is able to assess the degree of stenosis or regurgitation once the diagnosis is made and can identify when physiologic criteria are met for intervention.

Cardiac catheterization is performed when coronary assessment is indicated, primarily in patients over age 40, or if there is concern that primary coronary insufficiency is present or that coronary scarring or compression has developed following a Ross procedure or other aortic root replacement procedure. Magnetic resonance imaging (MRI) and computed tomography are indicated to assess ascending aorta size and to rule out dissection and aneurysm. Additionally, MRI can be used to quantify aortic regurgitation if symptoms and echocardiographic findings disagree.

**NATURAL HISTORY**

BAV is the most common congenital heart defect, occurring in up to 2% of the population. In many cases it is associated with normal physiology for years or even decades. Aortic stenosis or regurgitation may develop at any time. Dilatation of the ascending aorta occurs, caused by connective tissue aortopathy with a genetic basis. Many cases of neonatal and infant aortic stenosis requiring intervention have underlying BAV. If aortic valve physiology is normal in infancy and childhood, the typical age for surgical intervention is 60 years. Among adults requiring surgery for aortic stenosis, a congenital abnormality of the valve is considered the cause in 54%.

In a natural history study of 642 adults with BAV (mean age 35 years at baseline) followed for 9 years (mean), one or more primary cardiac events, including death, surgical intervention, aortic dissection, and heart failure, occurred in 25% of patients at a mean age of 44 years. Nevertheless, fatal events were rare, with actuarial survival comparable with that of the general population. In another large series of adults (mean age 32 years at baseline) with mean follow-up of 15 years, cardiac events occurred in 40% at a mean age of 52 years. Again, however, actuarial survival was indistinguishable from that of the general population. The frequency of adverse cardiovascular events in adults with BAV is stratified based on risk profile, with risk factors including older age, moderate or severe aortic stenosis, and moderate or severe aortic regurgitation (Fig. 29-14).

**TECHNIQUE OF OPERATION**

Many surgical techniques used for adults with BAV and its associated lesions are the same as those used in children with...
require either primary or repeat surgery for aortic arch obstruction and mitral valve disease in addition to left ventricular outflow tract surgery.

Reduction aortoplasty, with or without external aortic support, for ascending aorta dilatation is described and depicted in Figs. 29-15 and 29-16, respectively. Other variations on external aortic support are described by Robicsek and colleagues and by Cohen and colleagues. Some controversy remains about whether a supportive wrap is a beneficial accompaniment to reduction aortoplasty in patients with BAV. Some even question the utility of reduction aortoplasty.

RESULTS

Outcomes for adults undergoing aortic valve replacement for congenital aortic valve disease are similar to those for adults with acquired aortic valve disease (see Chapter 12). Early and midterm outcomes after reduction aortoplasty for dilated ascending aorta associated with BAV, either alone or in...
association with aortic valve repair or replacement, are excellent. In a series reported by Bauer and colleagues, 115 patients (mean age 56 years) underwent reduction aortoplasty. There were no early deaths (CL 0%-1.6%). At a mean follow-up of 40 months, there was no postoperative dilatation and no complications in the nine patients who underwent reduction aortoplasty. There were no reoperations in the entire series.

Others have raised concerns about outcomes when reduction aortoplasty is performed without external support, arguing that the results reported by Bauer and colleagues are unreliable because follow-up was not long enough and citing the two causes of aortic dilatation: the hemodynamic principles of the Law of Laplace and the intrinsic aortopathy found in these patients. These authors recommend external support for all cases of reduction aortoplasty. Cohen and colleagues report 102 adult patients (mean age 54 years) with ascending aorta dilatation, 80% of whom also had aortic valve disease. All underwent a procedure involving external polyester mesh support of the ascending aorta, with or without concomitant reduction aortoplasty, aortic valve surgery, or coronary artery surgery. There was no early mortality (CL 0%-1.8%) and no late mortality related to aortic disease. At a mean follow-up of 5.7 years, mean increase in aortic diameter was 2.6 mm.

Aortic root replacement with concomitant aortic valve replacement can be performed with low early mortality. Nazer and colleagues report early mortality of 2.1% (CL 0.9%-4.2%). Diminished late survival was related to older age at operation. Valve-sparing aortic root replacement has been reported. In one series of 190 patients, 60 (mean age 53 years) had BAV. There was no early mortality (CL 0%-3.1%) and no late mortality at 5-year follow-up. Function of the spared BAVs was similar to a comparison group of 130 patients undergoing valve-sparing root replacement with tricuspid aortic valves. In another series of 153 patients (mean age 51 years) with BAV, early mortality was 0.6% (CL 0.1%-2.2%). Survival was 99% at 5 years and 91% at 10 years. At 10 years, freedom from valve replacement was excellent (Fig. 29-17).

The Ross procedure, with concomitant ascending aorta reduction or polyester graft replacement, was reported by Conaglen and colleagues in 154 patients (mean age 32 years). There was no early (CL 0%-1.2%) or late mortality and no cardiac reoperations at a mean follow-up of 9 years.

**INDICATIONS FOR OPERATION**

Indications for intervention in adult patients with BAV include the standard symptoms and hemodynamic and physiologic thresholds associated with any form of aortic stenosis.

![Figure 29-16](image.png)
or regurgitation (see Chapter 12). If aortic stenosis exists without regurgitation and without a dilated ascending aorta, percutaneous balloon valvotomy is indicated. If isolated aortic regurgitation, combined aortic stenosis and regurgitation, or associated dilatation of the ascending aorta exists, then surgical intervention is indicated. If balloon valvotomy fails to relieve the gradient or causes important regurgitation, surgical intervention is indicated.

An ascending aorta diameter of 5 cm or more or a change in aortic diameter of 0.5 cm · y⁻¹ are absolute indications for intervention. Indications for surgery on ascending aortas with lesser degrees of aortic dilatation are not as clear. Most agree that an ascending aorta diameter of 3.5 to 4.9 cm should be surgically addressed if surgery is otherwise indicated to treat aortic valve disease. Many, but not all, recommend surgery for an ascending aortic diameter of 3.5 to 4.9 cm even if there is no indication for aortic valve disease; some recommend observation in this situation. Valve-sparing prosthetic aortic root replacement, composite prosthetic valve and root replacement, Ross procedure, reduction aortoplasty with or without external aortic support, and isolated external support of the ascending aorta have been recommended for surgical management of a dilated ascending aorta.

Clinical judgment comes into play when strict criteria for intervention are not met. For example, in the young adult, new-onset mild or moderate regurgitation and an enlarging ascending aorta that has not yet reached 5 cm in diameter may be considered for surgical intervention. Aortic root replacement at this point in the disease process may allow a valve-sparing procedure. Another example is the patient with severe aortic stenosis and an ascending aorta that is dilated, but does not meet criteria for replacement. The best advice is to surgically address the aorta and replace the valve.

In women of childbearing age, especially those planning pregnancy or likely to become pregnant, timing of intervention may be altered. Intervention may be considered when milder physiologic alterations are present, anticipating the cardiovascular demands during the third trimester of pregnancy. Additionally, choice of intervention may be altered. Mechanical valves, with the attendant requirement for anticoagulation therapy, are poor choices for the pregnant woman (see “Pregnancy and Contraception” under Special Circumstances in Section I).

### Section VIII Subaortic Stenosis

#### Definition

The definition, morphology, and basic physiology of subaortic stenosis are described in Chapter 47. In the adult it may present as a primary disease, either newly diagnosed or previously diagnosed with benign physiology, or as a secondary disease. In a report from 1978, 36 of 138 patients (26%) undergoing surgery for primary subaortic obstruction presented in adulthood. It is likely that in the current era, improved diagnostic imaging has resulted in a smaller percentage of patients presenting for surgery in adulthood.

#### Morphology

As with subaortic stenosis in infants and children, morphology may range from a discrete fibrous membrane, to mixed fibromuscular obstruction, to tunnel-like muscular obstruction. Accessory atrioventricular (AV) valve tissue may play a role in the obstruction. As in children, the angle formed by the ventricular septum and aorta (aortoseptal angle) is more acute in adults with isolated discrete subaortic obstruction. In contrast to the case in children, there is evidence that this angle, as well as other left ventricular outflow tract geometric abnormalities found in patients with isolated subaortic stenosis, does not remodel postoperatively in adults.

#### Clinical Features and Diagnostic Criteria

**Presentation**

Subaortic stenosis presents in a variety of ways in adults. It may be a primary and isolated lesion with the typical signs and symptoms of aortic stenosis, sometimes with associated aortic valve regurgitation. In one study, aortic regurgitation was present in 80% of patients, but was hemodynamically important in only 20%. Subaortic stenosis may also be a primary lesion associated with ventricular septal defect (VSD), atrioventricular septal defect (AVSD), or a conotruncal anomaly with subaortic conus. About half of all primary cases are isolated, and half are associated with other cardiac anomalies.

Subaortic stenosis may also be a secondary lesion that develops after surgical repair of a spectrum of anomalies, including left ventricular outflow tract obstruction, perimembranous VSD, posterior malalignment VSD with arch obstruction, AVSD, and conotruncal anomalies such as double outlet right ventricle or certain types of transposition of the great arteries. Signs and symptoms at presentation are similar to those of valvar aortic stenosis.

**Diagnosis**

Electrocardiography and chest radiography show typical findings associated with aortic stenosis (and aortic regurgitation if present). Echocardiography will demonstrate the morphologic characteristics of the subaortic region and proximity of the subaortic lesion to the aortic valve, assess aortic regurgitation, estimate the pressure gradient, and demonstrate...
left ventricular function. As with most complex intracardiac lesions in adults, transesophageal echocardiography may add important details to the surface echocardiogram. Cardiac catheterization plays a limited role in subaortic stenosis, primarily to assess the coronary arteries if necessary. There is no role for therapeutic catheterization. In complex cases, magnetic resonance imaging may provide a more detailed estimation of the left ventricular outflow tract.

NATURAL HISTORY

Subaortic stenosis is relatively uncommon among adults with congenital heart disease, accounting for 6.5% (134 of 2057 patients) of presenting cases in one series. In this series, 22% (29/134) presented with severe obstruction and no prior surgical history, 48% (64/134) had no indication for surgery and no prior surgical history, and 30% (41/134) had surgery for subaortic obstruction during childhood.

Subaortic stenosis is a progressive lesion that creates greater degrees of obstruction over time and causes progressive aortic valve damage, which leads to aortic regurgitation. In adults, progression of obstruction and aortic regurgitation is slower than in children. It is not unusual for an adult to be followed with known uncomplicated mild subaortic stenosis for a period of time, only to develop more progressive stenosis, aortic regurgitation, or infective endocarditis. Aortic regurgitation is more likely the higher the pressure gradient in the subaortic region. Severe obstruction carries the same risks as severe valvar aortic stenosis.

TECHNIQUE OF OPERATION

The appropriate operation for subaortic obstruction depends on the morphology of the obstruction—membranous, fibromuscular, or tunnel-like—and presence and severity of aortic regurgitation. Procedures include membrane resection, myectomy, aortic valve repair, aortic valve replacement, and Konno or modified Konno procedures. Operations and principles determining their application are described in Chapter 47, those for aortic valve replacement in Chapter 12, and those for aortic valve regurgitation in Chapter 35 (see Section II, Ventricular Septal Defect and Aortic Regurgitation).

RESULTS

Early mortality in the current era is 3% to 4%, with late survival substantially lower than that of the general population and a relatively high rate of reoperation. In a 1976 report of 36 adults undergoing surgery for subaortic stenosis, only 53% had an isolated anomaly and 25% presented with infectious endocarditis, reflecting the complex nature of the patients in this study. Early mortality was 8.3% (CL 3.7%-16%).

In a more contemporary series of 52 patients (mean age 25 years) reported in 2005, early mortality was 3.8% (CL 1.3%-8.8%). Concomitant aortic valve replacement was required in 29% because of chronic aortic regurgitation graded as 3+ or 4+. The mean age of patients requiring valve replacement was older than those not requiring replacement (37 vs. 21 years). Late mortality was 16% (Fig. 29-18). Recurrent obstruction requiring another operation occurred in five patients over a mean follow-up period of 17 years.

![Survival](image)

**Figure 29-18** Survival in 52 adult patients following resection of subaortic obstruction. (From Stassano and colleagues.)

<table>
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<th>No.</th>
<th>Procedures</th>
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<td>ASD closure</td>
</tr>
<tr>
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<td>ASD closure</td>
</tr>
<tr>
<td>VSD</td>
<td>14</td>
<td>VSD closure</td>
</tr>
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<td>Bicuspid aortic valve</td>
<td>9</td>
<td>Commissurotomy or AVR</td>
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<td>Commissurotomy</td>
</tr>
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<td>Valvular PS</td>
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</table>

From Erentug and colleagues. AS, Aortic stenosis; ASD, atrial septal defect; AVR, aortic valve replacement; PDA, patent ductus arteriosus; PS, pulmonary stenosis; RVOT, right ventricular outflow tract; VSD, ventricular septal defect.

In another series of 88 patients (mean age 20 years) reported in 2005, 66% (58/88) had discrete obstruction and 34% (30/88) had diffuse tunnel-like obstruction. Moderate or worse aortic regurgitation requiring a concomitant aortic valve procedure was present in 15%. Aortic valve hypoplasia requiring a Konno procedure was present in 17%. Associated cardiac anomalies requiring concomitant surgery were present in 45% (Table 29-9). Early mortality was 3.4% (CL 1.5%-6.7%) and late mortality 1.1% at a mean follow-up of 6.1 years. Diffuse tunnel-like obstruction was a risk factor for early mortality by multivariable analysis. Reoperation for progressive aortic regurgitation or recurrent left ventricular outflow tract obstruction was required in 16.5% of patients over the follow-up period (Fig. 29-19).

INDICATIONS FOR OPERATION

Surgical resection of subaortic stenosis is indicated in several circumstances. The first relates to classic obstructive physiology: peak echocardiographic gradient of 50 mmHg or greater or a lesser gradient associated with left ventricular hypertrophy and strain or documented symptoms. The
aorta and even descending aorta, renal artery hypoplasia, coronary artery obstruction and dysplasia, and branch pulmonary artery hypoplasia with multiple peripheral stenoses. The intima, media, and adventitia of the coronary arteries may all be involved with fibrotic and dysplastic changes.

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

#### Presentation

Because the pathologic processes in the arterial wall are diffuse and progressive, disease that was asymptomatic in childhood may lead to systemic hypertension (renal arteries and diffuse aortic hypoplasia), late-onset discrete systemic outflow obstruction (progression of supravalvar aortic stenosis), pulmonary hypertension (peripheral branch pulmonary artery stenosis and hypoplasia), or cardiac ischemia (coronary artery ostial obstruction, sinus of Valsalva inflow obstruction from progression of the supravalvar obstructive process, or coronary artery aneurysm or dissection). These modes of presentation can occur in the adult whether or not the patient underwent surgery in childhood to address supravalvar aortic stenosis.

#### Diagnosis

The electrocardiogram will show varying degrees of left ventricular hypertrophy, reflecting the degree of left-sided outflow obstruction. If there is coronary artery involvement, there may be signs of ischemia. The chest radiograph may also show signs of left ventricular hypertrophy. Surface echocardiography reliably demonstrates the abnormal supravalvar aortic morphology, but cannot completely define the coronary artery, pulmonary artery, or diffuse changes in the remainder of the aorta and its branches. Transesophageal echocardiography may further define the intracardiac and proximal aortic morphology, but has the same limitations as surface echocardiography with respect to more peripheral artery and coronary artery problems. Both magnetic resonance imaging and computed tomography (CT) are useful in defining the ascending and descending aorta and its major branches and the peripheral branch pulmonary arteries. Although CT can define some coronary artery abnormalities, cardiac catheterization and angiography are indicated for precise definition. Obstruction to coronary arterial flow may be caused by progression of the supravalvar stenosis leading to inhibition of blood entering the sinus of Valsalva, or from intrinsic coronary artery ostial obstruction from intimal thickening. In the most severe cases the sinus of Valsalva can be totally occluded as the free edge of the valve cusp fuses to the overhanging fibrous ridge of the discrete supravalvar ring.

#### NATURAL HISTORY

Supravalvar aortic stenosis is typically diagnosed and treated in childhood. In the William syndrome form, it is rare for the individual to reach adulthood undiagnosed, even if the cardiovascular manifestations are mild, because the distinctive associated facial and neurodevelopmental abnormalities make the diagnosis obvious.

#### TECHNIQUE OF OPERATION

Second relates to status of the aortic valve: presence of subaortic stenosis, regardless of gradient, is an indication for surgery if new-onset aortic regurgitation develops or more than mild regurgitation is present. Mild subaortic stenosis in the absence of aortic regurgitation, particularly if the membrane is in contact with or in close proximity to the aortic valve, is considered an indication for resection by some. Aortic valve repair is indicated at the time of resection if aortic regurgitation is more than mild. Aortic valve replacement is indicated for moderate or severe regurgitation if repair is not possible.
Other vascular procedures may be indicated, including reconstruction of stenotic or hypoplastic ascending aorta, arch, head and neck arteries, and branch pulmonary arteries.

**RESULTS**

Evidence-based outcome estimates for outcomes of supravalvar aortic stenosis repair in adults are based on case reports and the few adult patients included in larger pediatric series. Early mortality after repair of supravalvar aortic stenosis in adults is probably in the range of 2% to 5%. Mortality should be no higher than for similar operations in children unless important complicating factors are present. At least one large series, mostly involving children (median age 7 years), reports an early mortality of 9%; however, most of the deaths occurred in the 1950s and
1960s or involved patients brought to the operating room in extremis.145

It is probably true that adult patients with supravalvar aortic stenosis will demonstrate sequelae not usually seen in children, primarily related to the coronary arteries. Inan and colleagues report a case of a 21-year-old man with associated left main coronary artery stenosis caused by cusp fusion and thickening and intimal thickening of the coronary ostium.11 Surgical repair was uncomplicated. Yilmaz and colleagues report two cases, age 20 and 21 years, of associated coronary artery aneurysm. Both patients underwent repair of the supravalvar aortic stenosis without surgically addressing the aneurysms. Postoperatively, anticoagulation therapy was instituted. Both patients were doing well at midterm follow-up.17 Thistlethwaite and colleagues report on a 32-year-old patient with long-segment left main coronary artery narrowing successfully managed with supravalvar aortic repair and concomitant saphenous vein coronary artery bypass grafting.17

As in children, risk factors for late survival and reoperation are likely to be diffuse supravalvar aortic hypoplasia and concomitant aortic valve disease.145

INDICATIONS FOR OPERATION
Surgery is the only therapeutic option for supravalvar aortic stenosis; there are no percutaneous techniques applicable to this lesion. The hemodynamic indication for surgery is a 50-mmHg mean echocardiographic gradient. If symptoms are present, there is left ventricular hypertrophy or failure, or increased cardiac demand is expected (e.g., an active lifestyle, anticipation of pregnancy), surgery is indicated for less severe resting obstruction. Evidence of myocardial ischemia with obstruction to coronary flow is an indication for surgery regardless of aortic gradient.

Section X  Aortic Arch Obstructive Problems

DEFINITION
The definitions, morphology, and basic physiology of coarctation of the aorta and interrupted aortic arch are described in Chapter 48. Problems related to aortic coarctation are relatively common among adults with congenital heart disease. Often these problems relate to secondary disease, with the patient having undergone a surgical or interventional procedure as an infant or child. Patients can, however, present with native disease in adulthood.147,220,226,13,14,220

MORPHOLOGY
Many patients with a history of previous coarctation repair have some form of residual disease as adults, and lifelong follow-up is required after repair at any age. Residual disease may take many forms. There may be obstruction at the coarctation repair site or, particularly if the repair technique involves a prosthetic patch, aneurysm at the repair site. Diffuse aortopathy is recognized as part of the coarctation disease process, and this can contribute to chronic hypertension, dissection, aneurysm, and rupture. Intracranial aneurysm may be present in patients with coarctation, leading to intracranial bleeding and stroke.

A spectrum of associated left-sided cardiac structural anomalies can occur with coarctation, most commonly bicuspid aortic valve, but also other anomalies that, with coarctation, make up Shone complex. These are supramitral ring, parachute mitral valve, and subaortic membrane. All may be part of the presentation of either recurrent or residual coarctation, or well-repaired coarctation in the adult. With the exception of bicuspid aortic valve, these associated anomalies are much less likely to be part of the presentation of newly diagnosed coarctation in the adult, because most patients with multiple associated anomalies will present much earlier. These associated left-sided obstructive problems are not discussed further in this section. Aortic valve and subvalvar aortic obstruction are discussed in Sections VII and VIII of this chapter.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA
Presentation
The adult with unrepaired coarctation typically presents with systemic hypertension. This may be accompanied by symptoms such as headache and lower extremity weakness, especially with exercise. On further evaluation a differential between upper body and lower body blood pressure is commonly noted; however, long-standing obstruction leads to collateral development, which can blunt or even eliminate the pressure differential. A lower body pulse delay remains in all cases.

Interrupted aortic arch rarely presents in adulthood as primary disease; rather, the majority of patients present critically ill as neonates and either undergo surgical repair or die. Adults with secondary disease following prior repair of interrupted aortic arch will present with signs and symptoms similar to those of patients with prior coarctation repair. There will be, however, a higher prevalence of late aortic valve and subaortic problems.

Patients with previously repaired coarctation or interrupted aortic arch most commonly present with residual or recurrent coarctation or hypertension, but may present with any of the signs and symptoms related to aortic, coronary, or cerebral vascular disease, or associated cardiac structural anomalies. Aortic aneurysm at the repair site is particularly likely in patients with prior patch aortoplasty repair (Fig. 29-22).149 Even if there is no recurrent obstruction, adults with a history of coarctation repair in childhood have reduced exercise capacity compared with normal individuals, particularly if systemic hypertension is present or repair was performed at an older age.120

Diagnosis
In unrepaired coarctation, the electrocardiogram will show left ventricular hypertrophy. Chest radiography may show cardiomegaly from left ventricular hypertrophy, aortic silhouette irregularities such as the reverse-3 sign of unrepaired coarctation or dilatation and ectasia associated with prior repair, and rib notching from intercostal arterial collaterals. Echocardiographic imaging of the thoracic aorta is difficult in the adult,
although color Doppler may show an obstructive pattern at the coarctation site, flow in intercostal collaterals, and blunted pulsation distal to the coarctation. Echocardiography is essential for documenting associated intracardiac structural anomalies and myocardial function. Magnetic resonance imaging (MRI) and computed tomography (CT) are the preferred methods for precisely defining the morphologic details of both primary coarctation and previously repaired coarctation or interrupted aortic arch in the adult, particularly when three-dimensional reconstruction is obtained (Figs. 29-23 and 29-24). Accurate measurement of reduction in luminal diameter at the primary coarctation or repair site is an important factor used in management decisions. MRI can be used to calculate the amount of collateral flow present by subtracting flow in the aorta just distal to the primary coarctation or repair site from flow in the aorta at the diaphragm. It can also assess

**Figure 29-22** Cumulative incidence of descending thoracic aortic aneurysms after native coarctation repair by (A) patch aortoplasty (n = 494) or (B) other methods (n = 397). (From Knyshov and colleagues.19)

**Figure 29-23** Computed tomography images of a 36-year-old woman with severe native coarctation of the aorta. Sagittal multiplanar reformatted (A) and left lateral volume-rendered (B) images show severe aortic narrowing (white arrows) below left subclavian artery. Enlarged internal thoracic arteries and dilated posterior collateral intercostal arteries connecting to the postcoarctation descending thoracic aorta are seen. C, Anterior volume-rendered image shows enlarged internal thoracic arteries (black arrows) and dilated superior thoracic and thoracoacromial arteries (white arrows). D, Coronal maximum-intensity projection image shows dilated posterior collateral intercostal arteries causing rib notching. (From Turkvatan and colleagues.25)
functional elastic properties of the aortic wall.\textsuperscript{H1} These data may be particularly helpful in cases of both primary and recurrent coarctation when there is a smaller gradient than expected across the coarctation site and reduction in luminal diameter is equivocal.

MRA of the head is indicated in all adults to rule out intracranial aneurysm. Diagnostic cardiac catheterization is indicated primarily to assess the coronary arteries; however, in cases with questionable criteria for intervention, a catheter pullback peak-to-peak gradient across the coarctation may provide definitive information. Therapeutic catheterization may be indicated.

**NATURAL HISTORY**

If coarctation is unrecognized for many years, premature coronary artery obstructive disease, cerebrovascular disease, and aortic disease may lead to myocardial infarction, heart failure, stroke, intracranial hemorrhage, infective endarteritis, or aortic dissection or rupture. Aortic complications are more likely with advanced age and with presence of a bicuspid aortic valve.\textsuperscript{e97} Life expectancy is approximately half of normal in patients with unrepaired coarctation. Survival at 30-year follow-up after surgical repair ranges from 72% to 82%.\textsuperscript{W18}

**TECHNIQUE OF OPERATION**

There are many surgical options for addressing both native and recurrent coarctation in the adult. The actual techniques are no different from those used for coarctation in infants and children, which are described in detail in Chapter 48. Decision making used in choosing among these, however, is very different from that used in infants and children. The difference is based on several factors:

- Somatic growth does not have to be considered in the adult.
- Adults have much less elasticity in their aortic tissue than children.
- Adults are much more likely to have had one or more prior operations for coarctation.
- Adults are much less likely to have intracardiac anomalies requiring surgery concomitant with coarctation repair.

Thus, for native coarctation in the adult, it is more likely that an interposition graft will be required rather than resection and primary anastomosis, especially if there is any length to the coarctation or if proximal arch hypoplasia is present. For native coarctation, the surgical approach will usually be by left thoracotomy in adults, because intracardiac anomalies are relatively uncommon. Use of various forms of extended resection and primary anastomosis are essentially never an option in the adult because lack of elasticity in the adult aorta precludes the degree of mobilization required. Resection and primary anastomosis is reserved for discrete coarctation with no proximal arch hypoplasia. If coronary artery or aortic valve disease is present and requires surgical treatment, median sternotomy is used.\textsuperscript{J14, T15}

For recurrent coarctation, the surgeon must consider whether previous repairs were performed by sternotomy or left thoracotomy. If by sternotomy, and the recurrent obstruction is in the distal arch, then left thoracotomy may be the best approach. Resection and primary anastomosis is rarely possible in this setting or in any recurrent setting in the adult; most often, either patch repair or interposition grafting will be performed. If the previous operation was by left thoracotomy, a median sternotomy with cardiopulmonary bypass (CPB) may be the best approach, especially if the recurrent obstruction is in the proximal arch. If the obstruction is distal in the arch and relatively simple anatomic, and there has been only one previous thoracotomy, a repeat thoracotomy may be considered. CPB can also be considered when a thoracotomy is chosen, either for native or recurrent coarctation, if the repair appears to be complex (anticipated long aortic clamp time) and there are few or no collaterals (Fig. 29-25).\textsuperscript{B1} Deep hypothermic circulatory arrest has been described for complex coarctation repair via thoracotomy.\textsuperscript{G22} As the number of previous thoracotomies and anatomic complexity of the recurrent obstruction increase, the more attractive becomes the option of performing the repair using one of the many extracardiac graft reconstruction techniques.\textsuperscript{A18, A16, C3, D3, M13, S14, W7} Two of these techniques, one using median sternotomy and one left thoracotomy, are shown in Figs. 29-26 and 29-27. Right thoracotomy can also be used.

Therapeutic catheter-based intervention for recurrent obstruction is preferred in many institutions. Endovascular approaches, including balloon aortoplasty and covered stenting, may be used.\textsuperscript{G19, W3} In selected complex patients with previous surgery or with important comorbidities, hybrid approaches may be applicable (Fig. 29-28).\textsuperscript{C5, C6}

**RESULTS**

Early mortality after surgical repair of native coarctation in the adult is less than 1%, and hypertension is reliably improved and even normalized in many cases, with reduced requirement for antihypertensive medication.\textsuperscript{V16} Jatene and
Figure 29-25 Repair of coarctation of the aorta in adults. 

A, Through a posterolateral thoracotomy, lung has been retracted anteriorly with a “Kirklin fence.” Aortic cannula is shown in position in the descending thoracic aorta distal to site for distal aortic vascular clamp. Coarctation site and aortic arch have been dissected. “Patent ductus arteriosus” (PDA) represents either ductus or ligamentum arteriosum, which may or may not be present.

B, Lung has now been retracted posteriorly (temporarily) and pericardium opened posterior to phrenic nerve. Venous cannula has been inserted into left atrial (LA) appendage. C, Patient is placed on partial cardiopulmonary bypass. Venous drainage must be carefully controlled by perfusionist such that left atrium is not drained completely, allowing enough left ventricular filling so that upper body perfusion is maintained by left ventricular ejection. Proximal and distal vascular clamps have been applied. Ligamentum, if present, is ligated and divided. Dotted lines indicate extent of coarctation resection. In this case, two intercostal collateral vessels have been ligated and divided.
colleagues report on 50 adults (mean age 25 years) who underwent surgical repair of native coarctation via left thoracotomy. Procedures used included resection with anastomosis in 40%, patch augmentation in 44%, and interposition graft in 16%. There was no early mortality (CL 0%-3.7%). At a mean follow-up of 46 months, there was one late death due to endocarditis. Blood pressure was normal in more than 90%, with 75% free of antihypertensive medication (Fig. 29-29). The gradient was reduced from a mean of 61 mmHg preoperatively to a mean of 19 mmHg and was independent of the surgical technique used. Similarly, Bouchart and colleagues report on 35 adults (mean age 28 years) with native coarctation. Resection with anastomosis and interposition graft were the dominant techniques used. Mean follow-up was 165 months. There was no mortality (CL 0%-5.3%) and no reoperation for recoarctation over the course of follow-up. At follow-up, 66% (23/35) were normotensive without medication; however, 35% (8/23) had a hypertensive response to exercise testing at 6-month follow-up. Six patients underwent subsequent surgery for aortic valve disease. Wells and colleagues report on 26 adults (mean age 32 years) undergoing surgical repair of native coarctation, with a mean follow-up of 2.3 years. There was no mortality (CL 0%-7.0%). At rest, 88% were normotensive, but most remained on medication. Hashemzadeh and colleagues report on 38 adults (mean age 26 years) undergoing surgical repair using the techniques of resection with anastomosis, patch repair, and graft interposition, with a mean follow-up of 37 months. Results were similar to the previously cited studies, with no mortality (CL 0%-4.9%) and relief of resting hypertension in the majority of patients. Bhat and colleagues report on 84 adults (mean age 29 years) undergoing surgical repair of native coarctation, with a mean follow-up of 5.2 years. There was 1 early death (1.2%; CL 0.2%-4.0%) and no deaths at follow-up. All survivors experienced significant regression of hypertension, with 42% off medication, and persistent hypertension was observed in 31%. Bauer and colleagues report 15 patients over the age of 50 years undergoing surgical repair of native aortic coarctation, with a mean follow-up of 4 years. There was no mortality (CL 0%-21%). Two minor strokes occurred perioperatively with full resolution, and there was one case of endocarditis. Hypertension was relieved in 80% (12/15), but 73% (8/11) of evaluated patients who were normotensive at rest had a hypertensive response to exercise.

Complications after repair of native coarctation in adults are similar to coarctation repair in children, including blood loss, phrenic nerve injury, recurrent nerve injury, hypertension, residual coarctation, pseudoaneurysm, and paraplegia. Interventional procedures for native coarctation in the adult, either balloon angioplasty or stenting, provide similar gradient relief and hypertension control as surgery. Earlier reports of aneurysm formation and intimal tears following balloon angioplasty in up to 13% of patients may be reduced as experience increases and technology advances to include stents and covered stents. Reports as recent as 2008, however, show aneurysm formation in 7.5%. Several deaths have also occurred using interventional techniques. Long-term sequelae of endoluminal prostheses remain an important unanswered question, and this concern is the major objection to their use in native coarctation. It is also the major argument for surgical management of native coarctation, especially when end-to-end anastomosis can be achieved, thereby avoiding prosthetic material.

Early mortality for surgical repair of recurrent coarctation varies from 1% to 14%, depending on complexity of the surgery and presence of comorbidities. There are reports of no surgical mortality. Early mortality
of recurrent coarctation treated by stents and endografts, there was no early mortality and no paraplegia (CL 0%-16%). Surgical reconstruction of the left subclavian artery was necessary in two patients because of coverage of the origin of the artery and arm ischemia. At a mean follow-up of 12 months, three cases of leaks around the endograft were documented, one as late as 2 years after implantation. Long-term clinical effectiveness has not been demonstrated.

**INDICATIONS FOR OPERATION**

Intervention may be surgery or percutaneous catheter-based therapy. Indications for intervention include a gradient of 20 mmHg or more (documented by catheterization using extra-anatomic bypass techniques varies from 0% to 4.6%. Late outcome, ranging up to 22 years in these studies, is excellent, with no reported graft-related complications or reoperations.

Endovascular approaches, including balloon aortoplasty, stenting, and covered stenting, are as effective as surgery in relieving the gradient in adults with recurrent coarctation. These approaches avoid much of the morbidity associated with reoperative surgery and complex reconstruction; however, they are themselves complex procedures. Morbidity includes vascular injury at the site of percutaneous puncture, residual and recurrent coarctation, hypertension, aneurysm formation at the coarctation site, aortic leaks, and vascular compromise. In a series of 11 cases (mean age 47 years) of recurrent coarctation treated by stents and endografts, there was no early mortality and no paraplegia (CL 0%-16%). Surgical reconstruction of the left subclavian artery was necessary in two patients because of coverage of the origin of the artery and arm ischemia. At a mean follow-up of 12 months, three cases of leaks around the endograft were documented, one as late as 2 years after implantation. Long-term clinical effectiveness has not been demonstrated.

**INDICATIONS FOR OPERATION**

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in equivocal cases) across the coarctation and a luminal narrowing of 50% or more (by MRI, CT, or catheter-based aortography) at the coarctation site. If the gradient is less than 20 mmHg and luminal narrowing is less than 50%, MRI documentation of important collateral flow is an indication for intervention.

Some institutions consider percutaneous catheter-based balloon dilatation and stenting as an option for adult native coarctations that meet specific morphologic criteria, but others consider surgery to be the procedure of choice for all native coarctations, reserving percutaneous therapy for recurrent coarctation. Most institutions with experienced interventional cardiology teams consider percutaneous catheter-based therapy as the procedure of choice for recurrent coarctations that meet these specific morphologic criteria:

- Coarctation must be discrete.
- There must be no associated proximal arch hypoplasia.
- Coarctation must be remote from the origin of head and neck arteries.
- There must be no aneurysm, dissection, or important ectasia associated with the coarctation.
- No intracardiac anomalies requiring surgical repair are present.

Surgery is indicated for recurrent coarctation if any one of these criteria is not met or if percutaneous therapy is not successful. For those institutions that prefer percutaneous techniques for selected native coarctation, the criteria that must be met are the same as for recurrent coarctation.

### Section XI  Tetralogy of Fallot

#### DEFINITION

Definition, morphology, and basic physiology of tetralogy of Fallot are described in Chapter 38. Tetralogy of Fallot is common in adults presenting with congenital heart disease. Almost exclusively, adult patients have secondary disease, having undergone repair in infancy or childhood. Rarely, the adult with tetralogy will present with primary disease.

#### MORPHOLOGY

Most often, previously repaired patients present as adults with residual right ventricular (RV) outflow tract (RVOT) disease, either pulmonary stenosis, regurgitation, or both. This may develop in the native RVOT, in a prosthetic valve placed in the native RVOT, or in a RV-to-pulmonary trunk conduit. When stenosis is present, it may be subvalvar, valvar, or supravalvar. Residual RVOT disease is common because this problem is built into the standard initial repair. Pulmonary valve anular hypoplasia and abnormal cusp development occur in the majority of tetralogy patients. Initial repair involves a transanular patch in more than 50% of patients, causing obligatory important pulmonary regurgitation. Surgical pulmonary valvotomy is performed in many of the remaining patients, leaving them vulnerable to both regurgitation and stenosis.
Other less common reasons for adult presentation include residual ventricular septal defect (VSD), residual atrial septal defect, tricuspid regurgitation, aortic regurgitation, dilated aortic root, branch or peripheral pulmonary artery stenosis, stroke, and various arrhythmias.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Presentation**

The typical adult with previously repaired tetralogy of Fallot presents with signs and symptoms related to pulmonary regurgitation, including exercise intolerance and palpitations. If intervention is not undertaken at that time, RV dilatation progresses and right heart failure or atrial or ventricular tachycardia may be the mode of presentation. The effect of RVOT dilatation, “aneurysm,” and akinesis, independent of the pulmonary regurgitation itself, on the RV is currently the focus of attention. The role of these factors is not clear at this time. One study shows that the best predictors of reduced quality of life are reduced RV ejection fraction and later age at repair.

Many patients in developed countries are followed carefully into adulthood after infant or childhood tetralogy repair, and the presentation may be of an asymptomatic patient who at follow-up evaluation eventually meets a number of imaging, hemodynamic, and electrophysiologic criteria for intervention. These criteria continue to evolve and are designed to trigger intervention before irreversible myocardial or electrical damage occurs in the right atrium and ventricle.

The arrhythmia burden is substantial in repaired tetralogy patients, and it increases dramatically with age (Figs. 29-30 to 29-32 and Table 29-10).

Presentation in the adult may be altered by any of the residual or secondary lesions mentioned in Section I of this chapter.

Although about 15% of adult tetralogy patients have a dilated ascending aorta (associated with a history of long shunt-to-repair interval and with pulmonary atresia), it rarely leads to presentation. Of 671 acute aortic dissections reported in one large series, only one was in a patient with tetralogy of Fallot. A few additional isolated single case reports of aortic dissection and aneurysm in tetralogy patients
Table 29-10  Arrhythmia Burden in 556 Adults (Mean Age 37 Years) with Surgically Repaired Tetralogy of Fallot

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Prevalence %</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustained tachyarrhythmia:</td>
<td>29.9</td>
<td>26.2-33.7</td>
</tr>
<tr>
<td>Atrial tachyarrhythmia:</td>
<td>20.1</td>
<td>17.0-23.6</td>
</tr>
<tr>
<td>IART</td>
<td>11.5</td>
<td>9.0-14.3</td>
</tr>
<tr>
<td>AF</td>
<td>7.4</td>
<td>5.4-9.7</td>
</tr>
<tr>
<td>Other</td>
<td>6.7</td>
<td>4.8-8.9</td>
</tr>
<tr>
<td>Ventricular tachyarrhythmia:</td>
<td>14.6</td>
<td>11.8-17.7</td>
</tr>
<tr>
<td>VT</td>
<td>14.2</td>
<td>11.5-17.3</td>
</tr>
<tr>
<td>VF</td>
<td>0.5</td>
<td>0.1-1.4</td>
</tr>
<tr>
<td>At least one arrhythmia</td>
<td>21.4</td>
<td>18.1-24.9</td>
</tr>
<tr>
<td>intervention:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transcatheter ablation:</td>
<td>7.2</td>
<td>5.2-9.5</td>
</tr>
<tr>
<td>Implanted cardiac arrhythmia</td>
<td>18.3</td>
<td>15.3-21.7</td>
</tr>
<tr>
<td>device:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pacemaker</td>
<td>7.9</td>
<td>6.0-10.5</td>
</tr>
<tr>
<td>ICD</td>
<td>10.4</td>
<td>8.1-13.1</td>
</tr>
<tr>
<td>Sustained tachyarrhythmia and/or intervention</td>
<td>43.3</td>
<td>39.3-47.5</td>
</tr>
</tbody>
</table>

From Kairy and colleagues.871
Key: AF, Atrial fibrillation; CI, confidence interval; IART, intraatrial reentrant tachycardia; ICD, implantable cardioverter-defibrillator; VF, ventricular fibrillation; VT, ventricular tachycardia.

also exist; however, given the number of adults with tetralogy, these events are rare.813,817,821 Dilated ascending aorta, however, is associated with important aortic regurgitation.829

Diagnosis

The diagnosis is already known in the great majority of adults with tetralogy of Fallot. Further diagnostic workup is aimed at identifying residual defects (primarily pulmonary regurgitation) and determining when intervention is indicated. The electrocardiogram (ECG) is critical to evaluation, identifying the predominant rhythm (sinus, junctional, or atrial fibrillation or flutter), presence of ventricular ectopy, and QRS complex duration. Holter monitoring and formal electrophysiologic evaluation should be undertaken to fully characterize any rhythm disturbance (see “Arrhythmias” in Section I of this chapter).

Electrocardiography estimates severity of pulmonary regurgitation, RVOT obstruction, RV function and size, tricuspid regurgitation, residual ventricular and atrial septal defects, as well as left-sided valvar and ventricular function.

Magnetic resonance imaging (MRI) is particularly helpful in quantifying pulmonary regurgitant fraction, tricuspid regurgitant fraction, and RV end-diastolic volume.596,597 It may also provide important information about the peripheral branch pulmonary arteries. If MRI is contraindicated, computed tomography (CT) can be used to determine RV volume and to image the branch pulmonary arteries.828,829,830

Cardiac catheterization is indicated to assess the coronary arteries and to determine pulmonary vascular resistance, which may be abnormal, particularly in patients formerly palliated with shunts. Coronary arteries are imaged to rule out arteriosclerosis and to characterize the coronary artery anatomy if it is not already known. Specifically, the left anterior descending coronary artery arises from the right sinus of Valsalva and crosses the RVOT in about 10% of tetralogy patients and thus is vulnerable to injury during RVOT intervention. Catheterization may also be indicated to obtain complete hemodynamic evaluation if alterations in right or left ventricular function require further clarification.

NATURAL HISTORY

Tetralogy is a common form of congenital heart disease (5%-7% of all congenital defects), and most patients survive to adulthood after repair. Thirty-year survival after repair is 80% to 85%. Surgical cure is rare, however.814

When an adult presents with unrepaired tetralogy, the physiology is usually that of mild or mild to moderate RVOT obstruction.

TECHNIQUE OF OPERATION

The surgical procedures used in adults with tetralogy of Fallot will be for residual or recurrent disease in most cases. Rarely, the adult will present with unrepaired tetralogy, either with a history of previous palliative shunt or with no previous surgery. The procedures used in these patients are the same as in children and are detailed in Chapter 38. In adults with previously repaired tetralogy who have pulmonary regurgitation, porcine, xenograft, bovine pericardial, and allograft valved conduits may be placed into the RVOT. The technique of operation is described in Chapter 38, as is surgical reconstruction of the RVOT.

Catheter-based placement of a pulmonary valve is possible as a “valve-in-valve” procedure requiring a previously placed bioprosthetic conduit 18 to 20 mm in diameter. Peripheral or segmental pulmonary artery stenoses may be addressed by balloon dilatation, either proceeding the procedure or as a hybrid procedure. Catheter-based methods may be applicable for residual atrial or ventricular septal defects, branch pulmonary artery stenoses, aortopulmonary collateral arteries, and closure of previously placed surgical shunts.

RESULTS

Surgical outcomes after operations on the RVOT in adults with previously repaired tetralogy are excellent, with early mortality of 0% to 2%.520,521,711 Lesser performed operations, such as closure of residual atrial or ventricular septal defect or repair of branch pulmonary artery stenosis, probably have similar mortality. Late survival is also excellent, with mortality of 0.5% per patient-year.520 Sudden death from arrhythmias is the main mode of premature death. Ventricular tachycardia is the most common cause of this; however, acute atrial tachycardia and heart block may also contribute. Its risk factors include a long interval before repair (this risk is present whether the patient has received no operation or a palliative shunt); residual RVOT disease (regurgitation or stenosis); known ventricular ectopy; poor left ventricular function; and prolonged QRS duration. Prolonged QRS duration and ventricular ectopy both correlate with poorly functioning and dilated RVs and with cardiac events. Prolonged QRS also correlates with left ventricular dysfunction, and left ventricular dysfunction is a risk factor for sudden death.514,728
Table 29-11 Observed Annualized Cardiac Event Rate According to QRS Duration

<table>
<thead>
<tr>
<th>No.</th>
<th>Patient-Years</th>
<th>Events</th>
<th>Events/100 Patient-Years</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>90</td>
<td>483.8</td>
<td>13</td>
<td>2.7</td>
</tr>
</tbody>
</table>

**Preoperative QRS Duration**

| ≤180 ms + PO QRS reduction | 44 | 241.8 | 0 | 0 | NA |
| ≤180 ms – PO QRS reduction | 27 | 157.0 | 8 | 5.1 | 2.2-10.0 |
| >180 ms + PO QRS reduction | 14 | 75.3 | 3 | 4.0 | 0.8-11.6 |
| >180 ms – PO QRS reduction | 5 | 9.7 | 2 | 20.6 | 2.5-74.4 |

**Postoperative QRS Duration**

| ≤180 ms + PO QRS reduction | 52 | 294.8 | 2 | 0.7 | 0.1-2.4 |
| ≤180 ms – PO QRS reduction | 21 | 123.7 | 6 | 4.9 | 1.8-10.6 |
| >180 ms + PO QRS reduction | 6 | 22.4 | 1 | 4.5 | 0.1-24.9 |
| >180 ms – PO QRS reduction | 11 | 43.0 | 4 | 9.3 | 2.5-23.8 |

Modified from Scherptong and colleagues.511

\( P = .007 \) vs. the overall group.

\( P = .030 \) vs. the overall group.

Key: CI, Confidence interval; NA, not applicable; PO, postoperative.

Normalization of RV hemodynamics (placing a competent pulmonary valve and relieving RVOT obstruction) can reduce ventricular arrhythmias.52,B15,D12,E39,F2,D5,D7,G14,H15,H17,T11,W5 The operation can also reduce QRS duration in some cases, but not in others.16,M18 The study by Scherptong and colleagues showed that QRS duration improved in about two thirds of patients after operation, and this occurred whether the preoperative QRS was below or above 180 ms.511 Postoperative cardiac events were most likely to occur in the subset of patients with preoperative QRS of greater than 180 ms and no postoperative reduction in duration (Table 29-11). In another study, placing a competent pulmonary valve did not reduce QRS duration in any patient, and late follow-up showed no reduction in cardiac events.16 Why some patients show reduction in QRS duration after placement of a competent valve and others do not is unclear. Nevertheless, these studies imply that preserving RV function is probably the best way to minimize late fatal arrhythmias. This is best achieved by early primary repair with attention to myocardial preservation, and aggressive intervention in adults with residual or recurrent hemodynamic abnormalities that threaten to compromise RV function.

Improvement in both systolic and diastolic function and in RV dimensions has also been documented after placement of a competent pulmonary valve. Some studies, however, show continued RV dilatation and reduced function despite improvement in functional health status of the patient. These discrepancies may be due largely to timing of intervention, again underscoring the benefit of early intervention.52,A19,E6,F9,H12,T11,V10,V15

Performance of prosthetic pulmonary valves placed into the RVOT in adults with previously repaired tetralogy and pulmonary regurgitation has been studied by Fiore and colleagues.16 In comparing porcine (Medtronic Mosaic valve), bovine pericardial (Carpentier-Edwards), and pulmonary allograft vaulted conduit (Cryolife) prostheses, they found that allograft vaulted conduits initially had the lowest gradients; however, they also developed regurgitation and required reintervention sooner (Fig. 29-33). Outcomes for adult tetralogy patients undergoing right heart procedures and concomitant aortic valve or ascending aortic surgery have been reported by Stulak and colleagues.552 In their study of 81 patients, early mortality was 7.4% (CL 4.4%-12%); however, there was no mortality after 1991 in the last 56 patients (CL 0%-6.4%).

Adults presenting with unrepaired tetralogy of Fallot are becoming a vanishing subset. Most reports of large series are either from the 1960s and 1970s or, if more recent, are from countries with emerging healthcare technology.515 Attenhofer and colleagues recently reported on 52 patients (mean age 50 years) operated on between 1970 and 2007, half of whom had no previous palliation and half of whom did.521 Early mortality was 5.8% (CL 2.6%-11%). At 15-year follow-up, 29 of 48 early survivors had died at a mean age of 65 years. Previously palliated patients who died did so at a mean age of 59 years, and patients with no previous palliation...
who died did so at a mean age of 70 years. Survival in the entire group was lower than in the general population 10 years after repair, consistent with other evidence that earlier repair provides the most benefit. Surviving patients were functionally improved. Alizadeh and colleagues reported on 51 patients (mean age 22 years) operated on between 1995 and 2005. A previous systemic-to-pulmonary artery shunt had been performed in 16%. Early mortality was 2.0% (CL 0.05%-10%). During a mean follow-up of 42 months, one additional death occurred. Functional improvement was documented in survivors. Atik and colleagues reported on 39 patients (mean age 27 years) operated on between 1982 and 2001. A previous shunt had been performed in 10%. Early mortality was 5.1% (CL 0.6%-17%), and actuarial survival at 15 years was 68%. Again, functional improvement was seen in survivors. Lu and colleagues report on 57 patients (mean age 25 years) operated on between 1990 and 2004. Early mortality was 7.0% (CL 1.9%-17%), and survival was 73% at 14 years. Functional improvement was documented, with 76% of patients in New York Heart Association (NYHA) functional class I. Rammohan and colleagues report on 100 patients (mean age 20 years) operated on between 1991 and 1996. A previous shunt was present in 22%. Early mortality was 4% (CL 1.1%-9.9%), and there was one late death at a mean follow-up of 3.4 years. Of survivors, 94% were in NYHA functional class I.

These studies indicate that primary repair can be performed in the adult with varying, but generally low, early mortality risk, and with substantial improvement in functional status and quality of life. Late survival, however, is substantially lower than in the general population, and lower than for tetralogy patients who undergo operation earlier in life.

INDICATIONS FOR OPERATION

Decisions relating to intervention in the adult with previously repaired tetralogy of Fallot occur commonly and are complex. There are multiple potential defects, many of which may occur simultaneously and with varying degrees of severity. Appropriate intervention may be by surgery, percutaneous catheter-based intervention, or both. The adult congenital cardiologist, pediatric cardiologist, adult congenital cardiothoracic surgeon, and electrophysiologist should all be involved in formulating the individualized management plan for each patient. In patients with equivocal indications for intervention, cardiopulmonary exercise testing may be helpful.

Careful judgment should be used for the adult who presents with long-standing profound cyanosis and no previous surgery. This patient may struggle with severe right or even biventricular failure following primary repair even if no residual lesions are present and excellent myocardial protection is used. There are many reasons for this, including chronic cyanosis and long-standing RV hypertension.

There is another important variable: It must be appreciated that with markedly reduced pulmonary blood flow, this patient will have a combined ventricular output far less than normal, in the range of 1.3 to 1.5 times normal systemic output, rather than the normal combined ventricular output of 2 times normal systemic output. Primary repair of tetralogy, even when there are no residual defects, represents an acute volume load as biventricular output is obligatorily increased to 2 times normal systemic output. In the setting of a very noncompliant, small hypertrophied RV, the circulation may be unsustainable after repair. In such cases a preliminary systemic-to-pulmonary artery shunt procedure, followed by shunt takedown and repair after 3 to 6 months, should be considered. This approach will increase volume load during the shunt phase, effectively training the two ventricles to work at normal volumes prior to repair.

Catheter-Based Interventions

Catheter-based intervention may be applicable in selected cases of RVOT obstruction or regurgitation, residual atrial and ventricular septal defect, and branch and peripheral pulmonary artery stenosis that meet the same indications as for surgical intervention. Catheter-based intervention is preferred for closing acquired aortopulmonary collaterals and often for closing previously placed surgical shunts.

Catheter-based therapy may be considered for RVOT obstruction if the obstruction is at the valve level or beyond, but not if it is in the infundibulum. Balloon dilatation of valvar obstruction (either native valve or conduit), with or without stenting, is commonly performed; however, it is difficult to demonstrate objectively the efficacy of this procedure. Gradients can diminish but are not eliminated; however, regurgitation is made worse. The tradeoff in this physiologic change is of questionable benefit.

Catheter-based placement of a pulmonary valve in combination with balloon dilatation and stenting of obstruction is a more rational approach that has gained favor in recent years. This approach can also be used in selected cases of isolated regurgitation after repair. Catheter-based placement of a pulmonary valve, however, is only applicable in about 10% of repaired tetralogy patients with RVOT problems. Criteria for this procedure include requirement of a previously placed RV-to–pulmonary trunk conduit with a diameter of at least 16 mm, or previously placed bioprosthetic valve with a diameter of 18 to 20 mm. Thus, the great majority of repaired tetralogy patients—those with native RVOTs or transanular patches—are not candidates.

Most atrial septal defects are candidates for percutaneous device closure, with the criteria the same as for closure of isolated atrial septal defect. Selected muscular and patch-related VSDs are candidates for percutaneous device closure. Size and position of the defect must be such that impingement of the device on the tricuspid, mitral, or aortic valve is not of concern. Most acquired collaterals can be occluded with percutaneously placed coils or other occlusive devices.

Open surgical shunts are exceedingly rare in adult tetralogy patients in the current era; however, the occasional patient who reaches adulthood with palliated tetralogy may be a candidate for device closure. Branch and peripheral pulmonary artery stenosis can be considered for percutaneous balloon dilatation, particularly if surgical intervention is not in the immediate future of the patient. Stenting of branch pulmonary arteries should be avoided in most cases, even though it is fully acknowledged that some institutions recommend them. The central branch pulmonary
arteries are easily accessible surgically, even when the surgeon does not have particular expertise in pulmonary artery reconstruction. When placed in central pulmonary artery branches, stents do not relieve obstruction with the same efficacy as surgical reconstruction, and furthermore, stents can erode into the tracheobronchial tree and aorta.

Surgical Interventions

If surgical reconstruction of the RVOT is indicated, then balloon dilatation or stenting of central branch pulmonary artery stenosis should not be performed. Rather, the branch pulmonary artery obstruction should be repaired surgically as part of the RVOT procedure. If no immediate surgical procedure is anticipated for a patient, balloon dilatation of isolated central branch pulmonary artery stenosis is a reasonable approach, but stenting should be avoided.

If surgery is planned for RVOT disease, concomitant more peripheral stenoses in lobar or segmental pulmonary arteries may be addressed by balloon dilatation prior to surgery or at surgery. This decision should be made on an individual institutional basis depending on available surgical and interventional expertise. Stenting of peripheral lobar and segmental pulmonary arteries that do not respond to balloon dilatation should not be performed if surgical expertise is available for direct repair.

SPECIAL SITUATIONS AND CONTROVERSIES

A number of cardiac anomalies have morphologic characteristics similar to those of tetralogy of Fallot. These are all conotruncal anomalies. They include all types of pulmonary atresia with VSD, all types of truncus arteriosus, and some types of double outlet right ventricle, transposition of the great arteries (TGA), congenitally corrected transposition of the great arteries, and double outlet left ventricle. The similar characteristics include normally developed atria, atroventricular (AV) valves, and ventricles, with large conoventricular type VSD, overriding or transposed aorta, and pulmonary stenosis or atresia. It follows that surgical repair of these anomalies will be similar to that of tetralogy of Fallot. It also follows that many of the late complications and management issues seen in adults with these anomalies will be similar to those seen with tetralogy.

The majority of these anomalies will be repaired in infancy, and repair requires two main components: VSD closure such that the left ventricle aligns with the aorta, and RV-to-pulmonary trunk reconstruction, often involving a valved conduit. Thus, adults with these anomalies almost always present with secondary disease, having been repaired in infancy or childhood. Issues related to the late follow-up status of the RV and RVOT in all these anomalies are similar to those seen in tetralogy; each, however, has unique additional morphologic characteristics that can lead to other late management problems not typically seen in tetralogy. These are discussed in the following text.

Pulmonary Atresia with Ventricular Septal Defect

Definition

See Chapter 38.

Morphology

There are two forms of this anomaly. The duct-dependent form is similar to classic tetralogy of Fallot. Because of the atretic pulmonary valve, initial reconstruction in infancy typically involves a valved conduit. By the time these patients reach adulthood, essentially all will have a RV-to-pulmonary trunk conduit. Late problems in adults are similar to those in tetralogy patients who have received a conduit. Dilatation of the ascending aorta, and associated aortic regurgitation, is more common in tetralogy with pulmonary atresia than in classic tetralogy.

The other form of pulmonary atresia with ventricular septal defect does not have a ductus arteriosus, but instead has large aortopulmonary collateral arteries. Branch and peripheral pulmonary artery abnormalities, such as deficient arborization, hypoplasia, or complete absence, are the hallmark of this anomaly.

Clinical Features and Diagnostic Criteria

Because of the complex and variable pulmonary artery morphology of this anomaly, individual patients will be managed differently during childhood and will therefore present differently in adulthood. The spectrum of presentation includes primary disease that is newly diagnosed (rarely), primary disease that was previously diagnosed but with benign physiology (rarely), primary disease that was previously diagnosed but deemed inoperable, and secondary disease after previous repair or palliation.

In adults with newly diagnosed primary disease, mode of presentation will likely be with signs and symptoms of cyanosis, but also may be with complications related to longstanding mixed circulation, such as paradoxical embolus, endocarditis, arrhythmias, or heart failure. Formal evaluation with echocardiography to assess ventricular function and valve function, and cardiac catherization to assess the pulmonary artery and collateral morphology and physiology, are required.

Technique of Operation

Surgical management decisions are the same as for children diagnosed with this disease (see Chapter 38), although adults have a greater degree of pulmonary vascular obstructive disease and collateral loss as well as cardiac dysfunction. Unoperated adults with preserved cardiac function and a full complement of patent but partially stenotic collaterals may be operable and fully correctable. In the large series by Malhotra and Hanley, unifocalization and intracardiac repair was possible in selected patients as old as 45 years. If evaluation reveals that intracardiac repair is contraindicated, palliative shunt or conduit operations to improve oxygenation may be warranted if the dominant symptoms are from cyanosis. Heart-lung transplantation may be considered in patients with decompensated cardiac function (see Chapter 21).

In adults with previously diagnosed primary disease with benign physiology, careful evaluation is similarly warranted. The original assessment that the patient had benign physiology is likely to have been incorrect if that designation was based only on adequate systemic oxygen saturation and not on detailed morphologic and physiologic assessment of the individual collaterals. Appropriate evaluation of each patient in this category, as in the former category, will determine whether repair, palliation, or transplantation is indicated.
Chapter 29 Congenital Heart Disease in the Adult

Natural History

Unrepaired truncus arteriosus is rare in the adult, and when it is encountered it is almost always unreparable because of Eisenmenger physiology. There are no reported series or case reports of primary surgical repair of truncus in the adult. There are several case reports of unrepaired truncus presenting in adulthood with complications such as pulmonary hypertension with Eisenmenger physiology, endocarditis, and fatal truncal root dissection.

Technique of Operation

Because the truncal valve commonly has more than three cusps and the anulus is large, the regurgitant valve can often be repaired using techniques that are not usually applicable in true aortic valves (Figs. 29-34 to 29-36).

Results

Outcomes and techniques for truncal valve repair are reported, but mostly for younger patients. In the series of 17 repairs by Kaza and colleagues, there was a single older patient (age 42 years).

Indications for Operation

Patients with truncal regurgitation usually present for repair at the time of neonatal correction, or within the first 10 to 15 years after repair \[11,19,115\]; therefore, presentation in the adult is unusual. Indications for repair or replacement are standard.

Double Outlet Right Ventricle

Definition

The type of double outlet right ventricle (DORV) with subaortic VSD and pulmonary stenosis is discussed in this section (see Chapter 53). It is the most common form of DORV.

Morphology

DORV with subaortic VSD and pulmonary stenosis or atresia is managed surgically like tetralogy of Fallot. Late problems occur primarily in the reconstructed RVOT, as in tetralogy. Additionally, there are concerns about the left ventricular outflow tract (LVOT) because of the subaortic conus and the more complex patch (or baffle) that is required to close the VSD and align the left ventricle with the aorta. The result is a complex tunnel-like LVOT. A combination of hypertrophy of the conus muscle and patch distortion lead to a greater chance of late subaortic stenosis than in tetralogy of Fallot.
survive to adulthood have Eisenmenger physiology and are inoperable. Those with pulmonary stenosis who survive and are cyanotic from low pulmonary blood flow may be candidates for surgical repair, similar to individuals with unrepaired tetralogy of Fallot.

### Natural History

Individuals with DORV rarely survive to adulthood without surgical repair. Those without pulmonary stenosis who do survive to adulthood have Eisenmenger physiology and are inoperable. Those with pulmonary stenosis who survive and are cyanotic from low pulmonary blood flow may be candidates for surgical repair, similar to individuals with unrepaired tetralogy of Fallot.
CTGA with VSD and pulmonary stenosis or atresia shares certain features with tetralogy of Fallot: surgical repair requires VSD closure and placement of a conduit from the heart to the pulmonary trunk. The definitive repair in infancy or childhood is either the “classic” repair or the “double switch” repair. There are important sequelae in the adult after both operations. In the classic repair, VSD closure is straightforward, and the conduit is placed from the morphologic left ventricle to the pulmonary trunk. The expected late conduit problems are a concern with this anomaly, just as with the other anomalies under discussion in this section. However, obstruction in the conduit may be better tolerated because the morphologic left ventricle and mitral valve are part of the pulmonary circulation.

An additional important late problem following “classic” repair is function of the tricuspid valve and morphologic RV that are positioned in the systemic circulation. Premature failure of these structures is common at late follow-up after “classic” repair, as it is under any other circumstance when the RV is left in the systemic circulation. (This subject is covered in more detail in Sections XII and XIII of this chapter.) When this circumstance is encountered after “classic” repair, the option of training the left ventricle and subsequent reoperation to place the left ventricle in the systemic circulation, under any circumstance a controversial choice, is almost always inadvisable, because the left ventricle already has a large ventriculotomy in it (raising concerns about its long-term function in the systemic circulation), and the operation would require placing a prosthetic valved conduit from the left ventricle to the aorta. The alternative of cardiac transplantation is the better option.

In the other type of repair in infancy or childhood, the “double switch” repair, the left ventricle is aligned with the aorta via the VSD using a patch or baffle, a conduit is placed from the morphologic RV to the pulmonary trunk, and an atrial switch is performed. Because of the position of the heart and aorta in CTGA, the conduit must often be positioned in the midline in this operation. The late concerns of conduit compression from the sternum are similar to those previously discussed for TGA. Additionally, in the double switch repair, atrial baffle complications, including intra-atrial shunting, systemic or pulmonary venous obstruction, and sick sinus syndrome or junctional rhythm, can occur, similar to complications found after the Mustard or Senning operation for simple TGA.

Natural History
CTGA with VSD and pulmonary stenosis or atresia may present as primary disease in adulthood, but in the current era, most patients with this form of CTGA undergo surgery in infancy or childhood. This may involve initial palliation with a systemic-to-pulmonary artery shunt followed by later definitive repair, or initial definitive repair. After any kind of repair of CTGA, complete heart block is frequent, occurring either at the time of initial repair or spontaneously at any time.

Technique of Operation
In Connelly and colleagues’ series of 52 patients with all forms of corrected transposition presenting in adulthood, 64% underwent definitive surgical repair. The most common procedure was the “classic” repair for patients with associated VSD and pulmonary stenosis, performed in 80% (20/25) of the definitive repairs. In six of these patients, the
systemic tricuspid valve was replaced. Early mortality was 5%.
Two patients who had no systemic tricuspid valve regurgita-
tion preoperatively developed severe regurgitation after repair, probably related to shift of the ventricular septum after left ventricular pressure was reduced. Exercise testing in sur-
vivors was subnormal. There was no increase in systemic ventricular ejection fraction with exercise.

Results
In a series of 189 patients of all ages with all forms of corrected transposition, 152 had associated VSD and either pulmonary stenosis or atresia. Although mean age at surgery was 8 years, the upper end of the age range was 47 years, implying that at least some patients with VSD and pulmonary stenosis presented for initial repair in adulthood.

Double Outlet Left Ventricle
There are several forms of this extremely rare anomaly (see Chapter 54). In the repaired adult, in addition to the typical right-sided conduit problems, the LVOT must be monitored for late obstruction, just as in the other anomalies with left ventricular–to-aortic intracardiac patch or baffles. Commonly, repair involves complex closure of a VSD (with varying degrees of baffling required) and placement of a RV-to–pulmonary trunk conduit.

Section XII Transposition of the Great Arteries

DEFINITION
The morphology, physiology, and natural history of transposition of the great arteries (TGA) are described in Chapter 52.

MORPHOLOGY
There are several common morphologic variants of TGA: with intact ventricular septum (simple TGA); with ventricular septal defect (VSD); with arch obstruction; and with VSD and pulmonary stenosis or atresia. TGA with VSD and pulmonary stenosis or atresia is discussed in Section XI. The other variants require neonatal or infant surgical correction for the patient to survive.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presentation
The adult presentation of these variants of TGA will almost exclusively be that of secondary congenital heart disease follow-
ing early corrective surgery. The predominant corrective surgery for these variants between 1959 and about 1985 was some form of the atrial switch operation, either Senning or Mustard. The predominant corrective surgery between about 1985 and the present has been the arterial switch. Thus, currently, adults older than about age 25 almost certainly will present with a background of atrial switch surgery, whereas those under age 25 are likely to present with a background of arterial switch surgery. These two populations present distinctly differently in adulthood.

A small but notable subset of the population with prior atrial switch surgery is made up of patients with failing systemic right ventricles (RV) who have undergone pulmonary trunk banding in order to train the morphologic left ventricle (LV) in anticipation of atrial switch takedown and conversion to an arterial switch. These patients may enter adulthood at varying stages of LV training or after conversion to the arterial switch.

Survivors may have a spectrum of conditions, including atrial arrhythmias (most commonly junctional rhythm with sick sinus syndrome [50% at 20 years] but also atrial fibrillation and flutter [35% at 20 years]), ventricular arrhythmias (9%), heart block, systemic and pulmonary venous obstruction within the atrial baffle, atrial septal defect, systemic (morphologic right) ventricular failure, systemic (tricuspid valve) atrioventricular valve regurgitation, and dynamic LV outflow tract obstruction.

Systemic venous baffle obstruction within the superior limb leads to superior vena cava syndrome: swelling of the head and upper body, sometimes accompanied by headache or chylothorax. Systemic venous baffle obstruction in the inferior limb can lead to hepatic congestion, cirrhosis, ascites, and dependent peripheral edema. Baffle leaks will result in shunting, typically physiologically left to right, with pulmonary overcirculation; however, large defects may lead to mixing and systemic cyanosis or paradoxical embolus. Functional status of the systemic RV also influences magnitude and direction of the shunt.

Pulmonary venous pathway baffle obstruction leads to pulmonary venous congestion and pulmonary hypertension. All the sequelae mentioned in the preceding paragraphs may already be well established in childhood, and commonly, pacemaker placement and revision of the atrial baffle, due to either leak or obstruction, may have already been performed before adulthood is reached. These sequelae have a substantial effect on quality of life and survival. These multiple sequelae notwithstanding, systemic right heart function (RV dysfunction, tricuspid valve regurgitation, or both) is the major issue in adults being followed with an atrial switch operation. Some degree of systemic right heart dysfunction is present in most patients by the time they reach adulthood.

Patients with prior arterial switch present in adulthood with fewer sequelae than do those with prior atrial switch. Some studies indicate that patients are physiologically and functionally on par with the age-matched normal popu-
lation. One study of 65 patients shows, however, that exercise capacity was 73% of normal in patients studied at a mean age of 19 years.

Sequelae are not only less prevalent than after the atrial switch, those that occur are also distinctly different, reflecting the differences between the two operations. In a study of 65 patients by Tobler and colleagues, 17% (12/65) of adults had at least one important cardiac lesion. Arrhythmias accounted for 7%, with atrial flutter in three patients, sick sinus syndrome in one, and ventricular tachycardia in one. Structural lesions accounted for the other 10%, with RV dysfunction in three patients, severe pulmonary regurgitation in two, and LV dysfunction, severe tricuspid regurgitation, and LV outflow tract obstruction in one each. They also
noted aortic root dilatation (>36 mm diameter) in 31%, but no intervention was required. Aortic regurgitation occurred in 52%; however, it was mild or less in all. There were no documented coronary artery lesions in this series; however, in other series coronary lesions were noted in 7% of cases at late follow-up.9,25

Other arterial switch series emphasize RV outflow tract obstruction, coronary insufficiency and its sequelae, and aortic root dilatation and aortic regurgitation.14,16,24,26,51,17,32 RV outflow tract obstruction occurs in 5% to 15% of patients and tends to develop within several years of the arterial switch; rarely will this become a new problem late postoperatively. Most patients with serious stenosis will undergo revision of the RV outflow tract during childhood, and some will require multiple revisions. This may ultimately result in important pulmonary regurgitation or need for a prosthetic valve or valved conduit. As adults, these patients require further surgical management of the RV outflow tract for problems related to right-sided conduit failure.

Coronary artery problems develop late in up to 8% of patients after arterial switch.1,16 Some of these patients may be asymptomatic, but most will present with typical signs and symptoms of coronary insufficiency.

Aortic root dilatation is well documented late following the arterial switch, but it occurs in only a small percentage of cases.1,27,18

LV dysfunction may develop in patients with a history of initial atrial switch followed by late pulmonary trunk banding for LV training and conversion to arterial switch. The dysfunction is currently poorly understood, but is probably related to inadequacy of the LV training process in most cases. Coronary artery obstruction is usually not implicated. All patients with a history of LV dysfunction and late conversion to the arterial switch should undergo frequent evaluation to assess LV function.

Diagnosis

Evaluation of the adult with prior atrial switch surgery may include electrocardiogram (ECG), echocardiography, magnetic resonance imaging (MRI), computed tomography (CT), and cardiac catheterization. ECG documents baseline rhythm, status of sinoatrial and atrioventricular nodes, and presence of ventricular ectopy. Holter monitoring is commonly helpful if any disturbance is present.

Echocardiography is the most important tool in assessing the status of both systemic venous limbs of the arterial baffle, pulmonary venous pathway, baffle leakage, systemic RV function, and systemic tricuspid valve function. Transesophageal echocardiography may enhance the findings of surface studies. Nevertheless, it is acknowledged that echocardiography has limited ability to assess RV function.1,28,29 Coronary artery morphology is not well imaged by echocardiography.

MRI and CT provide superior imaging information about the atrial baffle and its pathways and the great arteries and extracardiac central veins, and can provide additional valuable information about the systemic RV and tricuspid valve. In particular, MRI can be used to calculate tricuspid valve mass and volume, ejection fraction, and tricuspid regurgitant fraction. Myocardial delayed enhancement can evaluate RV myocardial viability.1,18

Cardiac catheterization is critical in the evaluation. Angiography is the standard for imaging the coronary arteries. A complete hemodynamic evaluation, and in particular measurement of systemic RV end-diastolic pressure, provides crucial information for managing the systemic right heart.

Electrical, morphologic, and hemodynamic data obtained from these studies are used to determine management of the TGA patient with a systemic RV. Management options include medical (pharmacologic) management of rhythm or ventricular function problems, or both; surgery to correct rhythm and hemodynamic problems (atrial baffle leaks or obstruction, VSD, severe RV-to–pulmonary trunk obstruction, maze procedure for atrial flutter or fibrillation, standard atrioventricular sequential or biventricular pacemaker placement); initiation of a program to train the LV in preparation for conversion to an arterial switch by placing a pulmonary trunk band; completion of conversion to an arterial switch in a previously banded patient; and heart transplantation.

Routine evaluation in the adult with prior arterial switch includes ECG and echocardiography. Cardiac catheterization with coronary angiography should be performed at least once in the adult, and more frequently if coronary insufficiency is suspected by symptoms or by other studies.1,28 More frequent coronary angiography should also be considered if the original operative note from the arterial switch operation indicates an unusual coronary artery pattern or difficulty with coronary artery translocation. ECG is most helpful in showing ischemic changes either at rest or with exercise; however, it will also document atrial and ventricular arrhythmias.

Echocardiography assesses function of all four valves (with particular focus on the semilunar valves), ventricular function, and size of the aortic root. The coronary arteries cannot be fully assessed by echocardiography, but indirect evidence of coronary insufficiency, such as ventricular wall motion abnormalities and mitral regurgitation, can be.

MRI and CT with angiography are also used selectively, for example, when more precise imaging is needed than can be provided by echocardiography (for serial assessment of aortic root size), when qualitative functional valve assessment is needed (for serial assessment of aortic regurgitation), or when functional myocardial evaluation is needed (magnetic resonance myocardial delayed enhancement).

In atrial switch adult patients who are considered candidates for LV training and eventual conversion to arterial switch, baseline evaluation of the morphologic LV and mitral valve is required. This includes ECG for rhythm and ectopy; echocardiography to assess morphologic LV systolic function, wall thickness, and mitral valve function; cardiac catheterization to measure LV end-diastolic pressure; and MRI to determine LV mass. All of these studies are then repeated after placing a pulmonary trunk band according to a specific protocol, to determine if and when the patient becomes a candidate for conversion to arterial switch.

Electrophysiologic evaluation is indicated in all adults with TGA, regardless of the type of surgery, if clinical course, ECG, or Holter monitoring suggests important atrial or ventricular rhythm disturbance.

NATURAL HISTORY

Adults with prior atrial switch surgery survive to adulthood. Twenty-five-year survival is 65%, and is even better (80%) if TGA is not complicated by VSD.2 Late mortality risk after the first 5 years following surgery appears to be linear at 0.5% per year.112 Studies show a concerning trend in measures
using bicaval venous cannulation and aortic clamping with cardioplegia administration. The systemic venous component of the baffle is exposed using an incision into the morphologic right atrial free wall, which is part of the pulmonary venous pathway of the baffle. Patch augmentation of the affected limb of the systemic venous baffle is then performed.

An alternative option for superior limb obstruction is to perform a bidirectional superior cavopulmonary anastomosis. This option may be preferred if there is long-standing long-segment occlusion of the superior limb or very complex non-occlusive obstruction. This option is contraindicated if pulmonary vascular resistance is elevated above about 3 Wood units.

Another option for superior limb obstruction to consider when obstruction is complex is placing an extracardiac polytetrafluoroethylene (PTFE) conduit from the patent superior vena cava to the inferior vena cava at the level of the diaphragm, with the conduit positioned along the right lateral border of the heart. This option should be considered only if the inferior limb of the systemic baffle is fully evaluated and deemed large enough to carry the entire systemic venous output without obstruction. An option that may occasionally be considered for complex inferior limb obstruction is placing an extracardiac conduit in the reverse direction, from the patent inferior vena cava at the diaphragm up to the superior vena cava. The superior limb of the baffle must be large enough to carry the entire systemic venous return without obstruction.

Pulmonary venous baffle obstruction almost always occurs at the midpoint of the pathway as it crosses the plane of the (normal) atrial septum and wraps around the systemic venous component of the baffle. Surgical approach involves CPB as described previously for systemic venous baffle obstruction. Patch augmentation of the external wall of the morphologic right atrium (which is part of the pulmonary venous pathway), with the patch extending down onto the right pulmonary veins, usually relieves the obstruction.

Operation for baffle leakage is performed using the same exposure described previously for systemic venous baffle obstruction. The leak may be at the suture line or through multiple atrial muscle trabeculations remote from the patch suture line. After opening the morphologic right atrial wall and entering the chamber that accepts pulmonary venous blood, suture line leaks are usually obvious and are best closed with additional patch material. Muscular trabeculation leaks are best assessed by performing the additional step of opening the chamber that accepts systemic venous blood and examining the internal surface of the systemic venous pathway. Direct suture closure or patching of all communications from this vantage point is then carried out.

Subvalvar LV-to-pulmonary trunk obstruction is approached using CPB with bicaval venous cannulation and aortic clamping with administration of cardioplegia. Access to the subvalvar obstruction is through an incision in the pulmonary trunk, with retrograde exposure through the pulmonary valve. Muscular and fibromuscular resection is performed using the same techniques used for subaortic obstruction (see Chapter 47).

Tricuspid valve surgery in atrial switch patients is usually not indicated. When it is, it rarely involves valve repair. Very occasionally, a tethered septal leaflet will be an isolated cause of regurgitation in a patient with a history of atrial switch operation.

**TECHNIQUE OF OPERATION**

**After Atrial Switch Repair**

Several surgical options are available for superior and inferior vena caval baffle limb obstruction. The preferred approach involves direct revision of the systemic venous component of the baffle itself. This involves cardiopulmonary bypass (CPB)
Figure 29-39  Takedown of Mustard operation and conversion to arterial switch.  

A, In the months after placing a pulmonary trunk band, patient is followed with echocardiography, cardiac catheterization, and magnetic resonance imaging (see text for details) to assess biventricular function and acquisition of morphologic left ventricular (LV) mass, gradient across band, ejection fraction, LV end-diastolic pressure, and valvar function. If the LV fails to acquire a substantial amount of mass within 6 months and gradient across band predicts LV pressures below 70% of estimated right ventricular pressure, it is necessary to reoperate to tighten pulmonary trunk band. Optimal duration of banding, rate of LV mass acquisition, and gradient across band are likely to vary from patient to patient and have yet to be definitively established. However, compared with the rapid two-stage arterial switch for infants with transposition of the great arteries and intact ventricular septum, the process of LV mass acquisition is much more gradual, and the pulmonary trunk band is left in place substantially longer. The LV should be documented to be working at systemic-level pressure for about 1 year.  

B, After adequate LV mass acquisition, the Mustard configuration is converted to an arterial switch. Arterial switch is performed before Mustard baffle is removed, primarily to ensure that the switch is accomplished successfully before proceeding. Heart, aorta, pulmonary trunk, branch pulmonary arteries, and both cavae are exposed and dissected thoroughly and carefully through a midline sternotomy. Aorta and branch pulmonary arteries are mobilized extensively. Purse-string sutures are placed high in aorta and in both cavae, after which cardiopulmonary bypass is initiated with aortic and bivacal cannulation. Systemic (right) ventricle is vented through appendage of morphologically right atrium. Patient is cooled to 25°C. Aorta is then clamped and cardioplegia administered into aortic root. Aorta and pulmonary trunk are transected, and semilunar valves are inspected. After band around pulmonary trunk is removed, narrowed tissue at band site is excised and proximal and distal edges are trimmed carefully.  

C, After identifying coronary ostia, coronary arteries are mobilized on generous buttons of sinus wall. Counter incisions are made high in the facing sinuses of the proximal neoaorta (pulmonary trunk), and the coronary arteries are reimplanted with continuous 5-0 or 6-0 absorbable monofilament suture. In patients with abnormal coronary artery branching patterns, coronary reimplantation is modified as necessary.  

D, After coronary buttons are reimplanted into neoaortic root, the pulmonary trunk is brought anterior to ascending aorta (Lecompte maneuver). It is important that branch pulmonary arteries have been mobilized to the pulmonary hila to prevent tension on pulmonary trunk anastomosis, which may increase risk of postoperative supravalvar pulmonary stenosis. Distal ascending aorta is then anastomosed to neoaortic root in end-to-end fashion using continuous 4-0 or 5-0 absorbable monofilament suture. Coronary button defects in neopulmonary artery preferably are patched with autologous pericardium, and with allograft or synthetic patch material if pericardium is not obtainable.
Although a standard oblique atriotomy is the most common approach to performing a Mustard operation, other types of atrial incision may be used. In approaching a take-down of the Mustard baffle and reseptation of atria, original atriotomy should be identified and used. On opening pulmonary venous atrium, Mustard baffle is exposed. When Mustard procedure was performed, the coronary sinus septum may have been opened superiorly into the morphologic left atrium to more easily incorporate the coronary sinus into the systemic venous atrium. If that is the case, it will not be visible until the patch is removed. Suture lines are typically easy to identify. After incising the superior baffle suture line, entire patch is removed with sharp dissection using either a knife or scissors. Care should be taken when excising the patch around the opening of the superior vena cava because the sinoatrial node is located in close proximity to the anterior aspect of the suture line. After removing Mustard baffle, mitral valve and caval orifices are exposed. If the coronary sinus was incorporated into the systemic venous atrium, it will also be exposed. It is important to carefully remove as much scar tissue as possible from the suture lines, especially from the orifices of coronary sinus and cavae, to prevent any obstruction. A pericardial or polytetrafluoroethylene (PTFE) synthetic patch is then fashioned to recreate the interatrial septum. Patch is sewn to remaining rim of native atrial septum using continuous 4-0 or 5-0 polypropylene suture. In patients who had coronary sinus septum opened at time of Mustard procedure, the sinus orifice must be reconstructed by bringing the patch down and incorporating it as the posterior wall of the orifice. Alternatively, the patch can be carried along the suture line of the Mustard baffle, such that the coronary sinus drains to the left atrium. Before tightening final sutures, left atrium is de-aired by sustained pulmonary hyperinflation. A left ventricular vent is placed across mitral valve, through either the posterior suture line or a separate purse string. Clamp is removed from aorta, and right atrium is closed and pulmonary outflow tract reconstructed without cardioplegic arrest during rewarming.
Chapter 29 Congenital Heart Disease in the Adult

Right atriotomy is then closed with continuous 5-0 polypropylene as rewarming is commenced. Neopulmonary trunk is then reconstructed by anastomosing distal pulmonary trunk to reconstructed neopulmonary root using continuous 5-0 or 6-0 absorbable monofilament suture. A cardiotomy suction catheter is placed in pulmonary trunk to prevent backflow from obscuring operative field. (From Reddy and colleagues.)

Figure 29-39, cont’d

I. Right atriotomy is then closed with continuous 5-0 polypropylene as rewarming is commenced. J. Neopulmonary trunk is then reconstructed by anastomosing distal pulmonary trunk to reconstructed neopulmonary root using continuous 5-0 or 6-0 absorbable monofilament suture. A cardiotomy suction catheter is placed in pulmonary trunk to prevent backflow from obscuring operative field. (From Reddy and colleagues.)

with concomitant closure of a VSD. The tethered leaflet is iatrogenic. If systolic RV function is normal, repair of the tricuspid valve with partial closure of the septal anterior commissure at the site of tethering may be effective. More complex etiologies of tricuspid regurgitation in the setting of normal RV function are best managed using tricuspid valve replacement. Both bioprosthetic and mechanical valves are appropriate options. The decision is based on the typical advantages and disadvantages of each type of prosthesis.

Atrial switch takedown and conversion to arterial switch technique is shown in Fig. 29-39.

After Arterial Switch Repair

Repair of RV outflow tract problems after the arterial switch can usually be managed using normothermic beating heart CPB with a single venous cannula in the right atrium. Because of the Lecompte maneuver, access to the entire RV outflow tract, including subvalvar, valvar, and supravalvar areas, and branch pulmonary arteries, is excellent. Patch augmentation of obstructive lesions at any level is effective. Valvar obstruction may be managed by valvuloplasty, transanular patch, or valve replacement. Transanular patching will result in some degree of pulmonary regurgitation. Valve options include bioprosthetic valves and pulmonary and aortic allograft valved conduits. Isolated subvalvar obstruction can be resected, working retrogradely through the pulmonary valve, or by a longitudinal infundibular incision with resection or infundibular patching.

Coronary artery obstruction and aortic valve and root problems are managed with techniques described in Chapters 7 and 12. Surgical access to the aortic root, valve, and coronary arteries is more difficult than usual because of their posterior position behind the pulmonary trunk following the Lecompte maneuver. If the pulmonary branches and trunk are mobile, they may be dissected from the underlying aorta intact and retracted, allowing access to the aortic root. Often the pulmonary trunk is not easily mobilized, so it may be necessary to transect it just above the pulmonary valve or to transect the right pulmonary artery at its origin from the pulmonary trunk, mobilizing the pulmonary trunk to access the aortic root. Coronary ostial lesions may be managed by standard techniques of coronary artery bypass grafting or by ostial patching.

The classically described maze procedure is performed in patients with the arterial switch and atrial fibrillation, and an appropriately modified maze procedure is used when there is an atrial baffle in place (see Chapter 16).

Transplantation is performed with the appropriate arterial and venous anastomotic adjustments (see Chapter 21).

RESULTS

There are no large studies of adult TGA patients providing outcomes for the various operations described in this section. Based on outcomes for operations with similar complexity in non-TGA patients, early mortality for most of the procedures in patients with a history of either atrial or arterial switch should be in the range of 1% to 2%. The one exception is the
atrial switch patient undergoing conversion to arterial switch.\(^{14}\) In the series of one of the authors (FLH), early mortality was 20% (1/5; CI 3.2%-53%) among adult patients, with five additional patients not meeting criteria for conversion after LV training. Benzaquen and colleagues report one successful adult conversion.\(^{14}\)

**INDICATIONS FOR OPERATION**

In all adult patients with transposition, regardless of their surgical history, arrhythmias may require intervention. Indications for pacemaker insertion include sick sinus syndrome, symptomatic bradycardia, and selected patients with a stable junctional rhythm that does not meet bradycardia criteria. Although the atrial morphology may be altered, particularly in atrial switch patients, transvenous pacing systems can usually be placed. Surgical placement of epicardial pacing systems remains an option for those with unusual morphology, intracardiac shunts, or occluded central veins, and for those requiring biventricular pacing. Sudden death is described in adult atrial switch patients, mostly related to ventricular tachycardia and fibrillation.\(^{32}\) Placing an internal cardioverter-defibrillator (ICD) is indicated if a sudden death episode is documented or electrophysiologic evaluation demonstrates inducible ventricular tachycardia or fibrillation. The maze procedure, or appropriate modifications if atrial structures are altered, may be indicated for any adult patient with TGA if atrial fibrillation or flutter is present and other cardiac surgery is planned.

**After Atrial Switch Repair**

Both surgical and catheter-based interventional procedures are available for residual and recurrent lesions in adults with prior atrial switch surgery. Intervention for the structural lesions described in the following text is indicated if the lesions cause important symptoms or if hemodynamic alterations caused by these lesions meet standard criteria for intervention.

Catheter-based dilatation or stenting is the preferred method for treating symptomatic superior caval, inferior caval, and pulmonary venous pathway obstruction, and for baffle leaks. It is also an option, but not necessarily the preferred one, for supravalvar pulmonary trunk and branch pulmonary artery stenosis. Surgical intervention is indicated for these same lesions when catheter-based techniques are unsuccessful or contraindicated. As an example, catheter-based therapy may be contraindicated for long-segment occlusion of the superior baffle limb. Many consider surgical reconstruction the preferred method for treating supravalvar and branch pulmonary artery stenosis, whether these lesions occur alone or with valvar and subvalvar stenosis.

Surgical intervention for LV outflow tract obstruction in atrial switch patients is indicated only if LV pressure becomes suprasystemic or symptoms are attributable to the obstruction. Moderate or even severe obstruction, as judged by pressure gradient, may not affect LV function. Additionally, the argument has been made that some elevation of LV pressure may be beneficial, keeping the ventricular septum from bowing away from the RV, thereby stabilizing the subvalvar mechanism of the tricuspid valve and reducing development of systemic tricuspid valve regurgitation.

Surgical intervention may be indicated in selected cases of moderate or severe systemic tricuspid valve regurgitation, but only when systemic RV function is preserved. Repair of the tricuspid valve working under systemic loading conditions remains a challenge. In most cases, tricuspid valve regurgitation is associated with a dilated and poorly functioning systemic RV. The progression may be ventricular dysfunction leading to regurgitation; however, the causality may be the reverse as well. Either way, tricuspid valve repair or replacement is contraindicated when there is associated moderate or severe ventricular dysfunction.

Either pulmonary trunk banding with eventual conversion to an arterial switch or heart transplantation is indicated when RV dysfunction accompanies tricuspid regurgitation. There are no clear guidelines for choosing between these; however, important atrial or ventricular arrhythmias, morphologic LV dysfunction, and mitral valve dysfunction all strongly favor moving toward transplantation. Conversion to arterial switch remains controversial.\(^{112}\) Some institutions never recommend this option. The operation, however, can be performed successfully in highly selected cases in institutions experienced with it. Indications for proceeding with atrial switch take-down and conversion to arterial switch are complex. Several stages of selection are required. In the initial selection process, all patients with an atrial switch procedure can be evaluated. Generally, patients with normal or near-normal function of the systemic RV and tricuspid valve are not considered for conversion. Typically, moderate or severe systemic ventricular dysfunction or tricuspid regurgitation will be present, and these findings lead to further evaluation for conversion. However, other sequelae, such as baffle obstruction or leak, may also lead to additional evaluation. Candidates are eliminated from further consideration if important atrial or ventricular arrhythmias are present or if there is evidence of morphologic LV or mitral valve dysfunction.

In the unusual case that the LV is already working under conditions that will allow it to perform adequately in the systemic circulation (chronic moderate to severe LV outflow tract obstruction, or pulmonary hypertension from atrial baffle obstruction in the pulmonary venous pathway), the patient may proceed directly to atrial switch take-down and conversion to arterial switch without undergoing pulmonary trunk banding. In the more common case the LV will be chronically working under normal afterload conditions of the pulmonary circulation and will not be prepared for systemic workload conditions. These patients must enter a process of LV preparation by pulmonary trunk banding. The aim is to gradually achieve afterload conditions that allow the LV to remodel and hypertrophy such that it will be capable of working efficiently under the conditions of the systemic circulation. The training process takes a minimum of 1 year and may take longer. During this time it is likely that more than one banding procedure will be needed in order to achieve proper training.\(^{514}\) At each stage in the banding process, reevaluation with echocardiography, cardiac catheterization, and MRI is performed to obtain the data required to evaluate LV preparedness. The criteria used by one of the authors (FLH) before the LV is considered prepared are:

- Ventricular ejection fraction of 55% or greater
- Less than mild mitral regurgitation
- Ventricular systolic pressure 90% systemic or greater
- Ventricular end-diastolic pressure 10 mmHg or less
If these criteria are met, conversion is performed. In a series of 31 patients managed by one of the authors (FLH), 42% who began training with the band achieved criteria for conversion. Of those achieving conversion, five were adults aged 22 to 29 years. There was 80% survival in this group. An additional five adult patients who did not meet the criteria were turned down for conversion after attempted LV training. Age was not a deterrent to successful conversion as long as these strict inclusion criteria were adhered to. In the study by Poirier and colleagues of 39 patients undergoing banding, 71% underwent conversion; however, early mortality was 17% (CL 11%-27%) and late cardiac death 13%. This study identified older age as a risk factor, with no successful conversions in patients beyond age 16 years. The differences in these two series may be explained by the stricter training selection criteria used in the series with successful adult conversions.

After Arterial Switch Repair

Indications for surgery in adults with prior arterial switch and RV outflow tract lesions are the same as those for tetralogy of Fallot (see Section XI of this chapter). Indications for coronary artery surgery are similar to those in patients with arteriosclerotic disease (see Chapter 7) and include signs and symptoms of myocardial ischemia and coronary artery luminal narrowing of 50% or greater. Because coronary artery sequelae after the arterial switch are almost always limited to the ostium or adjacent proximal segment, direct ostial augmentation may frequently be indicated, although coronary artery bypass grafting remains an option as well.

Risk of aortic dissection and rupture associated with aortic dilatation after the arterial switch is not known. However, based on physiologic principles, it is reasonable to assume that it is the same as that in native aortic dilatation. Thus, it is reasonable to follow the indications for root replacement recommended for native aortic disease (see Chapters 25 and 12). If aortic valve function is normal, a valve-sparing root replacement should be considered. If root dilatation is accompanied by more than mild aortic regurgitation, root replacement with aortic valve replacement, or aortic valve repair, is indicated.

**Section XIII Congenitally Corrected Transposition of the Great Arteries**

**DEFINITION**

Definition, morphology, and basic physiology of congenitally corrected transposition of the great arteries (corrected transposition, CTGA) are described in Chapter 55. CTGA with pulmonary stenosis or atresia and ventricular septal defect (VSD), the single most common form, is discussed in detail under Special Situations and Controversies in Section XI of this chapter. All other forms are discussed in this section.

**MORPHOLOGY**

CTGA is a rare anomaly and thus is not often found in adults. It may present in adulthood as newly diagnosed disease, previously diagnosed disease with benign physiology, or secondary disease with a history of previous surgery. Presentation will be variable because all but 1% to 2% of patients have one or more major associated structural cardiac anomalies, including pulmonary stenosis, VSD, and systemic atrioventricular (AV) valve abnormalities, and these largely determine the nature of presentation. Even the rare patient without associated structural anomalies will eventually develop problems with conduction or with systemic right ventricular (RV) function.

There are several morphologic variants of CTGA:

- Without associated structural anomalies
- With VSD
- With pulmonary stenosis or atresia
- With structurally abnormal (“Ebsteinoid”) tricuspid valve
- With various combinations of these structural anomalies

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Presentation**

Initial presentation may be spontaneous heart block, which is well documented to occur at a rate of about 2% per year in CTGA. Patients with prior history of VSD closure will present in adulthood in the same way as unoperated patients without associated structural anomalies, that is, with systemic RV failure; however, the presentation may be more accelerated. Patients with prior placement of a prosthetic valve in the tricuspid valve position may present with dysfunction or outgrowth of the valve, whether it is a bioprosthetic or mechanical valve. These patients may also present with heart failure from progressive systemic RV dysfunction. Patients with a history of isolated pulmonary stenosis repair may present with recurrent stenosis, or, if one has been placed, with left ventricle–to–pulmonary trunk conduit failure. Patients with a history of double switch (arterial switch–type double switch) will present with a combination of all the sequelae seen after both the arterial and atrial switch (see Section XII, “Transposition of the Great Arteries,” earlier in this chapter). Signs and symptoms of systemic RV failure, systemic tricuspid valve regurgitation, and complete heart block are the same as in any patient with left-sided heart failure or heart block and therefore are nonspecific for CTGA. Evaluation will lead to the diagnosis.

**Diagnosis**

The electrocardiogram will show definitive evidence of ventricular inversion. The chest radiogram is not definitive, but may show abnormal contour of the ventricular shadow, a narrowed superior mediastinal shadow due to the position of the great arteries, and abnormal cardiac position such as mesocardia or dextrocardia. The echocardiogram is diagnostic, identifying AV and ventriculoarterial discordant connections, as well as the major associated anomalies such as VSD, pulmonary stenosis, and systemic tricuspid valve structural abnormalities and function. Apical displacement...
of the tricuspid valve is easily identified, and complexity of pulmonary stenosis, including valvar and subvalvar components, can usually be determined. Quantitative assessment of systemic RV function is often difficult by echocardiography. Magnetic resonance imaging (MRI) is used to assess systemic RV function and volume and to quantify systemic tricuspid valve regurgitation. Cardiac catheterization is often helpful in assessing systemic RV function, using both ventriculography and hemodynamics (RV end-diastolic pressure).

**NATURAL HISTORY**

The undiagnosed asymptomatic adult may present incidentally during evaluation for some other problem.\(^{511,517}\) The asymptomatic adult with known unrepaired CTGA may be referred to the adult congenital cardiac clinic simply because there is a known diagnosis. Most commonly, the unrepaired patient without associated structural anomalies, or with mild associated structural anomalies, will present in the fourth or fifth decade of life with signs and symptoms of systemic RV failure, systemic tricuspid valve regurgitation, or arrhythmias.\(^{511,519}\) In one single-institution study, by age 50 years, 66% of patients were in heart failure, but none died over a 10-year observation period thereafter.\(^{519}\) In a multi-institutional longitudinal study, 25% of patients with CTGA and no other structural anomalies presented with signs and symptoms of heart failure by age 45 years. If associated structural anomalies were present, heart failure by age 45 years increased to 67%.\(^{619}\)

Patients presenting in adulthood without prior surgery rarely have severe pulmonary stenosis, large VSDs, or severely abnormal systemic tricuspid valves, because the natural history of these associated anomalies rarely allows patients to reach adulthood in a healthy state. Isolated moderate, or even moderate to severe, pulmonary stenosis, however, may be well tolerated because the morphologic left ventricle will be working under afterload conditions that it tolerates well.

**TECHNIQUE OF OPERATION**

The surgical techniques recommended in this section—direct repair of associated anomalies and the double switch operation—are described in Chapter 55. Other techniques used to repair sequelae related to atrial and arterial switch operations are described in Chapters 7, 12, and 52.

**RESULTS**

Early surgical mortality in adults after repair of the associated anomalies found with CTGA is not well documented but is likely very low, similar to that associated with repair of these anomalies in younger patients. In the series of 44 patients (mean age 44 years) presenting in adulthood for surgery to correct various associated structural anomalies (atrial septal defect, VSD, severe aortic regurgitation, severe tricuspid regurgitation, severe mitral regurgitation, severe pulmonary stenosis), there were no early deaths (CL 0%-4.2%).\(^{511}\) Four patients who underwent tricuspid valve replacement for severe regurgitation required cardiac transplantation at a mean interval of 56 months after initial surgery. In another series, early mortality for VSD closure and placement of a left ventricular–to–pulmonary trunk conduit in adults was 5.8% (3/52; CL 2.6%-11%).\(^{635}\)

Isolated tricuspid valve replacement can be performed with low mortality. Mongeon and colleagues reported no early deaths (CL 0%-4.0%) in 46 patients (mean age 34 years) and actuarial survival of 69% at 10 years.\(^{531}\) Patients with initial right ventricular ejection fraction greater than 45% had better 10-year survival than those with lower ejection fraction, 94% vs. 55%.

Coronary artery bypass grafting for arteriosclerotic coronary artery disease has been reported in a 47-year-old diabetic adult with CTGA.\(^{84}\)

The double switch in adult patients with naturally prepared left ventricles has an early mortality that is probably similar to that in younger patients, about 2%. Extrapolating from experience with atrial switch conversions, requiring in CTGA left ventricular training, 50% will meet criteria to proceed to the double switch, for which early mortality is about 20%.

**INDICATIONS FOR OPERATION**

Surgery may be indicated in adults with unrepaired CTGA if additional structural anomalies are present and are causing symptoms, or if there are no additional structural anomalies but the systemic RV is failing. Options for surgery if structural anomalies are present include isolated surgical repair of the anomaly or anomalies causing the symptoms, double switch with concomitant management of the associated anomaly or anomalies, and cardiac transplantation.

Criteria for isolated VSD closure, pulmonary stenosis repair, or systemic tricuspid valve repair or replacement for regurgitation are generally similar to the criteria used for similar isolated anomalies in otherwise normal hearts; however, there are some notable modifications. The status of the systemic RV must be considered carefully when a small VSD is present. The already afterload-strained ventricle may not compensate for even a small volume load; thus, small VSDs may require closure if the systemic RV is dilated or dysfunctional. The same argument can be used when assessing systemic tricuspid valve regurgitation. Tricuspid valve repair is difficult in the systemic tricuspid valve, especially if there are structural valve abnormalities. Valve replacement is usually the procedure of choice. Pulmonary stenosis, on the other hand, may be better tolerated with a morphologic left ventricle in the pulmonary circulation, and surgical intervention may not be necessary for moderate or even severe obstruction.

The double switch is an option that should be considered in selected cases. It is an attractive option if the left ventricle is already prepared for a systemic workload due to a combination of VSD and pulmonary or subpulmonary stenosis (see Special Situations and Controversies in Section XI of this chapter). The double switch is less attractive when the left ventricle is unprepared for the systemic workload, as is the case when there are no, or minor, associated structural anomalies. The double switch in this setting will require preparatory left ventricular training (see Section XII, Transposition of the Great Arteries, earlier in this chapter). In unprepared adults without associated structural anomalies, there is no indication for surgery if systemic RV function and tricuspid valve function are normal or near normal. Occasionally, such patients will present with a request for double switch evaluation based on their own research. This approach may be pursued if the patient is fully informed of the left ventricular...
training process, including its risks, time course, likelihood of multiple banding procedures, and likelihood of success to double switch.

In unrepaired adults without associated structural anomalies who have untreated systemic RV failure, the options are left ventricular training and double switch or cardiac transplantation. The considerations are similar to those used to decide between these two options in patients with failing systemic RVs following the atrial switch for simple transposition (see Section XII, Transposition of the Great Arteries, earlier in this chapter). Double switch is not a good option when isolated pulmonary valve stenosis is present. Although the left ventricle is prepared, absence of a VSD renders a Rastelli impossible, and the pulmonary stenosis renders the arterial switch impossible unless a prosthetic root replacement is concomitantly performed. Occasionally, the pulmonary valve itself is normal or near normal, and there is isolated subvalvar left ventricular outflow tract obstruction. The double switch is a good option in this case, because the left ventricle is prepared, the arterial switch is possible, and the left ventricular outflow tract resection is relatively simple.

In selected unrepaired adults without associated structural anomalies who have important tricuspid regurgitation but preserved RV function (ejection fraction > 45%), tricuspid valve replacement may be considered instead of the double switch or transplantation. There is a single case report of a 64-year-old patient who presented with complete heart block and severe tricuspid valve regurgitation who underwent placement of a sequential AV pacemaker, resulting in markedly improved tricuspid valve function.

In adults with previous surgery for CTGA in whom the systemic ventricle remains the morphologic RV, indications for surgery and surgical options are generally the same as for unrepaired patients. Patients with left ventricle-to-pulmonary trunk conduits in place will eventually require conduit replacement for conduit failure. Moderate and severe conduit obstruction may be well tolerated when the left ventricle is in the pulmonary circulation, and in fact some elevation of left ventricular pressure may be beneficial, helping to stabilize the ventricular septum in midposition, thereby preventing systemic tricuspid valve regurgitation. When severe conduit obstruction is present and surgery is necessary, the fact that the left ventricle is prepared for the systemic circulation may make the double switch seem attractive; however, presence of the left ventriculotomy (from the conduit) and lack of a straightforward option for creating left ventricle to aortic continuity make the double switch inadvisable in most cases.

In adults with previous double switch surgery for CTGA, indications for surgery are a combination of the indications for surgery in patients with simple transposition and prior atrial switch and in patients with simple transposition and prior arterial switch. (See Section XII, Transposition of the Great Arteries, earlier in this chapter.)

**Figure 29-40** Probability of death according to severity of tricuspid valve deformity in 72 adult patients with Ebstein anomaly. Tricuspid valve deformity was estimated by echocardiographic measurement of amount of displacement of septal leaflet from true valve annulus. Patients were then placed in Group 1 (mild deformity), Group 2 (moderate), or Group 3 (severe). (From Attie and colleagues.)

### DEFINITION

**Great Arteries**

Prior arterial switch. (See Section XII, atrial switch and in patients with simple transposition and prior indications for surgery are a combination of the indications inadvisable in most cases.

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### MORPHOLOGY

A hallmark of Ebstein anomaly is its wide spectrum of morphologic deformity of the tricuspid valve and the associated wide spectrum of physiologic derangement. Severity of morphologic deformity generally correlates with severity of valve regurgitation, but there are exceptions. Unique to adults, the chronic abnormalities of the right heart in this disease may, over time, result in left ventricular alterations due to ventricular-ventricular interaction.

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

**Presentation**

Newly diagnosed adults commonly present with palpitations, dyspnea, or fatigue following new onset of atrial tachyarrhythmias, such as atrial flutter, atrial fibrillation, or reentrant tachycardia through an accessory pathway. In a group of
72 unoperated adults aged 25 years or older followed for 8 years, all but 5 patients were initially in New York Heart Association functional class I or II. Atrial arrhythmia was the most common clinical presentation in 51%, with flutter and fibrillation accounting for about half of these. Preexcitation was present in 44% on electrocardiogram. Onset of atrial arrhythmia commonly causes patients to progress to a worse functional class. Occasionally, adults present with untreated severe disease manifested by severe exercise intolerance, cyanosis, low cardiac output due to right heart failure, hepatic and renal compromise, and uncontrolled atrial and ventricular arrhythmias. Sudden death occurs and is associated with arrhythmias. Overall prognosis is poor in this subset of patients (Fig. 29-40).

Adults with previously diagnosed relatively mild disease will not have had prior surgery. These patients may present in adulthood with progression of cyanosis, progression of right heart failure symptoms, new-onset arrhythmias, or occasionally, paradoxical embolism.

Adults with prior surgery that included placing a bioprosthetic valve in the tricuspid position usually present with valve degeneration, manifested by a combination of predominant stenosis and some regurgitation. Adults with prior surgery that included tricuspid valve repair may also present with progressive tricuspid valve disease; however, recurrent regurgitation predominates, although stenosis after aggressive repair can also occur. Cyanosis in previously repaired patients is unusual because most surgical protocols involve closure of atrial-level shunts. Many repaired patients may have received a bidirectional superior cavopulmonary anastomosis as part of initial repair; upper body swelling, headache, and superior caval aneurysm may develop.

Some patients with complex disease have also received right ventricle–to–pulmonary trunk reconstructions in childhood. This will have important implications during adult life, creating sequelae such as pulmonary valve regurgitation, recurrent pulmonary stenosis, or conduit degeneration.

Patients with associated anomalies such as pulmonary stenosis or atresia, and left ventricular myocardial abnormalities such as noncompaction, typically have symptoms early in life and thus do not present in adulthood without prior surgery. Adults with prior surgery may also present with new-onset atrial or ventricular arrhythmias and right heart failure.

Diagnosis

The echocardiogram may show preexcitation due to a right-sided accessory bypass tract, prominent P waves, and right bundle branch block. The chest radiogram will show a variable degree of cardiomegaly due to right atrial enlargement, depending on severity of the morphologic and physiologic derangement. Echocardiography is diagnostic and in many cases is sufficient to proceed to surgery. It shows the structural alterations in the tricuspid valve, including apical displacement of the septal and posterior leaflets and the large abnormal anterior leaflet, the atrialized portion of the right ventricle, enlarged right atrium, and status of the atrial septum. It also provides physiologic information, including amount of tricuspid regurgitation, status of right ventricular function, and presence and direction of atrial-level shunting. Other associated anomalies, such as pulmonary stenosis or regurgitation, ventricular septal defect, and left ventricular noncompaction, can also be identified. Cardiac catheterization may be indicated if there is unexpected ventricular dysfunction or concern for arteriosclerotic coronary artery disease; assessment includes measurement of ventricular end-diastolic pressure and imaging of the coronary arteries. It is also indicated to calculate pulmonary vascular resistance if a bidirectional cavopulmonary anastomosis is being considered as part of the repair. Magnetic resonance imaging is capable of providing definitive information for diagnosis of Ebstein anomaly, including demonstration of all pertinent structural alterations discussed under echocardiography; additionally, it may provide quantitative functional information superior to that provided by echocardiography (Fig. 29-41).

Formal exercise testing may be helpful. In addition to measuring functional capacity, pulse oximetry can demonstrate onset or worsening of cyanosis with exercise. This information may be helpful in determining the best operative approach to the patient, as well as response to therapy.

Electrophysiologic evaluation should be considered in all adults presenting with Ebstein anomaly and is strictly indicated if there is evidence of arrhythmia by history, ECG, or Holter monitoring.

NATURAL HISTORY

Adults with mild deformity of the tricuspid valve may be asymptomatic and have normal survival (see Fig. 29-40). They typically have normal systemic arterial oxygen saturation, either without an atrial septal defect or with an atrial septal defect and left to right shunting. Patients with cyanosis from right to left shunting typically present earlier in life, partly because the cyanosis is obvious, but also because cyanosis is associated with a more severe form of the disease.

TECHNIQUE OF OPERATION

Surgical techniques used in adults with Ebstein anomaly are the same as those used in children (see Chapter 42). Surgery in adults with unrepaired Ebstein anomaly may include the following core procedures in various combinations, with the specific combination of procedures applied to an individual patient depending on the details of that patient’s physiology:

- Tricuspid valve repair
- Tricuspid valve replacement
- Closure of atrial septal defect
- Right atrial reduction plasty
- Bidirectional cavopulmonary anastomosis
- Maze procedure
- Targeted cryoablation
- In adults presenting with unsalvageable right heart dysfunction, the Fontan operation can be considered.

In general, decision making with respect to various core procedures that should be incorporated into the operation in an individual patient is similar to but not exactly the same as that in children. Repair of the tricuspid valve is preferred, with replacement the alternative if repair is not possible. This preference, however, is more difficult to justify in adults than it is in children because growth and rapid calcification of bioprostheses resulting from active calcium metabolism are
Figure 29-41  Magnetic resonance imaging (MRI) in 47-year-old man with unrepaired Ebstein anomaly. A, Gated T1-weighted spin-echo four-chamber view demonstrating right atriomegaly and inferior insertion of tricuspid valve leaflets within atrialized right ventricular cavity. B, Four-chamber view from cine-MRI demonstrating systolic flow dephasing (arrow) arising within right ventricular cavity, suggestive of Ebstein anomaly. C, Sagittal oblique view showing use of a selective saturation pulse through right atrium parallel to atrial septum (curved arrow). Signal loss (arrow) indicates right-to-left shunting through a small atrial septal defect. (From Eustace and colleagues.

Figure 29-42  Survival of 539 Ebstein anomaly patients (mean age 24 years at time of surgery) after surgical correction. (From Brown and colleagues.)

not of concern. In adults with severely deformed tricuspid valves, choice between a marginally adequate repair and a bioprosthesis may favor a bioprosthesis. Interestingly, Dearani and colleagues have shown that in 294 adults (mean age 20 years), 12-year freedom from reoperation was identical in patients with initial valve repair versus replacement (Fig. 29-42). Both bioprosthetic and mechanical valves have been used when valve replacement is required; however, long-term survival is much better when bioprosthetic valves are used.

Surgical electrophysiologic procedures are more likely to be part of the operation in adults than in children because atrial electrical degeneration becomes more frequent over time. A bidirectional superior cavopulmonary anastomosis is less likely to be part of the operation in adults, because individuals who reach adulthood without surgery generally...
have less severe structural changes and thus a more functional right heart.

Occasionally in mild cases of Ebstein anomaly, atrial septal defect may be the dominant structural anomaly. If there is a left-to-right shunt with both rest and exercise, catheter-based intervention and closure is appropriate. If cyanosis at rest is present, catheter-based intervention is contraindicated; surgery with a more extensive procedure than atrial septal defect closure alone is required and commonly will include addressing the tricuspid valve and performing a bidirectional cavopulmonary anastomosis. If there is left-to-right shunting at rest but right-to-left shunting with exercise, surgery is preferred, but catheter-based intervention may be considered in selected cases.

RESULTS

Early mortality following initial surgery to correct Ebstein anomaly in adults ranges from 0% to 5%. In the largest series of adult patients (539 patients, mean age 24 years), early mortality was 5.9% (CI 4.9%-7.2%); however, this experience dates back to 1972. For patients undergoing surgery between 2001 and 2006 in this series, early mortality was 2.7%. Twenty-year survival was 71% (Fig. 29-43). Preoperative risk factors for overall mortality were left or right ventricular systolic dysfunction, increased hemoglobin, male sex, right ventricular outflow tract obstruction, and hypoplastic pulmonary arteries.

In another series of 40 patients undergoing initial surgical correction at a mean age of 41 years, early mortality was 5% (CI 1.7%-11%), and 5-year survival was 84%. Survival was similar for patients receiving a concomitant superior bidirectional cavopulmonary anastomosis (23/40) and those who did not (17/40) (Fig. 29-44). Importantly in this study, the decision to include the cavopulmonary anastomosis was based on preoperative assessment of high operative risk (based on tricuspid valve and right ventricular characteristics), and thus, the authors inferred that the cavopulmonary anastomosis had a beneficial effect on survival. Chauvaud and colleagues prospectively assigned high-risk patients to two groups, those receiving a superior cavopulmonary anastomosis and those who did not. They showed a substantial early survival advantage for the group receiving the cavopulmonary anastomosis. Marianesci and colleagues also showed that use of the superior bidirectional cavopulmonary anastomosis reduced the need for tricuspid valve replacement.

Early mortality in adults undergoing initial surgical repair is lower than that in neonates and infants, and probably lower than that in children. The reason is that a relatively mild form of the disease usually exists in patients who initially present in adulthood. This advantage is partially offset, however, by an increase in associated degenerative changes over time in the myocardium and electrical system.

Functional status, substantially below normal in unrepaired adults, improves following surgery, as measured both by subjective patient response and objective exercise testing.

Khositseth and colleagues reported on 83 Ebstein patients (mean age 28 years) with preoperative indication for concomitant arrhythmia surgery. A variety of surgical arrhythmia procedures were performed, including ablation of accessory pathways, perinodal ablation for atrioventricular nodal reentrant tachycardia, and the maze procedure for atrial flutter or fibrillation. At a mean follow-up of 34 months, there was no recurrence of accessory pathway tachycardia or reentrant tachycardia, and a 25% recurrence of atrial flutter or fibrillation. Early mortality for concomitant arrhythmia procedures was 4.8% (CI 2.5%-8.6%).

Freedom from reoperation after bioprosthetic tricuspid valve replacement was 81% at 15 years in a series of 158 patients (mean age 19 years at surgery).

INDICATIONS FOR OPERATION

In unrepaired adult patients, cyanosis is an indication for surgical intervention. Progressive cardiomegaly due to tricuspid regurgitation, with right atrial and ventricular enlargement, is a relative indication for surgery, even if there are no symptoms. The natural history of the disease suggests that development of atrial flutter or fibrillation is likely if these findings are present. New onset of atrial arrhythmias in previously asymptomatic patients with relatively mild structural
disease is an indication for surgery. Any patient with important symptoms or reduced functional capacity should undergo surgery. These specific indications are no different from those in younger patients with Ebstein anomaly, described in Chapter 42.

In adult patients with prior repair, the preceding indications all apply. Progressive regurgitation of a previously repaired valve has the same sequelae as an unrepaird regurgitant valve. Patients with prior tricuspid valve replacement will eventually present with a degenerated bioprosthesis. Most commonly, stenosis will predominate, but mixed stenosis and regurgitation is almost always present. Occasionally, regurgitation will predominate. Predominant prosthetic valve regurgitation presents like native valve regurgitation, and indications for intervention are similar. Predominant prosthesis valve stenosis is an indication for surgery if the mean gradient is 10 mmHg or greater or if symptoms of reduced functional capacity, peripheral edema, or hepatic congestion are evident.

In adult patients with prior tricuspid valve repair, repeat valve repair may be indicated. However, there is a higher chance that valve replacement will be required than in primary surgery cases. In adult patients with degenerated prostheses, re-replacement is the only option.

Section XV Coronary Artery Problems Related to Congenital Heart Disease

DEFINITION

Definition, morphology, and basic physiology of congenital coronary artery anomalies are described in Chapter 46. Presentation of coronary artery problems related to congenital heart disease in the adult may be as newly diagnosed primary disease (primary congenital coronary anomalies), previously diagnosed primary disease with benign physiology (primary congenital coronary anomalies), or secondary disease (following congenital heart surgery for other anomalies). Coronary artery problems in the adult may also result from sequelae of acquired pediatric diseases in otherwise structurally normal hearts (Kawasaki disease).

MORPHOLOGY

Coronary artery problems related to congenital heart disease in the adult are uncommon and can be categorized into two main groups. One category includes the primary congenital coronary anomalies. The most important of these are coronary artery arising from the wrong aortic sinus, coronary artery arising from the pulmonary artery, and coronary artery fistula. Coronary artery fistulas are the most common of these, accounting for about half of all anomalies in adults. A more complete listing of coronary artery anomalies is shown in Box 29-5. These anomalies can be grouped into a four-tiered clinical-significance–based classification, as shown in Table 29-12. Table 29-13 lists the 62 anomalies (1.2%) found in one study of 5100 coronary angiograms. Mean age of the patients was 65 years. During a 5-year follow-up period, survival was 83%, and 71% of all cardiac events and 100% of all deaths occurred in patient with class III and IV anomalies.

The second category of coronary artery problems related to congenital heart disease encompasses otherwise normal coronary arteries that are at risk, either as a result of surgical procedures used to repair other congenital heart anomalies (e.g., arterial switch operation, Ross operation) or as the natural progression of certain congenital heart diseases (e.g., supravalvar aortic stenosis). Accelerated obstructive arteriosclerotic coronary artery disease, which can develop in patients with left-sided obstructive problems such as aortic coarctation, will not be discussed further in this section (see Section X earlier in this chapter). In patients with a postsurgical etiology, coronary obstruction is usually ostial or very proximal and results from manipulation and translocation of the coronary arteries, which cause some combination of malposition, scarring, torsion, tension, ischemia, or thrombosis. In the cases that occur in supravalvar aortic stenosis, obstruction may occur at the ostium, or even in the sinus, or the problem may be more distal because of arteriopathy.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presentation

Patients with coronary anomalies of any kind may present with classic signs and symptoms of coronary insufficiency, including angina, ventricular arrhythmia, sudden death, left ventricular dysfunction, or mitral regurgitation, or these anomalies may be more occult if coronary obstruction or insufficiency is less severe, completely absent, or develops slowly, allowing coronary artery collaterals to develop. Many of the more minor coronary anomalies are found incidentally.

Patients with coronary artery fistulas present with chest pain or dyspnea in 71% of cases, and with either fatigue, palpitations, heart failure, or syncope in another 20%. Only 9% are asymptomatic. Symptoms are much more likely in adults than in children, who are asymptomatic 79% of the time. In adults, spontaneous closure occurs in 3%, rupture in 4%, and aneurysm in 14%. Endocarditis has been reported. Fistulas are single in 74% to 90% of cases.

Anomalous origin of a coronary artery from the pulmonary trunk presenting as newly diagnosed disease in the adult will rarely involve the left main coronary artery because the natural history does not allow asymptomatic survival unless there is associated stenosis of the anomalous ostium or pulmonary hypertension. When it does present in the adult, severe left ventricular failure is present (see Chapter 46). Isolated anomalous origin of the left anterior descending, circumflex, or right coronary artery is more likely to present in the adult (Figs. 29-45 and 29-46).

The presentation of a coronary artery arising from the wrong aortic sinus is reviewed in detail in Chapter 46. Both the left main coronary artery arising from the right aortic sinus and the right coronary artery arising from the left aortic sinus can be associated with ischemia, and particularly with sudden death in young adult athletes either during or immediately after exertion.

Kawasaki disease acquired in childhood may result in chronic progressive degenerative changes in the coronary arteries, leading to coronary ectasia, aneurysm formation,
Anomalies of Origination and Course

Absent left main trunk (split origination of LCA)
Anomalous location of coronary ostium within aortic root or near proper aortic sinus of Valsalva for each artery:
- High
- Low
- Commissural
Anomalous location of coronary ostium outside normal coronary aortic sinuses:
- Right posterior aortic sinus
- Ascending aorta
- Left ventricle
- Right ventricle

Pulmonary artery—variants:
- LCA arising from posterior facing sinus (ALCAPA)
- Cx arising from posterior facing sinus
- LAD arising from posterior facing sinus
- RCA arising from anterior right facing sinus
- Ectopic location (outside facing sinuses) of any coronary artery from pulmonary artery:
  - From anterior left sinus
  - From pulmonary trunk
  - From pulmonary branch

Aortic arch
- Brachiocephalic artery
- Right carotid artery
- Internal thoracic artery
- Subclavian artery
- Descending thoracic aorta

Anomalous origination of coronary ostium from opposite, facing coronary sinus (which may involve joint origination or adjacent double ostia)—variants:
- RCA arising from left anterior sinus, with anomalous course:
  - Posterior atrioventricular groove or retrocardiac
  - Retroaortic
  - Between aorta and pulmonary artery
  - Intraseptal
  - Anterior to pulmonary outflow or precardiac
  - Posteroanterior interventricular groove
- LAD arising from right anterior sinus, with anomalous course:
  - Between aorta and pulmonary artery
  - Intraseptal
  - Anterior to pulmonary outflow or precardiac
  - Posteroanterior interventricular groove
- Cx arising from right anterior sinus, with anomalous course:
  - Posterior atrioventricular groove
  - Retroaortic

Single coronary artery

Anomalies of Intrinsic Coronary Arterial Anatomy

Congenital ostial stenosis or atresia (LCA, LAD, RCA, Cx)
Coronary ostial dimple
Coronary ectasia or aneurysm
Absent coronary artery
Coronary hypoplasia
Intramural coronary artery (muscular bridge)
Subendocardial coronary course
Coronary crossing

Anomalous origin of posterior descending from anterior descending branch or septal penetrating branch
Absent posterior descending or split RCA:
- Proximal distal posterior descendings, arising from separate RCA sources
- Proximal posterior descending arising from RCA, distal posterior descending arising from LAD
- Proximal posterior descending arising from RCA, distal posterior descending arising from Cx

Absent LAD or split LAD:
- Large first septal branch and small distal LAD
- Double LAD
- Ectopic origination of first septal branch

Anomalies of Coronary Termination

Decreased number of arteriolar/capillary ramifications (?)
Fistulas from RCA, LCA, or infundibular artery to:
- Right ventricle
- Right atrium
- Coronary sinus
- Superior vena cava
- Pulmonary artery
- Pulmonary vein
- Left atrium
- Left ventricle
- Multiple, right and/or left ventricles

Anomalous Collateral Vessels

Box 29-5 Classification of Coronary Anomalies Observed in Normal Human Hearts

Modified from Angelini and colleagues. 

| Key: Cx, Circumflex; LAD, left anterior descending coronary artery; LCA, left coronary artery; PD, posterior descending branch; RCA, right coronary artery. |

Diagnosis

The electrocardiogram may be normal or may show changes consistent with ischemia or myocardial infarction. Echocardiography and cardiac catheterization are indicated to establish etiology. Echocardiography may confirm the diagnosis, especially if the etiology is a primary coronary anomaly (coronary artery arising from the wrong aortic sinus or from the pulmonary trunk); however, more definitive imaging is almost always required (see Chapter 46). Echocardiography is also performed to assess function of the myocardium and valves. Cardiac catheterization with coronary angiography confirms or establishes the diagnosis, providing important confirmation of the abnormality, whether that is stenosis, and occlusion. Aneurysms have a tendency to thrombose and to develop stenosis at both their proximal and distal ostia.
### Table 29-12  Clinical Significance-Based Classification of Coronary Artery Anomalies in the Adult

<table>
<thead>
<tr>
<th>Class</th>
<th>Coronary Artery Anomaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Benign</td>
<td>Ectopic origin of LCx from right sinus</td>
</tr>
<tr>
<td></td>
<td>Separate origin of LCx and LAD</td>
</tr>
<tr>
<td></td>
<td>Ectopic origin of LCx from RCA</td>
</tr>
<tr>
<td></td>
<td>Dual LAD types I-IV</td>
</tr>
<tr>
<td></td>
<td>Myocardial bridge (score &lt; 5)</td>
</tr>
<tr>
<td>II. Relevant</td>
<td>Coronary artery fistula</td>
</tr>
<tr>
<td></td>
<td>Related to myocardial ischemia</td>
</tr>
<tr>
<td></td>
<td>Single coronary artery R-L, I-II-III, A-P</td>
</tr>
<tr>
<td></td>
<td>Ectopic origin of LCA from PA</td>
</tr>
<tr>
<td></td>
<td>Atretic coronary artery</td>
</tr>
<tr>
<td></td>
<td>Hypoplastic coronary artery</td>
</tr>
<tr>
<td>III. Severe</td>
<td>Ectopic origin of LCA from right sinus</td>
</tr>
<tr>
<td></td>
<td>Potentially related to sudden death</td>
</tr>
<tr>
<td></td>
<td>Single coronary artery R-L, I-II-III, A-P</td>
</tr>
<tr>
<td></td>
<td>Ectopic origin of LCA from PA</td>
</tr>
<tr>
<td></td>
<td>Atretic coronary artery</td>
</tr>
<tr>
<td></td>
<td>Hypoplastic coronary artery</td>
</tr>
<tr>
<td>IV. Critical</td>
<td>Class II and superimposed CAD</td>
</tr>
<tr>
<td></td>
<td>Related to sudden death/myocardial ischemia and associated with superimposed CAD</td>
</tr>
</tbody>
</table>

From Rigatelli and colleagues. Key: CAA, Coronary artery anomaly; CAD, coronary artery disease; LAD, left anterior descending coronary artery; LCA, left coronary artery; LCx, left circumflex coronary artery; PA, pulmonary artery; RCA, right coronary artery.

### Table 29-13  Occurrence of Different Types of Coronary Artery Anomalies in 5100 Angiograms

<table>
<thead>
<tr>
<th>Coronary Anomaly</th>
<th>n</th>
<th>Prevalence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ectopic origin of LCA from right sinus</td>
<td>5</td>
<td>0.098</td>
</tr>
<tr>
<td>Ectopic origin of LCx from RCA</td>
<td>13</td>
<td>0.25</td>
</tr>
<tr>
<td>Ectopic origin of LCx from right sinus</td>
<td>7</td>
<td>0.13</td>
</tr>
<tr>
<td>Atretic LCx</td>
<td>2</td>
<td>0.039</td>
</tr>
<tr>
<td>Ectopic origin of RCA from pulmonary artery</td>
<td>1</td>
<td>0.020</td>
</tr>
<tr>
<td>Ectopic origin of LCA from pulmonary artery</td>
<td>1</td>
<td>0.020</td>
</tr>
<tr>
<td>Dual LAD</td>
<td>2</td>
<td>0.039</td>
</tr>
<tr>
<td>Single coronary artery</td>
<td>5</td>
<td>0.098</td>
</tr>
<tr>
<td>Ectopic origin of the RCA from left sinus</td>
<td>2</td>
<td>0.039</td>
</tr>
<tr>
<td>Separated origin of LAD and LCx</td>
<td>16</td>
<td>0.31</td>
</tr>
<tr>
<td>Coronary artery fistula</td>
<td>2</td>
<td>0.039</td>
</tr>
<tr>
<td>Myocardial bridge</td>
<td>6</td>
<td>0.11</td>
</tr>
<tr>
<td>TOTAL</td>
<td>62</td>
<td>1.21</td>
</tr>
</tbody>
</table>

From Rigatelli and colleagues. Key: CAA, Coronary artery anomaly; CAD, coronary artery disease; LAD, left anterior descending coronary artery; LCA, left coronary artery; LCx, left circumflex coronary artery; RCA, right coronary artery.

**Figure 29-45** Coronary angiography showing retrograde filling of an anomalous left circumflex coronary artery (LCx) through collateral vessels after injection of contrast into (A) left anterior descending coronary artery (LAD) and (B) right coronary artery (RCA). Anomalous origin of LCx from right pulmonary artery is demonstrated. (From Korosoglou and colleagues.)

Asymptomatic adults known to have unrepaired coronary artery origin from the wrong sinus, coronary arising from the pulmonary trunk, or coronary fistula should be evaluated as described in the previous paragraph. If the anomaly involves an anomalous coronary origin, a fistula, an aneurysm, or a coronary obstruction (see Fig. 29-45). Magnetic resonance imaging and computed tomography with angiography may add important details regarding the morphology (see Fig. 29-46).
helpful in determining whether closure is indicated for small or moderate-sized coronary fistulas.

Asymptomatic adults with known history of previous surgery or another condition that puts the coronary arteries at risk should be managed with a high index of suspicion. Patients who have had arterial switch surgery should undergo noninvasive testing for myocardial ischemia every 3 to 5 years. This recommendation is based on the established occurrence of coronary artery occlusion and stenosis found incidentally at cardiac catheterization after this operation. If noninvasive testing is positive, further coronary imaging as described earlier in this section is indicated. Asymptomatic patients who have undergone a Ross procedure should have imaging of their coronary arteries at least once during adult life. Often this can be timed to be part of the preoperative evaluation in preparation for right ventricular outflow tract conduit revision. Asymptomatic patients with a history of repaired or unrepaird supravalvar aortic stenosis should undergo noninvasive testing for myocardial ischemia as adults every 1 to 2 years, based on the known association of diffuse arteriopathy and known occurrence of coronary events associated with this anomaly.

**TECHNIQUE OF OPERATION**

Surgical techniques used to treat adults with primary congenital anomalies of the coronary arteries are described in Chapter 46. Surgical techniques used for coronary artery obstruction in adult patients who have undergone surgery for a congenital heart defect are described in Chapter 7.

**RESULTS**

Early mortality following surgery for congenital anomalies and congenitally associated anomalies of the coronary artery system in adults is not well documented. Based on outcomes for similar problems in children, and on outcomes for adults with arteriosclerotic coronary artery disease and good ventricular function, a mortality of 1% or less represents a reasonable estimate. Long-term outcome in adults is not available. Early mortality for ligation of coronary artery fistulas in adults ranges from 0% to 4%.

**INDICATIONS FOR OPERATION**

Surgical correction is indicated for all coronary arteries arising from the pulmonary trunk, for all symptomatic patients with coronary arteries arising from the wrong sinus, and for asymptomatic patients age 50 years or younger with coronary arteries arising from the wrong sinus if the coronary artery passes between the great arteries, is intramural, or has evidence of angiographic narrowing (see Chapter 46). Coronary artery fistula closure, either by surgery or by catheter-based intervention, is indicated for patients with symptoms attributable to the fistula, regardless of the size of the left-to-right shunt, and for asymptomatic patients if the fistula causes a large left-to-right shunt. Catheter-based closure of a coronary artery fistula can be effective and is indicated if morphologic details allow occlusion without interruption of nutrient branches of the affected coronary artery. Currently, this is possible in a minority of cases. In a literature review of coronary artery fistulas in adults covering 1993 and 2004, 107 fistulas were identified. Definitive
management was noted in 67%, with 38% closed surgically, 24% medically managed, and 5% closed by percutaneous embolization.

If coronary abnormalities are detected in patients with a history of supravalvar aortic stenosis, management will depend on the nature and severity of the abnormality. Obstructive lesions should be managed like other more common arteriosclerotic lesions, with either coronary artery bypass grafting or catheter-based dilatation or stenting (see Chapter 7). Ostial reconstruction for ostial occlusion, more commonly recommended in children, remains an attractive option in the adult, along with bypass grafting.

Indications for intervention for coronary obstructive lesions identified in patients who have undergone an arterial switch operation or Ross procedure are:

- Any obstructive lesion associated with symptoms of ischemia
- Asymptomatic lesions with 50% or greater luminal narrowing
- Asymptomatic lesions with demonstrable flow disturbance

Intervention may be by surgery or catheter-based balloon dilatation or stenting, depending on the position and nature of the lesion (see Chapter 7).A1,H10,R2

Surgical management of coronary involvement in Kawasaki disease is limited and decision making complex. If ischemia is present, bypass grafting or catheter balloon dilatation and stenting may be indicated. Large saccular aneurysms may be asymptomatic but carry a risk of rupture, thrombosis, and occlusion of adjacent coronary arteries. Aneurysm resection and coronary reconstruction or bypass grafting may be indicated.

Section XVI Single Ventricle

DEFINITION

Definition and details of single-ventricle physiology are described in Chapter 41.

MORPHOLOGY

A spectrum of morphologic entities falls under the category of single-ventricle physiology. The most common is hypoplastic left heart syndrome (see Chapter 49), followed by tricuspid atresia (see Chapter 41) and then by less common entities, such as double inlet ventricle and common ventricle (see Chapter 56), unbalanced atrioventricular septal defect (see Chapter 58), certain forms of Ebstein anomaly (see Chapter 42), and certain forms of pulmonary atresia with intact ventricular septum (see Chapter 40). In addition, some patients are managed as having single-ventricle physiology even though their structural anomalies are characterized by two well-formed ventricles and two well-formed atrioventricular valves, because the surgical reconstruction that would be required to septate such hearts is either impossible or inadvisable. An example would be some forms of double outlet right ventricle with noncommitted ventricular septal defect (see Chapter 53). Adults presenting with congenital heart disease uncommonly will have single-ventricle physiology. This is because all morphologic entities that result in single-ventricle physiology combined account for only a small fraction of congenital heart disease. Furthermore, mortality rates are high in infancy and childhood, with fewer than 50% of patients surviving to adulthood. Nevertheless, the palliated state of all survivors dictates that this small group of patients will demand an inordinate amount of resources in the adult congenital heart disease program.

Adults with single-ventricle physiology rarely present with newly diagnosed disease, previously diagnosed disease with benign physiology, or previously diagnosed disease thought to be too complex for intervention; only 13 adult patients with mixed circulation were evaluated over a 10-year period in one large adult congenital referral center.A12 The great majority of patients will present in adulthood with secondary disease following prior surgery. The prior surgery will by necessity be palliative and will result in one of three basic physiologic states:

- Palliation with separated circulations (Fontan circulation)
- Palliation with partially separated circulation (superior cavopulmonary anastomosis, or Glenn, circulation)
- Palliation with completely mixed circulation and controlled pulmonary blood flow (mixed circulation with systemic-to–pulmonary artery shunt or pulmonary trunk band)

The general goal in infancy and childhood is to achieve Fontan circulation in all patients with single-ventricle physiology. Some patients will not meet criteria required to undergo the Fontan and will reach final palliation with a superior cavopulmonary anastomosis. Still others will not meet criteria for a superior cavopulmonary anastomosis and will reach final palliation with a systemic-to–pulmonary artery shunt or a pulmonary trunk band.

A deeper level of complexity exists in this patient population. Patients with Fontan circulation may have an atrio pulmonary Fontan, a lateral tunnel Fontan, or an extracardiac conduit Fontan. Additionally, the circulations may not be fully separated if a fenestration was created as part of the Fontan operation. Patients with Glenn circulation may have a bidirectional cavopulmonary connection or a unilateral cavopulmonary connection, and may or may not have additional sources of pulmonary blood flow through a surgically created systemic-to–pulmonary artery shunt or pulmonary trunk band, or through a congenitally stenotic pulmonary valve. Patients with completely mixed circulation may have a single source of pulmonary blood flow through a shunt or band, or may have multiple sources of pulmonary blood flow through various combinations of shunts and bands. All these variations have particular importance in the adult with respect to the nature of sequelae that will be encountered.

As a final level of complexity, single-ventricle patients with any of these palliated states may have had arch reconstruction, repair of anomalous pulmonary veins, valve repairs or replacements, or subvalvar ventricular outflow tract muscle resections. Some patients may have their morphologic tricuspid valve, pulmonary valve, and morphologic right ventricle functioning in the systemic circulation. All these factors will have management implications in the adult.
Presentation

Single-ventricle patients may undergo evaluation for surgical therapy in a number of circumstances:

- Structural problems such as arch obstruction, bulboventricular foramen obstruction, valve regurgitation, or pulmonary artery obstruction regardless of mixed, partially separated, or separated circulation
- Systemic-to-pulmonary shunt or pulmonary trunk band revision (or rarely, initial placement) in mixed circulation patients
- Advancement of mixed circulation patients to partially separated circulation by performing a superior cavopulmonary anastomosis
- Advancement of patients with partially separated circulation to separated circulation with a Fontan operation
- Addition of a second source of pulmonary blood flow in cyanotic patients with a superior cavopulmonary anastomosis
- Conversion of an atrio pulmonary connection Fontan to an extracardiac conduit or lateral tunnel connection Fontan

Adult patients with mixed circulation can present in a variety of ways. Progressive cyanosis is common, especially in patients with a systemic-to-pulmonary artery shunt. This often is accompanied by increasing exercise intolerance. Heart failure resulting from chronic cyanosis and volume overload is also common. This may be accompanied by onset of arrhythmias, atrioventricular valve regurgitation, and increasing exercise intolerance as well. Patients with chronic unrestricted pulmonary blood flow present with pulmonary hypertension with Eisenmenger physiology. Infective endocarditis may develop, either at the shunt or band site or at an abnormal valve. Paradoxical embolism may occur, resulting in cerebrovascular events or other end-organ dysfunction. Thrombotic complications may develop as a result of increased blood viscosity related to elevated hematocrit. Brain abscess is also described in this population.

Adult patients with partially separated circulation—those with a bidirectional superior cavopulmonary anastomosis—typically present with progressive cyanosis as upper body–to–lower body venovenous collaterals and pulmonary arteriovenous malformations develop. Because of the cyanosis and partial mixing of the circulations, all of the sequelae described for mixed circulation patients can also occur. Unless there is an additional source of pulmonary blood flow, superior cavopulmonary anastomosis patients will not have a volume-loaded ventricle, and thus ventricular failure is less common than in mixed circulation patients.

Adult patients with separated circulation—those with a Fontan—also present in a variety of ways. At baseline, they have greatly diminished lung function and aerobic capacity. Those with anatriopulmonary Fontan connection inevitably develop atrial dilatation, which is associated with atrial arrhythmias, atrial thrombus with possible pulmonary embolism, and right pulmonary venous obstruction. Low cardiac output commonly develops in adult patients, regardless of the Fontan connection, and is associated with exercise intolerance, protein-losing enteropathy, hepatic congestion and dysfunction, peripheral edema, pleural effusion and ascites, and plastic bronchitis. Obstruction in the Fontan pathway may accelerate these signs and symptoms, as may progressive elevation of pulmonary vascular resistance from chronic pulmonary emboli. Atrial shunting resulting in cyanosis is unusual; however, venovenous connection from the systemic circulation to the pulmonary veins may be a cause of cyanosis. Patients with lateral tunnel and extracardiac conduit Fontan connections do not develop atrial dilatation and thus are less likely to develop atrial thrombus with chronic pulmonary emboli and atrial arrhythmias. Atrial arrhythmias, however, such as flutter, fibrillation, and sinus node disease leading to junctional rhythm, can occur. Low cardiac output, and its sequelae as described for atrio pulmonary Fontan connection patients, also develops, but more slowly.

Diagnosis

The main utility of the electrocardiogram (ECG) is to identify atrial and ventricular arrhythmias. Holter monitoring and electrophysiologic evaluation may be indicated based on the ECG or symptoms. The chest radiograph is particularly helpful in identifying and following pleural effusions in Fontan patients. Effusions suggest low cardiac output and failing Fontan circulation, and all of the sequelae associated with it, including protein-losing enteropathy. Echocardiography is the mainstay for evaluating and following single-ventricle patients. The usual intracardiac structural and functional evaluation of the ventricle, valves, aortic arch, and arterial and venous connections is performed. In Fontan patients, additional evaluation of the Fontan pathway is performed, looking for obstruction at the inferior caval and pulmonary artery ends, for thrombus and low flow with spontaneous contrast formation, for flow characteristics and severity of dilatation of the inferior vena cava and hepatic veins, and for the status of a fenestration if one is present.

Cardiac catheterization is indicated in any symptomatic single-ventricle patient to assess a number of variables, including:

- Ventricular hemodynamics
- Coronary arteries
- Pulmonary vascular morphology, pressure, and resistance
- Cardiac output
- Qp/Qs ratio
- Status of surgical shunts
- Bands and cavopulmonary connections
- Assessment of pulmonary arteriovenous malformations, venovenous abnormal connections, and systemic-to-pulmonary artery collateral formation

Cardiac catheterization is a necessity in any single-ventricle patient with previously operated or unoperated mixed circulation, or partially separated circulation, who is being considered for Fontan completion surgery (see Chapter 41 for criteria for proceeding to the Fontan). It is also a necessity for any patient being evaluated for conversion from an atrio pulmonary Fontan to either an extracardiac conduit or a lateral tunnel Fontan.

Magnetic resonance imaging (MRI) and computed tomography with angiography may be useful in single-ventricle patients, usually to augment the structural and functional echocardiographic evaluation, particularly in the pulmonary
arteries and veins. MRI is also useful for functional evaluation of the ventricular myocardium.

**NATURAL HISTORY**

The best prognosis is for patients with S,L,L double inlet left ventricle with moderate pulmonary stenosis. Survival into the sixth decade is possible.\(^{A12}\) Ten-year survival after lateral tunnel and extracardiac conduit Fontan connection, the predominant Fontan operations performed over the last 20 years, is 90% or greater, much better than that observed after the atriopulmonary Fontan.\(^{544}\) Once low output and its sequelae develop, unless there is a structurally correctable problem such as Fontan pathway obstruction, valve regurgitation, or systemic ventricular outlet obstruction or coarctation, survival is limited, with 5-year survival of about 50%. Survival in Fontan patients nevertheless is much better than the approximately 50% 20-year survival for patients with mixed circulation and partially separated circulation.\(^{W13}\)

The chronicity of the abnormal hemodynamic state associated with Fontan circulation leads to additional challenges for adults not generally considered in younger patients. Prevalence and severity of chronic lower extremity venous insufficiency are much greater than in the normal population.\(^{V1}\) Also, intracardiac thrombus formation is noted in 12% of adult Fontan patients when it is looked for, and is attended by significant morbidity.\(^{T23}\) Atrial arrhythmias occur with increasing frequency in adults, noted in 41% of Fontan patients in one study, and arrhythmias were associated with atrial thrombus.\(^{G13}\) In an analysis of all adult Fontan patients presenting to a large clinic, 17% were found to have silent pulmonary emboli.\(^{V11}\)

**TECHNIQUE OF OPERATION**

Surgical techniques, including systemic-to–pulmonary artery shunt, pulmonary artery band, bidirectional superior cavopulmonary anastomosis, and extracardiac conduit and lateral tunnel Fontan operations, are described in Chapter 41. Therapeutic catheter-based procedures may be used to relieve various obstructions and to occlude abnormal venovenous connections, systemic-to–pulmonary artery collaterals, surgical shunts, and Fontan fenestrations.

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**Figure 29-47** Cryoablation left and right atrial maze (Cox-maze III) procedure in patient with tricuspid atresia undergoing an extracardiac conduit Fontan conversion. A, Superior (SVC) and inferior vena cavae (IVC) have been detached from right atrium in preparation for extracardiac conduit Fontan, and cardiacl stumps of SVC and IVC have been oversewn. Cryolesions are placed in four locations in the right atrium at \(-60^\circ\C\) for 90 seconds each. In this patient with tricuspid atresia, a linear cryoprobe is used to ablate tissue between atrial septal defect (ASD) and SVC stump, ASD and lateral edge of atriotomy, coronary sinus os and IVC stump, and area of atretic tricuspid valve anulus and IVC stump. B, Left-sided cryolesions are placed for patients with preoperative atrial fibrillation. They are placed around the pulmonary veins, at orifice of left atrial appendage, and between inferior pulmonary veins and mitral valve anulus. Appropriate adjustments, while adhering to the basic principles of the maze, must be made in placing the cryolesions for other single-ventricle morphology, for example, in patients with unbalanced atrioventricular septal defect or hypoplastic left heart. (From Weinstein and colleagues.\(^{W18}\))
The maze procedure is modified as appropriate for patients with the variable morphologic features associated with the spectrum of single-ventricle anomalies. Fig. 29-47 shows the cryolesions for a right and left atrial maze procedure applied to a patient with tricuspid atresia who is about to undergo an extracardiac conduit Fontan.

RESULTS
Systemic-to-pulmonary artery shunt and pulmonary trunk band procedures have a low surgical mortality in adults without important comorbid conditions, similar to the mortality of these same procedures in children (see Chapter 41). For shunt procedures it is about 5%, and for bands less than 1%.

Early mortality for the superior bidirectional cavopulmonary anastomosis and Fontan operation in adults is not well documented, but should not differ from outcomes in younger patients, about 2% to 5% for each, as long as selection criteria are met. Observed mortality in most series is higher than this, however, because these series span many decades, and the outcomes often reflect the era. In the largest single-institution study, 132 adults (mean age 23 years) underwent the Fontan procedure between 1973 and 2001, with an early mortality of 8.3% (CL 5.8%-12%). Other studies, including male gender, pulmonary artery pressure greater than 15 mmHg, and age greater than 30 years.

In the next largest series, Veldtman and colleagues reported 61 cases (median age 36 years) with an early mortality of 13% (CL 8.6%-19%); 15-year survival was 67%. Van den Bosch reported on seven adults undergoing the Fontan with one early death (14%; CL 2.3%-41%), and in a mean follow-up period of 15 years, there were two additional deaths and one cardiac transplantation. Gates and colleagues reported on 21 patients with an early mortality of 4.8% (CL 0.8%-15%), with one late death over a mean follow-up time of 7.4 years.

Podzolkov and colleagues reported an early mortality of 6.9% (2/29; CL 2.4%-16%) for the superior bidirectional cavopulmonary anastomosis in adults, and 8.3% for the Fontan in adults. Both values were similar to their outcomes in children. Gates and colleagues reported an early mortality of 6.9% (2/29; CL 2.4%-16%) for the superior bidirectional cavopulmonary anastomosis in adults, and 8.3% for the Fontan in adults. Both values were similar to their outcomes in children.

Early mortality after conversion of the atrioventricular Fontan to the cavopulmonary Fontan ranges from 0% to 25%. The wide range of mortality is likely related to the selection criteria used in individual series. In one of the largest series (containing both children and adults), Mavroudis and colleagues reported no early mortality (CL 0%-4.6%) and one transplant in 40 conversions and concomitant maze procedures (mean age 19 ± 9.0 years at conversion). At a mean follow-up of 2.5 years, functional status was improved, and there was one death and two additional transplants. In another study of 27 conversions in adults (mean age 30 years), there were two early deaths (7.4%; CL 2.6%-17%). Both patients who died had liver cirrhosis and had been evaluated and turned down for transplantation. Functional status improved following conversion. Most patients in this series (78%) also had concomitant maze arrhythmia surgery for atrial flutter or fibrillation, with late arrhythmia recurrence of 14% at 4.2-year follow-up. Another study of 10 adults (mean age 21 years) undergoing conversion and concomitant cryoablation showed one early death (10%; CL 1.6%-30%) and a second midterm death. At follow-up, all survivors improved functionally, and arrhythmia recurrence was 10%.

Sheikh and colleagues reported 15 conversions (mean age 20 years) with no early (CL 0%-12%) or late mortality and improved functional status at a mean follow-up of 43 months. Eleven of the 15 patients had arrhythmia surgery as well, with reduced requirement for medications at follow-up. Mott and colleagues reported no early (CL 0%-12%) or late deaths in 15 conversions with concomitant arrhythmia surgery (mean age 23 years) at 30-month follow-up.

INDICATIONS FOR OPERATION

![Graph showing survival rates after Fontan operation](image-url)
In adults with mixed circulation (usually previously operated, but rarely with no surgical history) and unclear physiology, full evaluation, including cardiac catheterization, will determine whether criteria are met to advance to a state of separated circulation. Criteria for advancing to a superior cavopulmonary anastomosis are the same as those for infants and children (see Chapter 41). If these criteria are met, however, in contrast to the situation in young patients, a superior cavopulmonary anastomosis will rarely be adequate as the sole source of pulmonary blood flow, because of severe cyanosis. A secondary source, either from a new or existing systemic–pulmonary artery shunt or pulmonary trunk band, or from native pulmonary blood flow across a naturally stenotic outflow tract to the pulmonary arteries, will be required.

If the criteria are not met to advance to a separated circulation in the adult with mixed circulation, and the patient is cyanotic due to reduced pulmonary blood flow, then further surgical management with a systemic-to-pulmonary artery shunt, or possibly a pulmonary trunk band revision (if one is in place already), is indicated. If the patient is cyanotic because of pulmonary hypertension, evaluation for heart-lung transplantation is the only surgical option.

If pulmonary overcirculation is present and pulmonary vascular obstructive disease is not, then shunt revision or pulmonary trunk band placement or tightening is indicated as appropriate. Such patients can be further evaluated with catheterization approximately 6 months after shunt or band revision to assess criteria for advancing to a separated circulation. If pulmonary vascular obstructive disease is present in the overcirculated patient, the only surgical option is heart-lung transplantation.

In adult patients with partially separated circulation, if criteria are met at cardiac catheterization (see Chapter 41), advancement to a separated circulation with a completion Fontan operation is indicated. If the patient does not meet criteria for a Fontan and is symptomatic from cyanosis, creation of an additional source of pulmonary blood flow (usually a systemic-to-pulmonary artery shunt) is indicated. If pulmonary arteriovenous malformations are partially the cause of cyanosis, the shunt should be placed to direct the systemic flow primarily to the lung with the dominant malformations. Rarely, large isolated arteriovenous malformations can be closed using percutaneous catheter-based methodology.

In adult patients with separated circulation, surgical intervention may be indicated in several circumstances. Any significant structural cardiac problem or systemic arterial, pulmonary arterial, systemic venous, pulmonary venous, or Fontan pathway obstruction is an indication for surgical correction if catheter-based intervention is contraindicated or unsuccessful. In symptomatic patients with low cardiac output due to elevated pulmonary vascular resistance, a surgical fenestration may be indicated in selected cases. Adult Fontan patients who are fully or nearly fully saturated, however, may not tolerate the increase in cyanosis that attends fenestration. All adult atrio pulmonary Fontan patients with acceptable ventricular function and low pulmonary vascular resistance should be considered for conversion to an extracardiac conduit or lateral tunnel Fontan connection. Conversion is strictly indicated if atrial flutter or fibrillation, pulmonary venous compression, atrial thrombus, or structural problems such as obstruction in the Fontan pathway are present.158,166

In all single-ventricle patients with severe ventricular failure, regardless of mixed, partially separated, or separated circulation, and normal pulmonary vascular resistance, the only surgical option is heart transplantation.62

If atrial flutter or fibrillation is present in single-ventricle patients undergoing surgery to correct structural problems, to advance to a more separated circulation, or to convert from an atrio pulmonary to a cavopulmonary Fontan, a maze procedure or one of its modifications is indicated as a concomitant procedure.166

Section XVII  Other Anomalies Rarely Requiring Surgery in the Adult

ISOLATED PULMONARY STENOSIS

Definition

Isolated pulmonary stenosis is a common congenital heart anomaly; however, it rarely requires surgery in the adult.311 The reasons for this are that the valve obstruction is often mild and self-limited, and percutaneous catheter-based valvotomy is often effective in those who need treatment.

Morphology

Two common morphologic subtypes of isolated pulmonary stenosis are recognized. The predominant type is the doming valve with three fused commissures but underlying well-developed valve cusp tissue. The less common type (=20%) is the dysplastic valve, defined by three cusps with fully formed commissures but thickened immobile myxomatous cusp tissue. This type of valve is associated with Noonan syndrome.311 Occasionally, isolated pulmonary valve stenosis will be caused by a bicuspid valve.

Technique of Operation

Because surgery for pulmonary stenosis in the current era is relegated to a second-choice role behind balloon valvotomy, most patients presenting for surgery will have unfavorable morphology and will likely require pulmonary valve replacement. The occasional patient with a doming valve that does not respond to catheter-based balloon dilatation, and the occasional patient with a doming valve who is undergoing cardiac surgery for another anomaly, are candidates for surgical commissurotomy. Most surgical cases, however, have either dysplastic morphology or one or more associated conditions, such as anular hypoplasia or valve regurgitation, and will require valve replacement. Occasionally, a dysplastic valve without regurgitation and with adequate anular size will respond to surgical valvuloplasty involving shaving of the thickened cusps.

Currently, the replacement option of choice is a bioprosthetic valve placed orthotopically. It may be necessary to patch augment the anular and supravalvular component of the right ventricular outflow tract or to resect muscle in the subvalvar component of the right ventricular outflow tract as well. Surgical reduction of the pulmonary trunk may be considered when there is associated marked post-stenotic dilatation of the pulmonary trunk, but this procedure is truly
In one series of 40 patients (age range 18-56 years), the gradient was reduced by catheter intervention but not eliminated (persistent gradient of $37 \pm 14$ mmHg). All patients had mild or less regurgitation, and there was a tendency for subpulmonic gradients to regress at 24-month mean follow-up (Fig. 29-49). Other studies with follow-up of up to 10 years after balloon dilatation show similar findings. Dysplastic valves are not as effectively treated by catheter-based balloon valvotomy, with generally unacceptable residual gradients.

Balloon valvotomy for the doming valve is currently the first line of therapy. Two studies comparing balloon treatment and surgery suggest that gradient relief and freedom from reintervention are better with surgery (Fig. 29-50); however, although these differences are important, they are small, and thus they are offset by a higher occurrence of important regurgitation, more ventricular ectopy, greater cost, and increased invasiveness associated with surgery.

Surgery (pulmonary valvotomy) for unselected cases of isolated pulmonary stenosis in the adult has an early mortality approaching zero. Long-term survival and freedom from reoperation are also extremely favorable, with no late mortality and 95% freedom from reintervention at 25 years. When valve replacement is necessary, long-term outcomes are similar to those for other patients with bioprosthetic valves in the pulmonary position.

### Indications for Operation

There are several indications for surgical intervention for isolated pulmonary stenosis:

- After catheter-based balloon dilatation with a residual peak echocardiographic Doppler gradient of greater than 60 mmHg in asymptomatic patients or a residual peak gradient of more than 50 mmHg in symptomatic patients
- In any patient with associated severe pulmonary regurgitation, anular hypoplasia, fixed subvalvar stenosis, supravalvar stenosis, or dysplastic valve morphology
- If other cardiac anomalies requiring cardiac surgery, such as coronary artery disease, ventricular septal defect, or tricuspid regurgitation, are present

If there is an associated atrial septal defect, combined catheter-based closure and balloon pulmonary valvotomy may be performed.

### TOTAL ANOMALOUS PULMONARY VENOUS CONNECTION

#### Definition

Definition, morphology, and basic physiology of total anomalous pulmonary venous connection (TAPVC) are described in Chapter 31.

#### Morphology

It is rare for adults with TAPVC to survive into adulthood unrepaired. A few isolated cases are reported. Characteristics

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*Figure 29-49* Peak pulmonary systolic gradient (PG) by echocardiography from right ventricle to pulmonary artery before, immediately after, and at mean follow-up of 24 months after balloon pulmonary valvuloplasty in 32 adult patients. Bars represent mean ± standard deviation. (From Kaul and colleagues.)

*Figure 29-50* Freedom from reintervention in adults with isolated pulmonary valve stenosis managed by surgery ($n = 54$) or balloon valvuloplasty ($n = 92$). Numbers represent patients remaining at risk. (From Peterson and colleagues.)
of individuals who survive include unobstructed supracardiac form of the disease, large intraatrial communication, and low pulmonary vascular resistance with increased pulmonary blood flow, resulting in only mild cyanosis.\textsuperscript{A17}

Clinical Features and Diagnostic Criteria

Clinical presentation is characterized by varying severity of cyanosis and signs and symptoms of right heart and pulmonary overcirculation. Echocardiography is diagnostic; however, cardiac catheterization is mandatory to assess the status of the pulmonary vascular bed. Magnetic resonance imaging (MRI) and computed tomography (CT) may be helpful.

Natural History

Recurrent pulmonary vein stenosis presenting in adults with a history of infant repair of TAPVC is rare. Recurrent obstruction following infant repair occurs in about 10% of cases in which the total anomalous connection was an isolated lesion (it is higher in single-ventricle and heterotaxy patients). Furthermore, recurrence almost always occurs in the first 6 months after initial infant repair.\textsuperscript{R28,J2,R11}

Technique of Operation

Surgical techniques used to repair this anomaly in adults are the same as those used in infants (see Chapter 31).

Results

Early mortality approaches zero. Arikawa and colleagues report two adult cases, aged 43 and 51 years, without mortality and with uneventful postoperative courses and improved functional status.\textsuperscript{A17} These authors also review the Japanese literature and report on six additional patients over age 40 years, with similar outcomes. John, Sukumar and their colleagues note that presentation in late childhood and adulthood implies a better prognosis than presentation in infancy. They report no early or late mortality in the former groups.\textsuperscript{J8} Berg and colleagues report on three patients, aged 22, 29, and 33 years, all with minimal cyanosis at rest, dyspnea, mild heart failure, and mild to moderate pulmonary hypertension. One patient had gone through an uneventful pregnancy. Another had concomitant important mitral regurgitation that was surgically repaired. There was no early or late mortality after repair, and all patients were functionally improved.\textsuperscript{R17}

VASCULAR RING AND ASSOCIATED ARCH ANOMALIES

Definition

Definition, morphology, and basic physiology of vascular ring are described in Chapter 51. Vascular rings rarely present in adults. Most reported cases are single case reports.

Morphology

In adults, the most common anomaly is double aortic arch (\textsuperscript{\textapprox}45\%), followed by right aortic arch with anomalous left subclavian artery with ligamentum arteriosum (\textsuperscript{\textapprox}30\%).\textsuperscript{G20}

Clinical Features and Diagnostic Criteria

Vascular rings in adults may be found incidentally\textsuperscript{K1,F3} or may present with symptoms of dysphagia lusoria or upper respiratory obstruction.\textsuperscript{J1,G20,G21,M39,N4,S34} It is more common for dysphagia to be the presenting symptom in adults than in children, although respiratory obstruction is still the most common presentation in adults (42% present with respiratory symptoms, 33% with dysphagia). Diagnosis can often be made by chest radiography, contrast esophagogram, and echocardiography; however, MRI or CT are critical, allowing more precise imaging of the vascular anomaly and also imaging of the vasculature relationship to adjacent structures, including the trachea and esophagus.

Pulmonary artery sling is rare in adults. The literature consists of case reports only. Most are asymptomatic, presenting as an incidental finding\textsuperscript{P23,N47}; however, some present with esophageal or tracheal obstructive symptoms, or both.\textsuperscript{J1} Diagnostic evaluation and indications for surgery are similar to those for vascular rings.

Natural History

Presentation in adulthood after vascular ring repair in childhood is rare. Ruzmetov and colleagues followed 183 childhood repairs for up to 35 years with no reports of late complications.\textsuperscript{R24} There is a single case report of late presentation of subclavian steal syndrome in an adult who underwent vascular ring repair in infancy.\textsuperscript{C30}

Technique of Operation

All rings can be approached effectively through a median sternotomy. However, the more traditional approach is through a lateral thoracotomy (see Chapter 51).\textsuperscript{K139}

Surgical management of pulmonary artery sling is described in Chapter 51. In adults, in contrast to infants, tracheal reconstruction is usually not necessary.

Results

There are no reports of perioperative deaths in the modern literature. Symptomatic improvement occurs reliably in patients presenting with dysphagia, but less reliably in those presenting with respiratory symptoms. In the case of late presentation of subclavian steal syndrome, the original repair involved division of the ligamentum and left subclavian artery, without subclavian artery reimplantation.\textsuperscript{C30}

Indications for Operation

Asymptomatic anomalies may be followed. Surgical repair is recommended in the presence of important symptoms.

COR TRIATRIATUM

Definition
There are sporadic reports of cor triatriatum sinister presenting in the adult, either in the form of isolated case reports or included in single-institution (mostly) pediatric series. \cite{C17,H22,K10,K26,O4,S5,V7} Cor triatriatum dexter has been reported in adults, usually as an asymptomatic incidental finding. \cite{M31,S6,Y4} When symptoms are present, they mimic right heart failure.

Morphology

In contrast to children (see Chapter 32), most adults do not have complex associated cardiac anomalies; however, associated cardiac structural anomalies have been found in some patients presenting in adulthood. \cite{C17}

Clinical Features and Diagnostic Criteria

Presentation of isolated cor triatriatum sinister in the adult is identical to that of mitral stenosis, including dyspnea, pulmonary hypertension, atrial fibrillation, right heart failure, and hemoptysis. In mild cases, presentation may be incidental. Thrombus was present in the accessory chamber in one adult. \cite{P10} Diagnosis can be made by echocardiography; however, MRI and CT define the morphologic details with more clarity. Cardiac catheterization is indicated to assess the state of the pulmonary vasculature.

Cor triatriatum dexter has been reported in adults, usually as an asymptomatic incidental finding. \cite{M31,S6,Y4} When symptoms are present, they mimic right heart failure.

Technique of Operation

Surgical techniques are similar to those used in children (see Chapter 32). If chronic atrial fibrillation or flutter is present, a concomitant maze procedure should be performed.

Results

In the few case reports documented in the literature, surgical repair has been performed without early mortality and with improvement in symptoms and reduction in pulmonary artery pressure.

Indications for Operation

Surgical repair is indicated if symptoms are present or if other changes, such as thrombus formation, develop. Surgical excision of cor triatriatum dexter is indicated if symptoms are present.

SINUS OF VALSALVA ANEURYSM

Definition

Definition, morphology, and basic physiology of sinus of Valsalva aneurysm are described in Chapter 36.

Morphology

These anomalies are rare in adults. When they occur, they are often associated with unicusp or bicuspid aortic valves. The aneurysm occurs most frequently in the noncoronary and right coronary sinuses, but can occur in the left.

Clinical Features and Diagnostic Criteria

Sinus of Valsalva aneurysms are generally asymptomatic until they rupture. However, they may cause problems from a mass effect without rupture, including coronary obstruction, aortic regurgitation, right ventricular outflow obstruction, and ventricular tachycardia. Thrombus formation with subsequent embolism can also occur. When rupture occurs, it is usually into a right-sided chamber, creating an aortic to right atrial or right ventricular fistula. Rupture may also cause cardiac tamponade. Rupture usually presents as an emergency with extreme hemodynamic instability. Sinus of Valsalva aneurysms are often detected incidentally or during imaging of abnormal aortic valves.

Natural History

The natural history of small and moderate aneurysms is unknown, and the risk of rupture of large aneurysm, although well documented, is not quantified.

Technique of Operation

The appropriate surgical procedure will vary from simple plication, to resection and sinus patch reconstruction, to aortic root replacement with coronary artery reimplantation. \cite{D10,H3,P11,R10,U1}

Indications for Operation

Treatment options are well defined. If surgery is required for aortic valve disease or any other cardiac problem, sinus of Valsalva aneurysms of any size should be addressed. If no other surgery is indicated, surgical correction of large and moderate-sized aneurysms is the best approach to prevent rupture and other sequelae. Small aneurysms should be followed carefully.

DOUBLE-CHAMBERED RIGHT VENTRICLE

Definition

This anomaly is rare in adulthood in developed countries. Two series with multiple patients are reported in the literature. \cite{L6,M19} Otherwise, there are only occasional individual case reports or mention of an occasional adult in series that include predominantly children. \cite{G1,S32} In the study by McElhinney and colleagues, it is reported that a literature review identified six case reports. \cite{M19} Larger series of adult patients are reported from countries with underdeveloped healthcare systems where this anomaly may go undiagnosed until adulthood. \cite{S33}

Morphology

In adulthood, as in childhood, there are almost always associated structural anomalies. In one series of 11 patients, 10 had associated anomalies, usually a ventricular septal defect, and in a series of 3 adults, all had associated anomalies, either atrial or ventricular septal defects. \cite{L6,M19}

Clinical Features and Diagnostic Criteria
Symptoms in adults are different from those in children. They include syncope, chest pain, and exertional dyspnea. New York Heart Association functional class ranges from II to IV in most patients. Diagnosis in the adult may be difficult. Electrocardiography (ECG) is non-specific, showing evidence of right ventricular hypertrophy, right atrial enlargement, and diffuse ST-wave changes. Transthoracic echocardiography often fails to make the diagnosis. The incorrect diagnosis is often tetralogy of Fallot, ventricular septal defect, or pulmonary valve stenosis. Transesophageal echocardiography may be more accurate. MRI has been reported to establish the diagnosis and may supplement echocardiography. Cardiac catheterization should be performed in all cases and establishes the diagnosis in all. It also should always be performed to assess coronary arteries and overall hemodynamics.

**Technique of Operation**

Surgical techniques are similar to those used in children. Usually a transatrial–transpulmonary artery approach will be effective, with a formal right ventriculotomy unnecessary. Associated anomalies should be addressed as well.

**Results**

Early mortality should be less than 1%. All patients reported in the literature have survived, and follow-up in the two series ranged from 15 to 270 months, with no late mortality, improved functional status, and a low occurrence of recurrent obstruction. Perioperative mortality due to low cardiac output has been reported, but only for patients undergoing surgery prior to 1965.

**Indications for Operation**

Surgery is indicated in the presence of symptoms, signs of myocardial strain or ischemia, or a gradient greater than 40 mmHg.

**REFERENCES**

A


B

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Atrial Septal Defect and Partial Anomalous Pulmonary Venous Connection

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An atrial septal defect (ASD) is a hole of variable size in the atrial septum. A patent foramen ovale that is functionally closed by overlapping of limbic tissue superiorly and the valve of the fossa ovalis inferiorly (in response to the normal left-to-right atrial pressure gradient) is excluded. ASDs generally permit left-to-right shunting at the atrial level. Partial anomalous pulmonary venous connection (PAPVC) is a condition in which some but not all pulmonary veins connect to the right atrium or its tributaries, rather than to the left atrium. The term connection is preferred to the term “return,” because connection is anatomical and return is governed by hemodynamic factors. PAPVCs may occur as isolated anomalies or may be combined with ASDs.

These two groups of anomalies are considered together in this chapter because they manifest similar physiology and result in similar clinical findings. Total anomalous pulmonary venous connection is considered in Chapter 31. ASDs typically occur in association with other cardiac anomalies, and these are considered in chapters dealing with those anomalies.

HISTORICAL NOTE

Clinical recognition of an ASD has been possible only in about the past 70 years. Among the 62 recorded autopsy cases of ASD analyzed by Roesler in 1934, only one had been correctly diagnosed during life.\(^\text{56}\) By 1941, Bedford and colleagues were able to make the diagnosis clinically in a number of patients.\(^\text{57}\) When cardiac catheterization came into general use during the late 1940s and early 1950s, secure diagnosis became possible. The first descriptions of PAPVC are attributed to Winslow in 1739\(^\text{115}\) and Wilson in 1798.\(^\text{111}\) The first diagnosis of PAPVC during life was reported by Dotter and colleagues in 1949.\(^\text{107}\)

A number of ingenious closed methods for repair of ASDs and related conditions were proposed and studied experimentally in the productive and expansive surgical era following the end of World War II in 1945. In 1948 in Toronto, Murray reported closing an ASD in a child by external suturing.\(^\text{110}\) Several other closed methods had clinical application, including Bailey and colleagues’ “atriocephoptomy” and Sondergard’s purse-string suture closure.\(^\text{22,51}\) However, limited applicability of these methods was always apparent, and they were soon abandoned.

Hypothermia, induced by surface cooling, and inflow occlusion for repair of ASDs was introduced during the early 1950s (see Historical Note in Section I of Chapter 2). Lewis and Taufic reported the first successful open repair of an ASD with this method in 1953.\(^\text{15}\) At about the same time, Gross invented the ingenious atrial well technique, a semi-open approach in which a rubber open-bottomed well or cone was sutured to an incision in a clamp-exteriorized portion of the right atrial wall.\(^\text{61,19}\) When the clamp was released, the blood rose into the well, and through this pool of blood, the surgeon could place sutures under digital control for direct or patch closure of the defect. Gibbon started the era of open heart surgery in 1953 when he successfully repaired an ASD in a young woman using a pump-oxygenator.\(^\text{69}\) Although these three methods—hypothermia and inflow occlusion, atrial well, and cardiopulmonary bypass (CPB)—were all used during the late 1950s and provided similar early results,\(^\text{58}\) by the late 1960s almost all surgeons used CPB exclusively for these repairs. Percutaneous catheter techniques for closing a fossa ovalis ASD using a polyester double umbrella device were introduced by King and Mills in 1974.\(^\text{124}\)

The first reported treatment for a type of PAPVC was lobectomy in 1950.\(^\text{119}\) In 1958, Neptune and colleagues reported repair using a closed technique in 17 patients with PAPVC of the right lung to the right atrium associated with ASD.\(^\text{55}\) It is not certain who first repaired the sinus venosus syndrome, but the malformation was clearly illustrated by Bedford and colleagues in 1957.\(^\text{114}\) Repair of PAPVC to the inferior vena cava was performed by Kirklin and colleagues at Mayo Clinic in 1960 and was also subsequently reported by Zubiate and Kay in 1962.\(^\text{117,22}\) Correction of anomalous connection of the left pulmonary veins to the left brachiocephalic vein and other forms of PAPVC was reported from the Mayo Clinic in 1953\(^\text{56,15}\) and later in 1956.\(^\text{17}\)

MORPHOLOGY

Types of Atrial Septal Defect

As viewed from the right atrial side (see Fig. 1-2 in Chapter 1), the normal atrial septum may have defects in almost any location (Box 30-1). Although the morphology of these defects has been known since the early descriptions by Robitansky in 1875,\(^\text{85}\) the advent of open heart surgery emphasized their surgically important aspects\(^\text{54,16}\) (Fig. 30-1).

Fossa Ovalis Defect

The most common ASD is the fossa ovalis type, also called foramen ovale type or ostium secundum defect. This defect lies within the perimeter inscribed by the limbus anteriorly, superiorly, and posteriorly (Fig. 30-2). The smallest defects are
Box 30-1  Types of Atrial Septal Defect

- Fossa ovalis defect
- Posterior defect
- Coronary sinus defect
- Sinus venosus defect
- Confluent defect
- Ostium primum defect (absence of atrioventricular septum)

*Fossa ovalis, posterior, and most confluent defects can be classified as secundum type.

*Varies in size from small valvar-incompetent foramina ovale ASD to complete absence of septum primum tissue with resultant ASD extending to inferior vena cava.

essentially valvar incompetent foramina ovale that occur beneath the superior limbus, between it and the valve (floor) of the fossa ovalis. The floor of the fossa ovalis (remnant of septum primum) may in this situation have multiple fenestrations of various sizes (Fig. 30-3). When more of the floor of the fossa ovalis is absent, a larger fossa ovalis defect is present. When all fossa ovalis tissue is absent, the ASD is confluent with the orifice of the inferior vena cava (IVC). The eustachian valve of the IVC then overhangs the ASD and must not be mistaken for its inferior edge at operation. Size of this type of ASD is also affected by any hypoplasia of the limbus that may be present. When the limbus is quite hypoplastic anteriorly, there is only a thin rim of tissue above the atrioventricular (AV) valves (formerly this was called an intermediate defect and was sometimes confused with an ostium primum defect). The limbus may also be hypoplastic superiorly or posteriorly.

Normally the IVC–right atrial junction is partly to the left of the plane of the limbus, so that when the floor of the fossa ovalis is absent and an ASD of fossa ovalis type extends to the IVC, the caval ostium overrides (or straddles) the defect onto the left atrium.\(^7\) This defect results in some right-to-left shunting of IVC blood to the left atrium in virtually all patients with a large fossa ovalis–type ASD (as documented in experimental studies\(^{69,455,510}\)) and severe shunting with cyanosis in a few patients.\(^{455}\) Also, the position of the normally connected right pulmonary veins next to the atrial septal remnant results in preferential left-to-right shunting of their venous drainage.\(^{832,510}\)

Posterior Defect

A defect in the most posterior and inferior part of the atrial septum, with absence, hypoplasia, or anterior displacement of the posterior limbus, is termed a posterior ASD. The orifices of the right pulmonary veins usually open directly into the area of the defect, but true anomalous pulmonary venous connection of the right lung frequently coexists. In the pure form of this type of ASD, the tissue of the fossa ovalis (including the posterior limbus) is present, and the ASD is an oval defect posterior to this tissue (Fig. 30-4).

Sinus Venosus Defect

The ASD that occurs in sinus venosus syndrome (subcaval defect, superior vena cava defect) is located immediately beneath the orifice of the superior vena cava (SVC), superior to the limbic tissue, and is usually associated with anomalous pulmonary venous connection of the right superior pulmonary vein to the SVC near or at the SVC–right atrial junction. The lowermost margin of the defect is a sharply defined crescentic edge of atrial septum, whereas its upper margin is devoid of septum, being continuous with the posterior SVC wall, which in turn is continuous with the upper edge of the left atrium. The SVC usually overrides the atrial septum onto the left atrium to some extent (see “Sinus Venosus Malformation [Syndrome]” later in this chapter).

Coronary Sinus Defect

Coronary sinus ASDs are part of unroofed coronary sinus syndrome. When the sinus is completely unroofed and no partition is present to separate it from the left atrium, the ostium of the coronary sinus is a hole in the atrial septum that permits free communication between left and right atria (see Chapter 33). Occasionally a fenestration may exist in this partition in the midportion of the coronary sinus, particularly in hearts with tricuspid atresia, or rarely the fenestration may be almost at the ostium of the coronary sinus.\(^7\) (Fig. 30-5).

Confluent Defect

Large ASDs may represent a confluence of two of the defects already described. Thus, a fossa ovalis defect coexisting with absence of the posterior limbus can present as a very large ASD with no septal remnant posteriorly. Another confluent defect occasionally seen is a combination of coronary sinus and fossa ovalis ASDs.

Ostium Primum Defect

An ASD occurs anterior to the fossa ovalis (and the anterior limbus) when the AV septum is absent. Such defects are called AV septal defects, AV canal defects, or ostium primum atrial septal defects and are considered in Chapter 34. When essentially the entire atrial septum is absent (common atrium), the defect includes absence of the AV septum (see “Atrial Septal Deficiency and Interratrial Communications” under Morphology in Chapter 34).

Types of Partial Anomalous Pulmonary Venous Connection

Sinus Venosus Malformation

The most common type of PAPVC is the defect present in sinus venosus malformation, in which PAPVC coexists with a superior caval ASD. In sinus venosus malformation, the right upper and middle lobe pulmonary veins (right superior pulmonary vein) attach to the low SVC or the SVC–right atrial junction, an arrangement present in about 95% of patients with a superior caval ASD.\(^{46,34,520}\) Most often, the anomalous pulmonary venous connection is through two anomalous veins from upper and middle lobes, one superior to the other, but there may be three or rarely four veins, with the uppermost entering the SVC near the ayzygos vein entry. Infequently, only part of the right superior vein connects anomalously, with the inferior (right middle lobe) portion of that vein connecting to the left atrium. Rarely, both the right superior and right inferior pulmonary veins connect anomalously to the low SVC or SVC–right atrial junction (Fig. 30-6).

The lowermost part of the SVC that receives the anomalous veins is usually wider than normal, although it may be relatively small, particularly when there is also a well-formed left SVC, which is not uncommon.\(^7\) The SVC typically overrides the atrial septum to some extent and extends partly into...
Figure 30-1  Anatomy of atrial septal defect (ASD), viewed from right atrium.  

Figure 30-2  Specimen with fossa ovalis atrial septal defect, viewed in anatomic orientation with superior vena cava above and inferior vena cava and its eustachian valve below. Limbus forms anterior, superior, and posterior rim of defect, and remnants of the floor (valve) of fossa ovalis form inferior rim. Key: CoS, Coronary sinus; D, atrial septal defect; E, eustachian valve; L, limbus; TV, septal leaflet of tricuspid valve.

Figure 30-3  Specimen with large fossa ovalis atrial septal defect viewed from opened right atrium in same orientation as Fig. 30-2. Thin remnant of septum primum (floor of fossa ovalis) shows numerous perforations. Key: D, Atrial septal defect; IVC, inferior vena cava; SP, septum primum; SVC, superior vena cava; TV, tricuspid valve.

Figure 30-4  Specimen with large posterior atrial septal defect, viewed from opened right atrium. Orientation is as in Fig. 30-2. Fossa ovalis is intact, but there is a patent foramen ovale. Right inferior pulmonary vein certainly drains anomalously, but is probably normally connected. Right superior pulmonary vein is anomalously connected to right atrium. Key: CoS, Coronary sinus; D, atrial septal defect; FO, fossa ovalis; IVC, inferior vena cava; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; SVC, superior vena cava.
Figure 30-5  Unusual example of small coronary sinus atrial septal defect near ostium. Other anomalies include patent foramen ovale, ventricular septal defect, mild aortic regurgitation, and possible mitral regurgitation. Key: CoS, Coronary sinus; D, atrial septal defect; FO, fossa ovalis; IVC, inferior vena cava; TV, tricuspid valve.

Figure 30-6  Unusual example of sinus venosus malformation. A, Specimen with typical subcaval atrial septal defect (ASD), but with both right superior and right inferior pulmonary veins entering superior vena caval–right atrial junction. In addition, the left pulmonary veins form a common channel connected to left atrium and right superior vena cava. Left superior vena cava and mitral atresia were also present. B, Interior of right atrium showing the subcaval ASD high in the septum and enlarged coronary sinus ostium to which is connected the left superior vena cava. Key: CoS, Coronary sinus; D, atrial septal defect; FO, fossa ovalis; IVC, inferior vena cava; RAA, right atrial appendage; RIPV, right inferior pulmonary vein; RSPV, right superior pulmonary vein; RSVC, right superior vena cava.
the left atrium, resulting in a right-to-left shunt of some SVC blood to the left atrium. In a few patients, SVC overriding is severe enough to produce a large right-to-left shunt and marked cyanosis. The overriding may also be complete, so that the SVC drains directly and completely into the left atrium. The relationship between anomalous connection of the SVC to the left atrium without an ASD and sinus venosus ASD is indicated by connection of pulmonary veins from the right upper lobe to the cardiac end of the SVC in some patients with PAPVC. This relationship also occurs in patients with no ASD but in whom the pulmonary veins from the right upper lobe are connected to the cardiac end of the SVC, with the SVC connected to the left atrium by a large opening, and to the right atrium by a small opening.

Rarely, a typical high superior caval ASD is present without anomalous pulmonary venous connection; right pulmonary veins connect to the left atrium but more superiorly than normal.

**Right Superior Pulmonary Vein to Superior Vena Cava**

Occasionally the entire right superior pulmonary vein connects to the SVC without an associated superior caval ASD. The connection is then usually well above (superior to) the SVC–right atrial junction, and the lower part of the SVC is not dilated. Rarely, even when no superior caval ASD is present, the connection may be in the typical low position of sinus venosus syndrome. At times, only a portion of the right superior pulmonary vein draining one or two segments of the right upper lobe connects directly to the SVC. The PAPVC may be isolated or associated with a fossa ovalis ASD.

**Right Pulmonary Veins to Right Atrium**

Right pulmonary veins may connect directly to the right atrium, either in toto, where they may connect as two or three separate veins, or only through the superior (or rarely inferior) right pulmonary vein. This anomaly may exist as an isolated defect, without an ASD or with only a patent foramen ovale, with the plane of the atrial septum altered from coronal to near-sagittal because of leftward displacement of its lateral attachment. The plane of the right pulmonary vein is actually altered minimally from normal. Because the posterior limbus is present in such defects, the veins are clearly anomalously connected to the right atrium. In ASDs with absence of posterior limbus (posterior ASD), and at times in large fossa ovalis ASDs, the plane of division between right and left atria posteriorly can be questionable, and thus the atrial connection of the right pulmonary veins in this area is debatable. In such defects, however, true anomalous connection of the right pulmonary veins may be present (see Fig. 30-4).

**Right Pulmonary Veins to Inferior Vena Cava**

An anomalous right pulmonary vein, generally draining the entire right lung but occasionally only the middle and lower lobes, may descend in a cephalad-to-caudal direction toward the diaphragm, more or less parallel to the pericardial border but with a crescentic (scimitar) shape, and then curve sharply to the left just above or below the IVC–right atrial junction. The anomalous pulmonary venous trunk usually passes anterior to the hilum of the right lung but occasionally is posterior to it. Entrance into the IVC is just superior to the hepatic vein orifices. The atrial septum may be intact, or a fossa ovalis ASD may be present. Occasionally the anomalous vein also connects to left atrium, and rarely scimitar syndrome can exist with connection of the anomalous vein only to left atrium. Pulmonary venous drainage is then normal. (Rarely, the left lung may connect via a scimitar-shaped vein to the IVC.)

Right-sided scimitar syndrome occurs as an isolated malformation in a minority of cases. In most patients, anomalies of the right lung are also present. The most common anomaly is right lung hypoplasia, which is associated with a marked mediastinal shift and dextroposition of the heart, and in its severe form with the entire heart lying in the right side of the chest. Blood supply to the hypoplastic right lung comes mainly from a branch of the abdominal aorta in the region of the celiac axis, which ascends through the inferior pulmonary ligament to supply the lower lobe, or more often the entire right lung. A small pulmonary artery may be present, but often the central and hilar portions of the right pulmonary artery are absent. Occasionally a true right lower lobe bronchopulmonary sequestration may exist, with secondary intrapulmonary cyst formation.

Associated cardiac anomalies are often present in scimitar syndrome. In one study, for example, 11 of 13 infants had associated malformations, seven of whom had left-sided hypoplastic conditions. Diaphragmatic anomalies occurred in about 20% of the cases reviewed by Kielty and colleagues. These defects included herniation of the right lung through the foramen of Bochdalek and abnormal attachments of the diaphragm.

**Rare Connections of Right Pulmonary Veins**

Rarely, right pulmonary veins connect anomalously to the azygos vein or coronary sinus, with or without a fossa ovalis ASD.

**Left Pulmonary Venous Connections**

Left pulmonary veins may connect to the left brachiocephalic vein by way of an anomalous vertical vein. Anomalous drainage is usually from the entire left lung, but may be only from the left upper lobe. A fossa ovalis ASD coexists in some patients, and in others the atrial septum is intact. Rarely, left pulmonary veins connect anomalously to the coronary sinus, a right-sided SVC, or the right atrium.

**Bilateral Partial Pulmonary Venous Connection**

Partial but bilateral anomalous pulmonary venous connection is rare. The most common variant is probably the defect in which the atrial septum is intact, the left superior pulmonary vein attaches to the left brachiocephalic vein by way of an anomalous vertical vein, and the right superior pulmonary vein attaches to the SVC–right atrial junction. In another form, a common pulmonary venous chamber is present (see “Pulmonary Venous Anatomy” under Morphology in Chapter 31 for definition), and some veins from both lungs connect to it. All but one lobe or only one lobe from each side may connect to the sinus. The common venous sinus may connect to the right atrium or brachiocephalic vein.

**Cardiac Chambers in Atrial Septal Defect and Related Conditions**

Typically in ASD and related conditions, the right atrium is greatly enlarged (at least grade 3 or 4 on a scale of 1 to 6)
and thick walled. The left atrium is not enlarged. This discrepancy occurs in the absence of any flow or pressure restriction between the two, speculatively because the right atrial wall is more distensible than the left.

Right ventricular (RV) diastolic size is increased, often greatly, because of volume overload imposed by the left-to-right shunt. Whereas normal RV diastolic dimensions are between 0.6 and 1.4 cm · m⁻², in patients with large left-to-right shunts at atrial level they average 2.66 cm · m⁻² and may be as large as 4 cm · m⁻². Consequently, the cardiac apex is often formed by the RV.

Morphologically, the left ventricle (LV) is normal or slightly decreased in size. However, important LV dynamic abnormalities are present in most patients (see “Mitral Prolapse”).

Mitral Valve and Atrial Septal Defects

Mitral Prolapse

Mitral valve prolapse occurs in association with fossa ovalis ASD, sinus venosus syndrome, and probably other types of ASDs and related conditions that result in left-to-right shunts at the atrial level. Prevalence of true prolapse is about 20%, increasing with age and with magnitude of the pulmonary-to-systemic blood flow ratio (Qp/Qs).

Schreiber and colleagues have clarified a previously confused subject by relating mitral valve prolapse to abnormalities of LV shape in patients with ASD. Alteration in LV configuration results from leftward shift of the ventricular septum, a process that begins as a slight decrease in the normal rightward convexity and progresses with time to flattening and then reversal, with a resultant central bulge into the LV. This process is a response to RV enlargement, which is secondary to volume overload. This etiologic basis of mitral valve prolapse is supported by its decreased degree or elimination in most cases by ASD closure, with return of LV geometry to normal.

Mitral Regurgitation

Mitral prolapse in ASD can lead to mitral regurgitation, as does ordinary mitral prolapse. True prevalence of regurgitation in unselected patients varies because older patients and those with larger pulmonary blood flows have a higher prevalence of this abnormality and prolapse. Prevalence of mitral regurgitation severe enough to require correction at the time of ASD repair is about 5% or less. The data of Leachman and colleagues strongly suggest that this type of mitral prolapse can also precipitate chordal rupture, as it can in Barlow syndrome.

Cleft Mitral Leaflets

Cleft anterior or posterior mitral leaflets that cause mitral regurgitation are reported to occur occasionally in patients with ASD. However, judging from some of the illustrations of such “clefts,” they may simply be spaces between commissural and main leaflets in prolapsed valves.

Lungs and Pulmonary Vasculature

Pulmonary arteries are considerably dilated and elongated when pulmonary blood flow is increased. This dilatation involves even the smallest branches, which tend to compress the smaller airways, with resultant retention of secretions and bronchiolitis.

Hypertensive pulmonary vascular disease develops infrequently in patients with ASD, and then usually not until the third or fourth decade of life (see “Pulmonary Vascular Disease” under Morphology in Section I of Chapter 35). This contrasts sharply with ventricular septal defects (VSDs), complete AV septal defects, and patent ductus arteriosus, in which pulmonary vascular disease may be present early in life. In ASD, pulmonary vascular disease is caused mainly by secondary thrombosis in the dilated pulmonary artery branches, with changes in the intima and media of vessels usually playing a minor role. Haworth has suggested, however, that an increase in pulmonary arterial smooth muscle may be the only finding.

Associated Cardiac Conditions

ASDs and related conditions may coexist with almost all varieties of congenital heart disease, but such cases are not considered here unless the left-to-right shunt at atrial level is the dominant hemodynamic lesion. A wide spectrum of cardiac anomalies coexist with ASD as the dominant lesion (Table 30-1).

Valvar heart disease may coexist with hemodynamically important ASDs. Six cases with moderate or severe rheumatic mitral stenosis and a hemodynamically significant ASD (Lutembacher syndrome) were observed among 443 patients with an ASD at GLH (1957-1983). Eleven cases of moderate or severe mitral regurgitation were observed; in three, regurgitation was rheumatic in origin. Both mitral stenosis and regurgitation increase left-to-right shunting.

Tricuspid regurgitation of variable severity frequently complicates ASDs in older patients with heart failure, the mechanism generally being RV and tricuspid anular dilatation.

Related Conditions

Rarely, ASD may occur in patients with Marfan, Turner, Noonan, or Holt-Oram syndromes.

Table 30-1 Associated Cardiac Anomalies in Patients with Atrial Septal Defect or Partial Anomalous Pulmonary Venous Connection

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>No.</th>
<th>% of 443</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left superior vena cava</td>
<td>24</td>
<td>5</td>
</tr>
<tr>
<td>Mild or moderate pulmonary artery stenosis</td>
<td>16</td>
<td>4</td>
</tr>
<tr>
<td>Peripheral pulmonary artery stenosis</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Azygos extension of inferior vena cava</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Small ventricular septal defect</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Small patent ductus arteriosus</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Mild coarctation of aorta</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Small coronary artery–pulmonary trunk fistula</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Anomalous right subclavian artery</td>
<td>2</td>
<td>0.01</td>
</tr>
<tr>
<td>Dextrocardia (isolated)</td>
<td>1</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Data from 443 patients undergoing repair at GLH from 1957 to 1983. Some patients had more than one anomaly, so the figures are not cumulative.
CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Symptoms, clinical features, and signs in ASD and related conditions producing left-to-right shunting at the atrial level are related largely to size of the left-to-right shunt. Thus, in general, when $Q_p/Q_s$ is less than 1.5, there are neither signs nor symptoms of the shunt, and this is often true with a $Q_p/Q_s$ up to 1.8. When $Q_p/Q_s$ is larger than this, signs of the shunt are usually present, and symptoms appear eventually (see “Changes in Pulmonary/Systemic Blood Flow Over Time” later under Natural History). Infants present an exception to these generalizations. Their clinical features are often atypical; for example, splitting of the second heart sound is unrelated to $Q_p/Q_s$.

Determinants of Interatrial Shunting

Left-to-right shunting across a nonrestrictive (>2 cm in an adult) ASD under ordinary circumstances is a function of the relative compliance (reflected in the diastolic pressures) of RVs and LVs. RV compliance in particular is unpredictable and is one factor causing variability in $Q_p/Q_s$. A compliant distensible RV (in association with a normal pulmonary vascular bed) will permit a large shunt; a less compliant one (such as may result from pulmonary hypertension or from morphologic RV changes occurring later in life) permits a more modest shunt. LV compliance tends to decrease with age, which tends to increase $Q_p/Q_s$ as patients become older. Shunting is increased by systemic hypertension when this results in decreased LV compliance.

Mitrail regurgitation or stenosis increases $Q_p/Q_s$. When the ASD is small and flow is restrictive, left-to-right shunting is limited. Even then, mitral stenosis may elevate left atrial pressure sufficiently that a large left-to-right shunt through all phases of the cardiac cycle results, leading to a soft continuous murmur.

Symptoms

Symptoms may persist for several decades, but when they occur, they consist of effort breathlessness and a tendency toward recurrent respiratory tract infections. Palpitation from paroxysmal atrial tachycardia or atrial fibrillation may occur later in life. Older adults may present with chronic heart failure with fluid retention, hepatomegaly, and severe cardiac cachexia. Occasionally an infant with ASD and a large left-to-right shunt, often in association with PAPVC, may have heart failure with tachypnea, but this is uncommon. In such infants, other associated malformations may contribute to the heart failure.

Atypical presentations occur. Rarely, an unequivocal history of cyanosis may bring a patient with an uncomplicated ASD to medical attention. For example, a large fossa ovalis ASD extending to the IVC may cause streaming of blood from the IVC into the left atrium, with resultant cyanosis. This coincides with occasional bidirectional shunting in patients with otherwise uncomplicated ASDs, usually older patients. For the same anatomic reasons (see Morphology, earlier), patients may present with paradoxical emboli or cerebral infarctions. This presentation occurred in 9 (2%) of a Mayo Clinic series of 546 patients.

Infrequently the presentation may be modified by presence of severe pulmonary hypertension, in which case cyanosis, effort intolerance, and hemoptyis may be present.

Signs

Clinical signs diagnostic of a large shunt at the atrial level ($Q_p/Q_s > 1.8$ to 2.0) are:

- Overactive left parasternal systolic lift
- Fixed splitting of the second heart sound throughout the respiratory cycle (absent when large $Q_p/Q_s$ is from PAPVC with an intact atrial septum)
- A soft pulmonary midsystolic flow murmur (in second and third left intercostal spaces)
- A mid-diastolic tricuspid flow murmur (in fourth and fifth left intercostal spaces) present in borderline situations only on inspiration

This last sign is occasionally absent, however, particularly in older patients and in those with a larger shunt.

In addition, an extremely large shunt produces a more marked left-sided precordial RV lift, occasionally some prominence of the left anterior chest wall, and leftward displacement of the cardiac apex. Many such patients are short and thin. When heart failure is present, jugular venous pressure is elevated, the liver is enlarged, and there is gross cardiomegaly.

Tricuspid regurgitation produces systolic liver pulsation and a greater tendency to ascites and peripheral edema. Important pulmonary hypertension is evident clinically by accentuation of the second heart sound and a more marked RV and pulmonary artery lift. A pulmonary regurgitation murmur may be heard, as well as a murmur of tricuspid regurgitation.

Chest Radiography

Chest radiography reflects the large $Q_p/Q_s$. The right atrium and right ventricle are large. The pulmonary trunk shadow in the upper left portion of the cardiac silhouette is enlarged, and right and left pulmonary arteries are enlarged to the periphery of the lung field. In general, pulmonary vascular markings are increased, or plethoric. The shadow of the transverse aortic arch is abnormally small. Patients with heart failure may have interstitial pulmonary edema and areas of pulmonary consolidation and atelectasis. These signs are probably secondary to compression of smaller airways by enormously enlarged small pulmonary vessels.

The chest radiograph may suggest the specific anatomic diagnosis. Occasionally the right superior pulmonary vein can be identified lying more superiorly than normal (Fig. 30-7), leading to suspicion of sinus venous syndrome. A crescentic shadow more or less parallel to the right-sided heart border (Fig. 30-8) suggests the diagnosis of anomalous pulmonary venous connection of right pulmonary veins to IVC (scimitar syndrome).

Electrocardiography

Electrocardiogram (ECG) almost always shows the pattern of incomplete right bundle branch block and a clockwise frontal loop. Left axis deviation and a counterclockwise loop strongly suggest an AV septal defect, although this pattern occurs in about 10% of patients with fossa ovalis ASDs.
PART VII Congenital Heart Disease

localization of subcaval defects and anomalous pulmonary venous connection is usually possible. Addition of Doppler color flow interrogation allows a reasonable estimate of $Q_p/Q_s$.

Magnetic Resonance Imaging

Limitations of echocardiography in delineating anomalous pulmonary venous connection can be largely overcome with magnetic resonance imaging (MRI). Anatomic detailing of pulmonary venous connection and calculation of $Q_p/Q_s$ are generally reproducible.

Cardiac Catheterization and Cineangiography

When diagnosis of a typical and apparently uncomplicated ASD has been made by noninvasive methods in children, adolescents, and young adults, cardiac catheterization is not required. The surgeon then becomes responsible for confirming the type of ASD at operation and presence or absence of any anomalous pulmonary venous connections. Cardiac catheterization and appropriate cineangiography are indicated in infants (because of possible associated anomalies), in many adults (for assessing possible pulmonary hypertension and status of mitral valve), and in any patient in whom noninvasive tests suggest PAPVC. Coronary angiography is performed in patients older than 35 to 40 years.

Assessment of operability in patients with pulmonary hypertension is particularly challenging. Even in Eisenmenger syndrome with shunt reversal at atrial level, pulmonary artery pressure ($P_{PA}$) is rarely more than two thirds that of systemic pressure. (There is no transmission of systemic pressure across the defect, as is the case with large defects at ventricular or ductus levels; see “Cardiac Catheterization” under Clinical Features and Diagnostic Criteria in Chapter 35.)

The most reliable criterion of inoperability is the absolute level of pulmonary vascular resistance normalized to body surface area ($R_pI$) and calculated when possible using measured, rather than assumed, oxygen uptake. $Q_p/Q_s$ or resistance ratios are much less discriminating. In fact, precise criteria have not been established as accurately for ASD as for VSD. Using VSD criteria (with no reason to believe these are not equally applicable to ASD), a resting $R_pI$ of 8 U · m$^2$ or more may preclude complete operative closure. In this event, $R_pI$ must also be calculated while using a pulmonary vasodilator (isoproterenol, tolazoline, or 100% oxygen).

If arterial desaturation (<97%) exists when measured by the usual finger sensor, cardiac catheterization is indicated in both adults and children. Interventions such as 100% $O_2$, exercise, and nitric oxide (NO) are appropriate to gauge pulmonary vascular reactivity, response of pulmonary vascular resistance, and reversion to a strictly left-to-right shunt condition. If arterial oxygen saturation ($S_{aO_2}$) increases to normal levels and pulmonary vascular resistance falls, operation can be done even in the presence of intermittent arterial desaturation (right-to-left shunt).

A vasodilator must produce a fall in $R_pI$ to below 7 U · m$^2$ before the patient can be considered operable, because only then can pulmonary vascular disease be expected to regress. Otherwise, disease is likely to progress despite closure of the ASD. Progressive pulmonary vascular disease is less well tolerated when the atrial septum is intact, because the right side of the heart is then unable to decompress.
through a right-to-left shunt at atrial level; thus, ASD closure under such circumstances usually decreases life expectancy.

Cardiac catheterization and angiography are also useful in defining anatomic details of related conditions that can cause shunting at the atrial level. Increased \( \text{SaO}_2 \) in the low SVC provides presumptive evidence of sinus venosus syndrome, and this becomes virtually certain if the catheter can be passed through a subcaval ASD into the left atrium. An indicator dilution curve obtained after injecting dye into the SVC may show some right-to-left shunting, which is generally completely absent in patients with a fossa ovalis ASD (who may have right-to-left shunting from the IVC). In addition, curves obtained after injection into the right pulmonary artery generally show a much larger left-to-right shunt, a result of the anomalously draining right pulmonary veins, than curves obtained after injection into the left pulmonary artery.

Identification of the specific anatomic details of sinus venosus syndrome is best accomplished by angiography after right pulmonary artery injection, because the typical location and drainage of the right superior pulmonary vein can then be seen. Pulmonary artery injection may confirm anomalous connection of the right pulmonary veins to the right atrium or IVC (see Fig. 30-8), of left veins to brachiocephalic or other veins, or of bilateral anomalous pulmonary venous connections. When anomalous connection of the right pulmonary veins to the IVC is demonstrated, aortography should
Survival

In 1970, Campbell published the most detailed study available on survival of patients with ASD treated nonsurgically. Transformation of these findings into conventional survival format and comparison with life expectancy of the general population provide good insight into the life expectancy of patients with ASD (Fig. 30-10). Campbell’s data support the idea that only 0.1% of individuals born with a large ASD and no other important cardiac anomaly die in infancy, and that few who are unrepaired die in the first or second decade. About 5% to 15% die in the third decade, usually with pulmonary hypertension and Eisenmenger syndrome. Premature late death with heart failure occurs in an increasing proportion after the fifth decade. Even so, probably no more than 25% of persons born with a large ASD die from the defect, because lethal manifestations of the disease tend to occur so late in life that other unrelated conditions cause death first.

The natural history of patients with sinus venosus syndrome and most other types of PAPVC and ASD is similar to that of patients with large fossa ovalis ASD. Patients with sinus venosus syndrome in the fourth to sixth decades present with heart failure or severe pulmonary hypertension from pulmonary vascular disease. The natural history of scimitar syndrome is not clear. Presumably, patients

NATURAL HISTORY

The natural history of persons born with ASDs and related conditions producing left-to-right shunts at atrial level is not known precisely, but its general characteristics have been described. Calculations of $Q_p/Q_s$ are of particular importance in patients with isolated PAPVC of only part of one lung. An operation is not indicated when the ratio is less than 1.8 (see Indications for Operation later in this chapter). This approach is especially relevant with isolated connection of some of the right upper lobe veins to the high SVC, because diversion or transfer to the left atrium is quite difficult (and probably needless). Even when only the right superior pulmonary vein is involved and the atrial septum is intact, the shunt may be greater than this, presumably because right atrial and caval pressures are distinctly lower than left atrial pressures, producing a larger-than-usual pulmonary venous gradient.

Figure 30-9 Transesophageal echocardiogram of fossa ovalis atrial septal defect. A, Arrow indicates dropout of atrial septum with clear evidence of tissue superiorly and inferiorly (above atrioventricular valves), diagnostic of fossa ovalis (secundum) defect. B, Blood flow is directed through the defect left to right from left to right atrium. C, Negative image of left-to-right flow during injection of saline (as contrast). Key: LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. (From Lang and Marcus.)

also be done to identify any anomalous systemic arteries from the abdominal or thoracic aorta to the right lower lobe. If the right lung is small, if the right lower lobe is contracted or seems otherwise abnormal on chest radiography, or if the patient gives a history of hemoptysis or recurrent pulmonary infections, bronchoscopy or bronchography is also indicated.
without important anomalies of the right lung and with a large left-to-right shunt have a life history similar to patients with a large fossa ovalis ASD. Those with right lung hypoplasia, however, often have a life history dominated by their pulmonary pathology, including hemoptysis and recurrent pulmonary infections. When there is isolated PAPVC of part of one lung and Qp/Qs is less than 1.8, life expectancy may be normal. Rarely, paradoxical emboli occur in patients with sinus venous syndrome (from SVC) as well as in those with fossa ovalis ASDs (from IVC).

Pulmonary Hypertension

In a UAB surgical series, 14% of patients catheterized had pulmonary hypertension with mean PPA greater than 25 mmHg. In a GLH surgical series, systolic PPA was greater than 50 mmHg in 13% of catheterized patients and 11% of the total series (Fig. 30-11). Prevalence of elevated RpI (≥4.5 U · m²) was 4.5%, and rare (1%) in patients younger than 20 years of age. In a few high-altitude locations, however, prevalence of pulmonary hypertension is greater. Cherian and colleagues reported that in their region of India, pulmonary hypertension was present in 13% of patients younger than age 20. Ghisla and colleagues in 14%. Pulmonary hypertension is particularly prevalent in patients with scimitar syndrome, partly due to increased pulmonary blood flow but also to stenosis of the anomalous vein, presence of systemic arterial collaterals to the right lung, or reduction of the pulmonary vascular bed on the right side.

Functional Status

Probably only about 1% of patients born with a large ASD have symptoms during the first year. Most are asymptomatic through the first and second decades, although many are short and thin. Effort intolerance and easy fatigability may develop in the second or third decade or as late as the fifth or sixth decade. These symptoms progress gradually to fluid retention, hepatomegaly, and elevated jugular venous pressure, leading to gradually increasing disability. These phenomena are well exemplified in the surgical experience, in which preoperative New York Heart Association (NYHA) functional class and age at operation are moderately well correlated (r = .61, P < .05) (Table 30-2). When heart failure becomes advanced, both mitral and tricuspid regurgitation are likely to have developed.

Spontaneous Closure

Spontaneous closure of a hemodynamically significant isolated ASD occasionally occurs in the first year. Cockerham and colleagues found closure in 22% of 87 patients, and Ghisla and colleagues in 14%. Smaller left-to-right shunts were present in patients whose defects spontaneously closed than in those whose did not. Spontaneous closure is uncommon after the first year, although Ghisla and colleagues found that closure occasionally occurred in the second year.

Table 30-2 Relationship between New York Heart Association Functional Class and Age at Operation

<table>
<thead>
<tr>
<th>Preoperative NYHA Class</th>
<th>Age (Years)</th>
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<tr>
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<td>Mean</td>
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<tr>
<td>I</td>
<td>16</td>
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<td>II</td>
<td>32</td>
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<tr>
<td>III</td>
<td>50</td>
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<td>IV</td>
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Changes in Pulmonary/Systemic Blood Flow Over Time

As already noted, decreasing LV compliance increases $Q_p/Q_s$ in patients with ASD, and this may develop during the fifth and sixth decades. Systemic arterial hypertension accelerates this process and may unmask an ASD that was not an important shunt before onset of decreased LV compliance. It is also likely that most ASDs increase in size as time passes; this has been clearly demonstrated in the case of patent foramen ovale. The direct relationship between $Q_p/Q_s$ and the tendency toward mitral valve prolapse also support the concept that the shunt increases with age. These increases in $Q_p/Q_s$ with time do not occur when the shunt is due to anomalous pulmonary venous connection without ASD. $Q_p/Q_s$ decreases when pulmonary hypertension develops, a result of decreased RV compliance that accompanies RV hypertrophy (see “Determinants of Interatrial Shunting” under Clinical Features and Diagnostic Criteria).

Right Ventricular Function

RV volume overload and consequent increased RV diastolic dimensions are characteristic of patients with a hemodynamically significant ASD or PAPVC. The ventricular septum is displaced posteriorly and leftward under such circumstances, but systolic anterior motion of the septum occurs. These features are well tolerated by the RV for many years, much longer than for the volume-overloaded left ventricle and probably longer than for volume overload produced by acute tricuspid or pulmonary valve regurgitation. RV failure eventually occurs, however, with decreased RV ejection fraction and hypokinesia. Doty and colleagues demonstrated loss of coronary reserve in patients with ASD and volume-induced RV hypertrophy, which contributes further to development of RV failure. Associated signs and symptoms of elevated systemic venous pressure then develop (peripheral edema, elevated jugular venous pressure, hepatomegaly, and finally ascites), often with tricuspid regurgitation.

These RV phenomena have been documented by several studies. Liberthson and colleagues found increased RV volume but normal (64%) ejection fraction in 9 asymptomatic patients with a mean age of 25 years. However, 11 symptomatic patients with a mean age of 52 years had diffuse RV hypokinesia and ejection fraction averaging 36%, in addition to increased RV volume. In a possibly related finding, adult patients with ASD but without pulmonary hypertension occasionally have marked pulmonary valve regurgitation, which disappears after ASD repair.

Left Ventricular Function

Most adult patients with hemodynamically significant ASD or PAPVC have normal LV systolic dimensions but subnormal diastolic dimensions. Some loss of LV functional reserve is present in most adult patients and in some children with ASD. In contrast to normal persons, such individuals do not increase LV ejection fraction during maximal exercise (Fig. 30-12), although resting ejection fraction is usually within normal limits. These preoperative LV abnormalities likely result from effects of the volume-overloaded right ventricle. Even in the absence of symptoms of systemic venous hypertension from RV failure, LV structure and function are influenced by increased RV volume rather than changes in LV compliance.

Ativoventricular Valvar Dysfunction

As discussed earlier, important mitral regurgitation is present in 2% to 10% of adults with large ASDs, and both mitral and tricuspid regurgitation may become prominent in older patients who develop heart failure. When viewed at operation, the tricuspid valve does not appear to be intrinsically abnormal. Presumably, regurgitation develops because of anular dilatation and lack of proper shortening of the tricuspid anulus during systole, secondary to RV enlargement resulting from long-standing volume overload.

Supraventricular Arrhythmias

After the third decade, supraventricular arrhythmias complicate the natural history of patients with large ASDs and related conditions in increasing numbers over time. Most often this begins with paroxysmal atrial fibrillation, which gradually becomes permanent. Atrial fibrillation was present in 15 (20%; CL 15%-26%) of 75 patients over age 40 operated on by Magilligan and colleagues. Of 19 patients preoperatively in NYHA class III or IV, 47% (CL 34%-64%) had this
arrhythmia, compared with 11% (CL 6%-17%) of 56 patients in class I or II. St. John Sutton and colleagues found that 56% of their patients over age 60 had atrial fibrillation at operation.\textsuperscript{S15}

In addition, more subtle abnormalities of conduction system function develop. Benedini and colleagues found concealed sinus node dysfunction in 17 (65%; CL 53%-76%) of 26 adult patients with fossa ovalis ASD, which became evident only with electrophysiologic testing.\textsuperscript{R5} Such abnormalities are less common in children with ASDs.\textsuperscript{R8}

Systemic Arterial Hypertension

Adult patients with hemodynamically important ASDs are likely to have systemic arterial hypertension. In a Mayo Clinic study, 25 (38%) of 66 patients had systemic arterial blood pressure above 150/90, a higher proportion ($P < .01$) than an age-matched general population.\textsuperscript{S15} As noted, this relationship may result partly from the effect of hypertension on shunt size.

**TECHNIQUE OF OPERATION**

Fossa Ovalis Atrial Septal Defect

Anesthetic management, positioning and preparation of the patient, median sternotomy, and preparations for CPB are discussed in detail in Section III of Chapter 2 and in Chapter 4. An alternative to the midline skin incision may be used for cosmetic reasons; in this approach, a bilateral fourth inter-space submammary skin incision is made and a skin flap raised superiorly and inferiorly before the sternum is incised vertically in the usual way. However, some surgeons have expressed concern regarding breast development and symmetry late following right submammary incisions in females. Alternatively, a right anterolateral fifth intercostal space incision may be used if the patient expresses concern about the cosmetic effects of a midline scar. Repair of ASD may also be accomplished using the small lower sternotomy approach and also a small vertical right parasternal incision. Each requires modification of the setup for caval cannulation (see Section III in Chapter 2).

In children and young adults with uncomplicated ASDs, routine placement of a left atrial pressure monitoring catheter is usually unnecessary, but such monitoring should be done routinely in older patients, whose left atrial pressure may be considerably higher than right atrial pressure after repair.

After the incision is made and pericardial stay sutures are placed, intrapericardial anatomy is assessed. The characteristic large right atrium and RV of ASD are noted, as well as the normal-sized left atrium and LV. A left SVC in the fold of Marshall is sought. The external position and connections of the right and left superior and inferior pulmonary veins are noted. Optimally, TEE is available to establish the position of the ASD, relationship of the pulmonary veins, and function of the mitral and tricuspid valves.

The patient is heparinized and arterial cannula inserted. Direct caval cannulation with two angled cannulae is generally employed. CPB is established, with the perfusate temperature at 34°C. The cardioplegic needle or aortic root catheter is now placed in the ascending aorta, the aorta clamped, and cold cardioplegic solution injected. Rewarming of the patient with the perfusate is begun once the heart is cold and isolated. The caval tapes are “snugged,” and the right atrium is opened obliquely (Fig. 30-13). A left atrial suction catheter is not inserted through the left atrial wall in fossa ovalis ASD, because it is unnecessary and imposes a remote risk of cerebral air embolism.

A few fine stay sutures are placed on the edges of the atriotomy incision. Blood in the left atrium is suctioned only enough to clearly expose the edges of the ASD; evacuation of more blood than this from the left side of the heart needlessly exposes the patient to risk of air entrapment and subsequent air embolization. An exception to this policy is presence of mitral valve pathology.

The entire right atrial internal anatomy is examined, particularly identifying the limbus and defining any rim of the ASD. The relationship of the defect to the ostium of the

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**Figure 30-13** Internal anatomy of a fossa ovalis (secundum) atrial septal defect as seen through usual atrial incision. Key: ASD, Atrial septal defect; IVC, inferior vena cava; SA, sinoatrial; SVC, superior vena cava.
limbic tissue with the first and last bites of this stitch (Fig. 30-14), which must be inferior to any remaining fenestrations. Great care is taken to avoid confusing the eustachian valve of the IVC with the remnant of the floor of the fossa ovalis. Such an error results in connecting the IVC to the left atrium, which can occur when the operation is done under circulatory arrest and there is no IVC cannula, or when direct caval cannulation is used. After this half purse-string stitch is tied, the ASD becomes slitlike. Before last stitch is tied, anesthesiologist places positive pressure on lung to express air from left atrium. Completed repair.

Key: CS, Coronary sinus; RSPV, right superior pulmonary vein.

Possible fenestrations in the valve (floor) of the fossa ovalis are sought; these are usually between the fossa ovalis and limbus anteriorly or near the IVC inferiorly. When present in thin tissue, fenestrations may be joined to the main defect by excising sufficient tissue to create an edge strong enough to hold sutures well, or the fenestrated tissue simply may be imbricated into the suture line.

Usually the fossa ovalis ASD is closed directly (see “Direct Suture versus Patch Repair” under Special Situations and Controversies later in this chapter). The suturing is begun at the inferior angle by placing a half purse-string stitch. Care is taken to catch good, substantial anterior and posterior limbic tissue with the first and last bites of this stitch (Fig. 30-14), which must be inferior to any remaining fenestrations. Great care is taken to avoid confusing the eustachian valve of the IVC with the remnant of the floor of the fossa ovalis. Such an error results in connecting the IVC to the left atrium, which can occur when the operation is done under circulatory arrest and there is no IVC cannula, or when direct caval cannulation is used. After this half purse-string stitch is tied, the ASD assumes a slitlike appearance. The suture line is now carried superiorly, catching tough limbic tissue anteriorly and posteriorly. To avoid damaging the AV node, the sutures must not be placed too far from the edge anteriorly.

Before the last few stitches are pulled up, a clamp or tissue forceps is placed in the aperture, and the anesthesiologist inflates the lung to expel any air from the left atrium. The suture line is snugged while lung inflation is maintained, and

Figure 30-14  Repair of fossa ovalis atrial septal defect (ASD). A, Usual oblique right atriotomy is made and retracting sutures placed. B-C, After exposure is arranged and all structures examined (orifices of pulmonary veins, valve of inferior vena cava [eustachian] coronary sinus), the first sutures are taken as a half purse-string stitch. If ASD extends to inferior vena cava (IVC), initial sutures are placed in floor of the IVC; eustachian valve of the IVC must be noted so that it is not erroneously included. D, After first set of stitches is tied, ASD becomes slitlike. E, Before last stitch is tied, anesthesiologist places positive pressure on lung to express air from left atrium. F, Completed repair. Key: CS, Coronary sinus; RSPV, right superior pulmonary vein.
Coronary Sinus Atrial Septal Defect

Because coronary sinus ASDs are close to the AV node (Fig. 30-15), stitches must be placed near the edge of the defect superiorly in tissue that may not be strong. For these reasons, patch closure is generally advisable. Additionally, when a coronary sinus ASD is identified, presence of a completely or partially unroofed coronary sinus must be ruled out (see Technique of Operation in Chapter 33). 

**Sinus Venosus Atrial Septal Defect**

Preparation and positioning of the patient are as usual. After sternotomy, the pericardium is cleared of pleural reflections bilaterally, and a large pericardial piece is removed and set aside between moist towels or in 0.6% glutaraldehyde. After the remaining pericardium is widely opened, stay sutures are placed and the anatomy examined. The right superior pulmonary vein is easily seen attached to the low SVC or SVC–right atrial junction. At this point, the pulmonary vein (or veins) should be differentiated from the azygos vein, which is slightly more cephalad and directed more medially. Size of the SVC is noted, as is the possible presence of a left SVC, in which case the right-sided SVC is likely to be small. The right atrium and RV are usually considerably enlarged.

**Posterior Atrial Septal Defect**

If the anomaly is a pure posterior ASD, closure by direct suture is possible in a manner similar to that described in the previous text. If the posterior ASD is confluent with a fossa ovalis ASD, the defect may be too large for direct closure. Then a patch of pericardium, knitted polyester velour, or polytetrafluoroethylene (PTFE) is used.
clamped, and cold cardioplegia infused (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). The caval tapes are secured. In infants, repair may be done with a single venous cannula and hypothermic circulatory arrest. When the aorta is clamped, the perfusate temperature is stabilized at 25°C to 32°C.

When configuration of the superior pulmonary vein is usual and the SVC–right atrial junction is wide, the right atrium is opened through the usual oblique incision beginning at the base of the right atrial appendage and extending down toward the IVC cannula (Fig. 30-16). This does not damage the sinoatrial node or its artery. Stay sutures are placed. A pump sump-sucker is placed across the foramen ovale into the left atrium (or through a stab wound), or no left atrial vent may be used. The repair directs pulmonary venous drainage through the ASD into the left atrium while closing the interatrial communication (see Fig. 30-16). A pericardial baffle forms approximately the anterior half of this internal conduit. Width of the pericardial patch should be about 1.5 times the diameter of the ASD, and length about 1.25 times the estimated length of the distances from the superior edge of the anomalous vein to the inferior edge of the ASD. This ensures an adequate pulmonary venous pathway and does not obstruct the SVC.

After the ASD repair is repaired, the sump (if used) is removed and the created defect closed. Rewarming is begun, and with suction on the needle vent in the ascending aorta, the aortic clamp is released. The right atriotomy is closed, and the operation is completed as usual (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

When the right superior pulmonary veins enter more cephalad in the SVC (more than about 2 cm above the cavoatrial junction) or when the SVC is small (as in the presence of bilateral SVCs), the single patch technique described above may require a long tunnel or create possible SVC obstruction, or both. Because of concerns about the potential for sinus node dysfunction with incisions across the cavoatrial junction, the Warden operation may be used (Fig. 30-17). After extensive mobilization and division of the azygos vein, the SVC is divided cephalad to the anomalously connected right pulmonary veins. The central end is closed, and as a final step the distal end is anastomosed to the right atrial appendage. Particular care is needed to completely excise all trabeculated muscle within the appendage and the associated pathway into the right atrial chamber. From within the right atrium, the inferior lip of the subcaval ASD is joined to the right atrial wall, anterior and lateral to the caval orifice. This closes the interatrial communication and diverts pulmonary venous drainage from the anomalously connected right pulmonary veins to the left atrium.

Another alternative is the V-Y-plasty technique. A vertical atriotomy is made posteriorly and extended into the SVC posterior to the sinus node and just in front of the anomalous veins (Fig. 30-18) in preparation for a V-Y-plasty enlargement of the SVC.

Others have recommended near-routine use of a two-patch technique, in which the original incision is extended across the cavoatrial junction below the sulcus terminalis and just anterior to insertion of the anomalous pulmonary veins. After placing the internal baffle, the incision is closed with an autologous or bovine pericardial patch.

Anomalous Connection of Right Pulmonary Veins to Right Atrium

The operation begins exactly as described for sinus venous malformation, including opening the right atrium through the usual oblique incision. The interior of the right atrium is examined, anomalous connections of the right pulmonary veins and normal connections of the left pulmonary veins to the left atrium are confirmed, and any defects in the atrial septum are identified.

When the atrial septum is intact, repair can often be accomplished by making a longitudinal incision in it next to the atrial wall posteriorly and resutting it to the lateral right atrial wall in front of the right pulmonary vein orifices. Alternatively, and particularly when geometry in the right atrium does not lend itself to this simple repair, the fossa ovalis and posterior limbic tissue may be excised and a pericardial, PTFE, or knitted polyester patch used for baffle reconstruction (Fig. 30-19).

When an ASD is present, repair is similar. When the defect is large and of the fossa ovalis or confluent type, a patch similar to the one shown in Fig. 30-19 is used. Occasionally, and particularly when the associated ASD is posterior, repair by direct suture is possible.

Anomalous Connection of Right Pulmonary Veins to Inferior Vena Cava (Scimitar Syndrome)

Initial stages of the operation for scimitar syndrome proceed as described for sinus venous malformation. An internal conduit is then constructed within the right atrium to conduct the right pulmonary venous blood from its entrance into the IVC across the atrial septum into the left atrium.

In small infants, the entire repair may be done during hypothermic circulatory arrest. In older patients, part of the repair can be performed during hypothermic circulatory arrest; alternatively, the entire repair can be performed during conventional CPB at 20°C to 28°C. In the latter approach, the IVC tape may be passed inferior (caudal) to the entrance of the anomalous pulmonary vein into the IVC, and a right-angled metal cannula can be used to cannulate the IVC inferior to this point. This possibility depends on whether the anomalous vein enters at the IVC–right atrial junction. Alternatively, the common femoral or external iliac vein can be cannulated for IVC return.

In any case, CPB is established with two venous cannulae, and if part of the repair is to be made with circulatory arrest, the IVC tape is placed on the cardiac side of the IVC entrance of the anomalous vein. The aorta is clamped and cold cardioplegic solution infused. After caval tapes have been tightened, the right atrium is opened with the usual oblique incision and carried down to the IVC. If present, the valve of the fossa ovalis is completely excised to create a large ASD (Fig. 30-20). The pericardial patch is trimmed according to the measurements made, and stay sutures are applied at the four corners.

Circulatory arrest is established with the patient’s nasopharyngeal temperature at 18°C when this modality is used, and the IVC cannula is removed. Otherwise, repair proceeds during CPB. The pericardial patch is sewn into place so as to form the anterior wall of a conduit between the entrance of the anomalous vein and the defect created in the atrial septum (see Fig. 30-20). If repair has been done during circulatory
Figure 30-16  Repair of sinus venosus malformation, which typically consists of subcaval atrial septal defect (ASD) associated with partial anomalous pulmonary venous connection of right superior pulmonary vein (RSPV) to low superior vena cava (SVC). A, Usual atriotomy is away from sinus node. B, Incision can be extended superiorly and medially to sinoatrial node. Subcaval ASD is superior to limbus. At times the SVC overrides the defect to drain in part directly into left atrium. ASD is far removed from tricuspid valve and atrioventricular node. First stitches for inserting pericardial patch are shown at right lateral edge of SVC orifice at its junction with laterally placed orifice of RSPV. Patch is sewn into place with continuous 4-0 or 5-0 polypropylene suture. Suture line continues medially in an anterior and posterior direction to form a tunnel or roof leading the anomalous RSPV through ASD. C, Convex roof of tunnel has been completed, and blood from anomalously connected RSPV drains beneath this roof into left atrium. Pathway from SVC to right atrium is unobstructed. When SVC is cannulated directly, exposure is good through this incision, and augmentation of the atrial closure is not necessary. D, Transverse section through repair seen from below.
Figure 30-17  Warden operation for sinus venosus malformation with right upper and middle lobe pulmonary veins entering superior vena cava (SVC). A, Right upper and middle pulmonary veins entering SVC. Right atrial appendage is amputated. B, High SVC or innominate vein is cannulated. Dashed line indicates the transecting incision in SVC. C, Cephalad end of transected SVC is anastomosed to amputated right atrial appendage. For mobilization, azygous vein is divided. D, Small incision is made in right atrial wall. Lateral edge of SVC orifice is sutured to lower rim of subcaval atrial septal defect (ASD), or the pathway is completed with a pericardial or polytetrafluoroethylene patch. Cardiac end of transected SVC is closed. E, Right pulmonary vein blood now flows (arrows) across the roofed ASD into left atrium. Key: RA, Right atrium; RAA, right atrial appendage. (From Warden and colleagues.)
Figure 30-18  V-Y atroplasty technique for enlarging superior vena cava (SVC). A, Initial incision is longitudinal and does not cross SVC–right atrial junction unless SVC enlargement is believed to be required. In such cases, a secondary incision is then added to create a V flap of right atrial wall. B, SVC is enlarged by advancing tip of V flap to apex of SVC incision. C, Augmentation is completed with a continuous suture line (X in B is brought to Y in C).

Figure 30-19  Repair of anomalous connection of right superior and inferior pulmonary veins to right atrium without atrial septal defect. A, Right atrial incision is the usual oblique transverse one, and fossa ovalis and posterior limbus are excised. B, Repair is made by replacing excised portion of atrial septum with a patch, sewn to right of (anterior to) the right pulmonary vein orifices. Key: LA, Left atrium; RA, right atrium.
Figure 30-20  Repair of partial anomalous pulmonary venous connection, right pulmonary veins to inferior vena cava (scimitar syndrome).

A, Usual oblique right atriotomy is made, extending it to inferior vena cava (IVC). B, Valve (floor) of fossa ovalis (septum primum) is excised, creating an atrial septal defect that extends almost to IVC. C, During a short period of circulatory arrest or with sucker trickle flow, IVC cannula is removed. Distance between inferior aspect of orifice of anomalous vein entrance into IVC and superior limbus is measured, as is width of fossa ovalis. Pericardial patch is trimmed in a rectangular shape, with length about 1.25 times the measured length and width about 1.5 times the width of the fossa ovalis. Using a continuous polypropylene suture, patch insertion is begun at inferior aspect of orifice of anomalous pulmonary vein in IVC, after this orifice and that of the hepatic vein are positively identified. Suture line between patch and floor of IVC is carried to patient's left and then up toward and onto anterior limbus, where it is held. With the other arm of original suture, patch is attached above orifice of anomalous vein as suture line is carried superiorly. IVC cannula is reinserted, and cardiopulmonary bypass is resumed at usual flow. D, Patch is then attached successively to posterior limbus, superior limbus, and anterior limbus, and tied there to other end of suture. E, Patch now forms approximately half of an intraatrial internal conduit conducting right pulmonary vein blood across defect created in the fossa ovalis into the left atrium. This is drawn in parasagittal section. Key: ASD, Atrial septal defect; LA, left atrium; RA, right atrium; SVC, superior vena cava.
arrest, the IVC cannula is reinserted, caval tape retightened, CPB reestablished, and rewarming with the perfusate begun. The anomalous vein is observed from time to time to ensure pressure in it is not elevated, because its drainage is now temporarily obstructed by the IVC tape. The right atrium is closed and the caval tapes promptly released. With suction on the aortic needle vent, the aortic clamp is released.

Alternatively, the anomalous pulmonary vein can be disconnected from its low insertion at the cavoatrial junction and reimplemented higher on the right atrial wall with connection via a baffle to the left atrium. As a third option, after disconnection, the anomalous vein can be implanted directly onto the left atrial wall at its rightmost aspect because this area is “bare” (having no natural entrance of right pulmonary veins). Usually, repair of the anomalous venous connection should be complemented by interrupting the aberrant systemic subpulmonary collateral supply to the right lower lobe. This can be accomplished by surgical ligation or catheter intervention. In neonates, it may be sufficient simply to interrupt the aberrant arterial supply and leave the anomalous venous connection intact.

Anomalous Connection of Left Pulmonary Veins to Brachiocephalic Vein

When the atrial septum is intact or there is only a valve-competent foramen ovale, operation is performed using a closed technique. The left chest is entered through a posterolateral incision (Fig. 30-21). The left groin should be prepared and draped for possible surgical access in case cannulation of the left femoral artery and vein are needed for CPB bypass. The anomalous left vertical vein is dissected up to the brachiocephalic vein. Left superior and inferior veins are dissected and mobilized as much as possible. A tape is placed around the left pulmonary artery.

The pericardium is opened, usually behind the phrenic nerve, and a large window is made. A clamp is placed across the very base of the left atrial appendage, and most of the appendage is amputated. The left pulmonary artery is temporarily occluded, the left vertical vein is ligated flush with the brachiocephalic vein, a clamp is placed across its proximal portion, and it is divided as near the ligature as safety allows. The vein is positioned with great care to avoid any rotation and is anastomosed to the base of the left atrial appendage. At least part of the anastomosis is made with interrupted sutures to avoid any possible purse-string effect. Before releasing the clamps, care is taken that no air is in the vein.

When there is an associated fossa ovalis ASD, both the left anomalous pulmonary venous connection and ASD should be repaired. (The first patient undergoing repair of this type of anomalous pulmonary venous connection, reported by the Mayo Clinic in 1953, required later closure of the ASD, at which time the previously made anastomosis was functioning well.) This repair can all be accomplished through a median sternotomy with CPB. The anastomosis between the vertical vein and left atrial appendage can be modified when CPB is used. Ports and colleagues make a long incision in the lateral aspect of the left atrial appendage, carrying it down onto the left atrium. The anomalous vein is cut transversely, then a T extension is made posteriorly. The end-to-side anastomosis is thus extremely wide. Alternatively, a side-to-side vertical vein–left atrial anastomosis is made, ligating the vertical vein at its junction with brachiocephalic vein.

Other Anomalous Pulmonary Venous Connections

Bilateral PAPVCs and rare right or left anomalous connections require individual techniques using principles described for standard repairs.

Treatment of Associated Mitral or Tricuspid Valve Disease

Mitral stenosis is treated by valvotomy. Mitral and tricuspid regurgitation are treated by anuloplasty when possible (see “Repair of Mitral Regurgitation” under Technique of Operation in Chapter 11). If mitral valve replacement is necessary, great care is required because the anulus tends to be friable.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Convalescence of most children and adolescents who had repair of an uncomplicated ASD, as well as most adults operated on before they have reached NYHA functional class IV, is uneventful. They are extubated in the operating room or within a few hours of leaving it. Arterial blood pressure is monitored until the next morning via an arterial catheter, and the atrial pressures via any polyvinyl catheters placed at operation.

Occasionally, older patients have unusually high left atrial pressures (20 to 25 mmHg) in the early hours after repair, presumably because systolic and diastolic LV functions are more impaired than usual by the aging process or by coexisting coronary artery disease, systolic arterial hypertension, or residual important mitral regurgitation that has been underestimated preoperatively. In contrast to a few examples reported in the literature, in which urgent reoperation was performed and the ASD reopened because of severe left-sided heart failure with pulmonary edema, in 35 years of experience with this malformation at GLH, Mayo Clinic, and UAB, no ASD has been reopened. A partial explanation for this may be that ASD closure has not been recommended when the primary problem was LV cardiomyopathy. However, because of these considerations, left atrial pressure is routinely monitored intraoperatively and for about 24 hours postoperatively in older patients.

Occasionally, when mitral regurgitation has been underestimated preoperatively and there are signs of severe pulmonary venous hypertension postoperatively, an urgent echocardiographic study may be required. If important residual mitral regurgitation is detected, reoperation may be necessary to repair or replace the mitral valve.

All patients over age 35 years at operation receive sodium warfarin prophylactically beginning on the evening of the second postoperative day and continuing for 8 to 12 weeks after repair. The rationale is that both pulmonary and systemic arterial embolization occur after repair in patients older than 35 years. Occurrence is particularly high in elderly patients in atrial fibrillation (see Results in text that follows), in whom permanent anticoagulation is usually warranted.
RESULTS

Early (Hospital) Death

Hospital mortality for repair of ASDs and related conditions has approached zero for many years in most cardiac surgical centers throughout the world. In the presence of pulmonary hypertension in the elderly, the imponderables are greater in predicting expected early mortality, but in any case it is generally less than about 3%.

Time-Related Survival

Time-related survival of patients with ASD or PAPVC repaired during the first few years of life is that of the matched general population. When operation is performed later in childhood
or in early adult life, survival is nearly as good.\textsuperscript{55} In older patients, repair of ASD improves life expectancy.\textsuperscript{\texttrademark} However, survival is lower than in the matched population.\textsuperscript{\texttrademark} In an observational study, Konstantinides and colleagues compared surgical closure of ASD to medical treatment in 179 patients over age 40 (mean age 56 ± 9 years). Ten-year survival of the surgically treated patients was 95% vs. 84% for those treated medically.\textsuperscript{\texttrademark}\textsuperscript{10}

Modes of Death

The rare patient who dies in hospital after repair of an ASD or PAPVC usually has a serious coexisting condition such as pulmonary vascular disease or old age. The exception is the rare occurrence of death from air embolization, which is about the only risk in repair of ASDs and the reason for using the particular surgical techniques described (see Technique of Operation earlier in this chapter). Premature late death likewise occurs infrequently and almost exclusively in the types of patients just described. Horvath and colleagues found that premature late death occurred more often in patients undergoing surgery in adulthood when preoperative systolic P\textsubscript{A} was 30 mmHg or greater than when it was less (survival 85% ± 1% vs. 99% ± 6% at 10 years; \textit{P} < .0002).\textsuperscript{\texttrademark}\textsuperscript{10}

Neurologic failure from cerebral embolization or hemorrhage is the most common mode of late death in elderly patients, most of whom have hypertension. Heart failure is the next most common mode of death, again in elderly patients. In rare instances, late death results from severe supraventricular arrhythmias.

Incremental Risk Factors for Death

In contrast to most types of congenital heart disease, patients with ASD or PAPVC rarely have serious important coexisting cardiac anomalies. Therefore, this incremental risk factor is absent. Likewise, neither morphology of the ASD nor morphology of most types of PAPVC is a risk factor for death. Again, in contrast to most types of congenital and acquired heart disease, preoperative functional class is not a confirmed
risk factor for death, probably because the operation is relatively atraumatic and requires only a short duration of CPB and global myocardial ischemia.

**Pulmonary Vascular Disease**

Preoperative pulmonary hypertension severe enough to indicate important pulmonary vascular disease is a risk factor for death, and if severe enough, death may occur early after operation.\(^{2,11}\) This risk factor appears in various forms in different analyses; in the study by Murphy and colleagues, for example, pulmonary vascular disease appears as the level of systolic PPA.\(^{11}\) Elevation of RpI becomes a major risk factor when greater than 6 U · m\(^{-2}\) and may be an irreversible risk when it reaches about 12 U · m\(^{-2}\) (see Special Situations and Controversies later in this chapter).

**Older Age at Operation**

Neither older age at operation nor young age at operation is a risk factor for hospital death. Older age is a risk factor for premature late death, identifiable after the first decade and becoming progressively more powerful as age increases.\(^{11,12}\) Patients in the first decade have about a 98% chance of surviving at least 25 years after repair, those in the third decade a 93% chance, and those in the fourth decade an 84% chance; patients older than about 40 years have even less probability of long-term survival.\(^{14}\) St. John Sutton and colleagues found that 10-year survival was 64% after repair of ASD in patients older than age 60, importantly better than that of similar nonsurgically (“Unoperated”). \(^{7,11}\) -2 Fig. 30-22 -

Late survival of patients over age 60 years after undergoing repair of atrial septal defect (hospital survivors only) compared with survival of an age-gender-matched general population (“Expected”) and with that of patients of the same age treated nonsurgically (“Unoperated”). (From St. John Sutton and colleagues.\(^{13}\))

**Anatomic Type of Interatrial Communication**

The anatomic type of interatrial communication or PAPVC does not appear to affect survival.\(^{2,14,15,11,15,16}\) An exception may be scimitar syndrome, with the right pulmonary veins connecting anomalously to the IVC. Increased risk is caused primarily by abnormalities in the right lung rather than by PAPVC itself.

**Functional Status**

Asymptomatic children have no symptoms after operation, but symptomatic infants undergoing repair of ASD may also experience complete relief of symptoms.\(^{2,14}\) Older symptomatic patients typically show improvement.\(^{2,15,16}\) Forfang and colleagues found that ASD closure in patients over age 40 improved symptomatic state by one NYHA functional class in every patient.\(^{14}\) Both Konstantinides and Gatzoulis and their colleagues reported improved functional status in their surgically treated groups that were over age 40.\(^{1,15,16}\) Even patients undergoing surgery after age 60 showed striking functional and symptomatic improvement: \(^{2,14}\) 87% improved at least one NYHA functional class.

Among the 31 patients preoperatively in NYHA class III or IV in the study by St. John Sutton and colleagues, only two (6%) remained severely disabled.\(^{15}\) This striking symptomatic improvement, even in older patients whose cardiomegaly does not always regress, has been documented by Pearlman and colleagues.\(^{14}\) Excellent treadmill exercise performance and normal maximal oxygen consumption were found in all 14 consecutive patients studied late after repair of ASD, despite 9 with persistently large RV diastolic dimensions.

**Hemodynamic Results**

Important hemodynamic changes occur immediately after closure of an uncomplicated ASD. Mean pressure in the ascending aorta increases, as does mean aortic blood flow.\(^{11}\) There is an immediate reduction in pulmonary blood flow.\(^{11}\) Right atrial pressure decreases and left atrial pressure increases; Søndergard and Paulsen found an average immediate rise of 8 mmHg.\(^{14}\) The small amount of available information indicates that in older patients, RpI drops negligibly late after operation.

**Ventricular Function**

RV diastolic dimensions are strikingly decreased after operation\(^{11}\) but are still above normal in many patients\(^{17,11,16}\) (Fig. 30-23). This finding is consistent with Young’s early observation that some children had important residual cardiomegaly years after complete repair of their ASD, which he correctly ascribed to the secondary cardiomyopathy resulting from chronic RV volume overload.\(^{11}\) Pearlman and colleagues showed an effect of older age at operation in this regard; 7 (64%; CL 44%-81%) of 11 patients aged 10 years or younger at operation had normal or near-normal RV diastolic volumes late postoperatively, whereas only 3 (21%; CL 10%-38%) of 14 patients older than age 25 displayed this finding (\(P\) [Fisher] for difference = .04).\(^{14}\)

In adult patients with preoperatively decreased RV wall motion and ejection fraction, most of whom have elevated right atrial pressure and are importantly symptomatic,
Figure 30-23 Effect of atrial septal defect repair on echocardiographic right ventricular internal dimension (RVID) at end-diastole, left ventricular dimension (LVD) at end-diastole (D) and end-systole (S), and left ventricular fractional shortening (FS). Shaded area, Normal range of fractional shortening (29%-45%); open circles with bars, mean values; solid symbols, three symptomatic patients with marked drop in ejection fraction during exercise. Key: LV, Left ventricular; NS, not significant; Pre, preoperative; Post, postoperative. (From Bonow and colleagues.)

Figure 30-24 Left ventricular ejection fraction at rest and during exercise after repair of atrial septal defect. Open circles with bars, Mean values. (From Bonow and colleagues.)

reduction in RV size after surgical repair is less, and ejection fraction, although higher than preoperatively, remains abnormally low (47% in the experience of Libethson and colleagues17). These patients are improved by operation but do not become asymptomatic. Analogies between this and response to surgery of the volume-overloaded LV are apparent (see “Left Ventricular Structure and Function” under Results in Chapter 12).

Postoperatively, in contrast to the preoperative condition, LV ejection fraction increases normally with maximal exercise (Fig. 30-24). Even in patients who have undergone repair in adult life, exercise ejection fraction is usually normal. This favorable change is the result of ablation of the RV volume overload by closure of the ASD. Also, LV diastolic dimensions, when abnormally small preoperatively, increase to normal within 6 months of operation.8,11,31 The abnormalities of LV geometry present preoperatively are also corrected by repair of the ASD.

Arrhythmic Events

Closure of ASDs in children has been shown to improve AV conduction, decrease AV nodal refractory periods, and improve sinus node function in most patients early postoperatively.8,10,31 Presumably this improvement results from reduction in RV and right atrial volume after ablation of the left-to-right shunt at the atrial level. However, Bolens and Friedli found loss of sinus node function after operation and an atrial ectopic rhythm.8,10 Although possibly the result of direct surgical damage to the sinus node, these effects may represent the unmasking of preoperatively concealed sinus node dysfunction.8,15

Little specific information is available on arrhythmias late after repair of ASDs in infants and children, but presumably these are uncommon. Forfang and colleagues, as well as other groups, found that arrhythmic symptoms regress less frequently than other symptoms.15 Thus, most adult patients with atrial fibrillation preoperatively continue to experience it late postoperatively.11,31 Shah and colleagues, however, as well as Konstantinides, noted a persistent occurrence of new arrhythmias and thromboembolic events in adults followed long term after surgical repair.33,34 Furthermore, at least in patients over about age 40, almost half of those not in atrial fibrillation preoperatively develop it late postoperatively.10,31,33 This tendency to atrial fibrillation or flutter late postoperatively may be less when venous cannulation is directly into the venae cavae rather than through the right atrial appendage.33

These same findings apply after repair of PAPVC, particularly of sinus venous malformation, so the pessimistic view expressed by Clark and colleagues is not justified.8,14 Twenty-three (79%; CL 69%-87%) of the 29 patients followed by Trusler and colleagues after repair of sinus venous malformation were in sinus rhythm late postoperatively, and 6 were in junctional rhythm (one of whom had it preoperatively).7,10,33,34

Also, prevalence of changed heart rhythms after repair is similar in patients with fossa ovalis ASDs and those with sinus venous malformation. Twenty-six (84%; CL 74%-91%) of 31 patients undergoing repair of sinus venous malformation had no change in their preoperative rhythm during the first 7 days after operation, compared with 190 (92%; CL 89%-94%) of 207 such patients undergoing repair of fossa ovalis defects (P|χ²| = .16) (Rouse RG, MacLean WH, Kirklin JW;
unpublished study, 1979). Trusler and colleagues reported similar findings; 4 of 29 children had sick sinus syndrome or junctional rhythm late postoperatively, and all 4 had an atriotomy across the cavoatrial junction.\(^{16}\)

**Thromboembolism**

Both systemic and pulmonary emboli tend to occur in patients with ASDs. Among 587 hospital survivors of ASD repair at Mayo Clinic between 1953 and 1963, Hawe and colleagues found postoperative embolization as late as 11 years after repair.\(^{16}\) A higher incidence was found in patients over age 40, especially those with atrial fibrillation (Fig. 30-25).

**Reintervention**

Recurrent ASD has required reoperation in about 2% of patients. Recurrence of ASD is more likely in older patients with heart failure preoperatively. Reoperation is likewise rarely necessary after repair of PAPVC. In the UAB experience, 1 of 56 hospital survivors required reoperation for partial patch dehiscence resulting in partial SVC obstruction and diversion of the SVC largely to the left atrium. At reoperation an entirely new patch was placed with a good result. Two of 12 patients required reoperation after repair of scimitar syndrome because of stenosis of the surgically created channel. Both had right lung hypoplasia with a Qp/Qs of 1.6. Reoperation carries negligible risk. When occurring beneath a pericardial or polyester tunnel, however, stenosis may be difficult to relieve.

**INDICATIONS FOR OPERATION**

Presence of an uncomplicated ASD or of PAPVC with evidence of RV volume overload is an indication for operation. The indication can be restated as a Qp/Qs of 1.8 or more and at times, if the anomaly is uncomplicated, of greater than 1.5. An exception is patients with scimitar syndrome who have severe hypoplasia of the right lung and a Qp/Qs of less than 1.8; operation, usually lobectomy or pneumonectomy with ligation of the anomalous arterial supply, may be required in these patients because of complications of bronchopulmonary sequestration. Isolated PAPVC of a part of one lung without an ASD is not an indication for operation when Qp/Qs is less than 1.8, particularly because the shunt under such circumstances does not increase with age. Isolated PAPVC of a whole lung is an indication for repair; whenever an entire lung drains anomalously and the atrial septum is intact, only the opposite, correctly draining lung can return oxygenated blood to the systemic circuit. If this normal lung is importantly compromised (e.g., by pneumonia, pneumothorax, or atelectasis from inhaled foreign body or tumor), potentially fatal hypoxia occurs.

Optimal age for operation is 1 to 2 years because of the deleterious effects of longer periods of RV volume overload. However, opportunity to intervene surgically as early as age 1 year is not always present, because diagnosis is often made later in life. Very young or very old age is not a contraindication to operation. Mainwaring and colleagues, however, caution that infants presenting with major symptoms and large fossa ovalis defects may not benefit from ASD closure.\(^{13}\) The inference is that these young patients’ failure to thrive is not related to presence of the defect.

Pulmonary vascular disease of sufficient severity to raise RpI to 8 to 12 U · m\(^{-2}\) at rest and to prevent its decrease to less than 7 with a pulmonary vasodilator is a contraindication to operation (see “Cardiac Catheterization and Cineangiography” earlier in this chapter). Such conditions are usually present with a resting Qp/Qs of less than 1.5 in patients with elevated P\(a\)O\(_2\), but may be present with a Qp/Qs of 2.0. These ideas are inferential and based on postoperative studies in patients with VSDs and elevated RpI.\(^{16}\) Of considerable importance is the interaction of pulmonary and systemic vascular resistance with exercise. As a practical consideration, a marked decrease in peripheral pulse oximetry with exercise strongly suggests sufficient increase in pulmonary vascular resistance to cause right-to-left shunting at the atrial level with exertion. This finding indicates need for extreme caution in proceeding with repair, because loss of the “pop-off” hole during exertion could induce syncope or sudden death.

Associated tricuspid or mitral regurgitation, which occurs especially in older patients, is not a contraindication to operation. If important, such conditions are repaired at closure of the ASD. Grading of mitral regurgitation by angiography and echocardiography may be misleading when major runoff occurs from left to right atrium through the ASD, and the regurgitation becomes more important when the ASD is closed. For these reasons, moderate mitral regurgitation is usually an indication for mitral valve repair.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Closure of Atrial Septal Defects by Percutaneous Techniques**

At least some ASDs can be closed with transcatheter techniques and a device known as the “clam shell,” introduced and manipulated percutaneously.\(^{87}\) The procedure has been successfully performed on an outpatient basis. Currently, 60% to 70% of patients with a fossa ovalis ASD are treated by percutaneous techniques at institutions with the necessary devices and experienced operators. The procedure is limited
to “central” defects with well-defined margins and size of 5 to 20 mm. Potential complications of percutaneous ASD closure include device migration, embolization requiring urgent operation, and residual shunts. With experience, these complications are rare. Simple foramen ovale defects permitting right-to-left shunting and a paradoxical embolus in elderly patients are ideally managed by transcatheter closure.

Direct Suture versus Patch Repair

Cardiac surgeons vary as to the frequency with which they use a patch (usually pericardium, PTFE, or knitted polyester velour) to close ASDs. For example, this approach was used in 17% of patients in a Mayo Clinic experience, approximately 30% of those in a GLH experience, and 3% of those at UAB. Provided a patch is used when the defect is particularly large or the tissues are unduly friable, there appears to be no difference in end results, including early or late thromboembolic complications. Under such circumstances, the ease and simplicity of direct suturing support its use in most patients.

Patch Material in Atrial Septum

Pericardium is the material of choice for interatrial patches (1) when a regurgitant jet may strike the patch, such as after repair of AV septal defects (prosthetic patches may produce severe hemolysis under these circumstances); (2) when pericardium forms part of the wall of an intracardiac conduit, the precise contour (position) of which is primarily determined by pressures on the two sides; and (3) when the patch is sewn to a very delicate area. In other situations, knitted polyester and PTFE patches are suitable alternatives.

Complications after Repair of Sinus Venosus Malformation

When the SVC is normal or enlarged and the pulmonary veins enter at or near the cavoatrial junction, late postoperative narrowing of the SVC is rare after repair of sinus venosus malformation by the techniques described. For this reason, minimal information is available to recommend more complex repairs.

In the unusual situations of a small right SVC (usually in the setting of bilateral SVC) or right pulmonary veins entering well above the cavoatrial junction, controversy exists regarding the optimal repair technique. Evidence exists to implicate occasional SVC stenosis when an autologous pericardial patch has been placed across the cavoatrial junction, and early and late sinus node dysfunction may be more likely secondary to disruption of blood supply to the sinoatrial node. However, several experienced groups report good results with “two-patch” techniques. Others prefer the Warden procedure in this setting (see Technique of Operation earlier in this chapter). Sinus node dysfunction is rare with this technique, but occasional stenosis at the SVC–right atrial connection has been reported. Thus, currently the standard one-patch technique appears optimal for the most common variant of sinus venosus ASD with PAPVC to the cavoatrial junction and a normal or
enlarged SVC. Long-term data have not generated a consensus about the optimal technique in the setting of a small SVC or pulmonary veins entering well above the cavoatrial junction.

Pulmonary Venous Obstruction after Repair of Scimitar Syndrome

The long intracardiac baffle often required to repair anomalous connection of right pulmonary veins to the IVC carries a greater risk of late baffle obstruction compared with other forms of PAPVC. Baffle length, relative stasis caused by the sudden change in direction of blood entering the baffle, and other factors may contribute to this complication. In a series of 15 patients with a baffle repair of scimitar syndrome, Alsoufi and colleagues from Toronto reported pulmonary venous stenosis in 7 of 10 undergoing late cardiac catheterization. Insufficient follow-up data are available to conclude whether alternative techniques, such as direct reimplantation of the anomalous vein, will yield better long-term results.

Repair in Presence of Increased Pulmonary Vascular Resistance

Some information indicates that a few patients with high RpI (>6 U · m²) may benefit from closure of an ASD using a flap-valve patch (Fig. 30-26). The flap opens right to left, such that if right atrial pressure exceeds left atrial pressure in severe pulmonary hypertension, the right atrium will decompress to the left atrium, supporting systemic cardiac output (see “Lateral Tunnel Fontan Operation with Deliberately Incomplete Atrial Partitioning” in Section IV of Chapter 41). It is inferred that as PPA and RpI decrease late postoperatively, the flap valve will close by cicatrix.

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Chapter 30  Atrial Septal Defect and Partial Anomalous Pulmonary Venous Connection

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Z
Total Anomalous Pulmonary Venous Connection

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Definition
Total (totally) anomalous pulmonary venous connection (TAPVC) is a cardiac malformation in which there is no direct connection between any pulmonary vein and the left atrium; rather, all the pulmonary veins connect to the right atrium or one of its tributaries. Although not part of the malformation, a patent foramen ovale or atrial septal defect is present in essentially all persons with TAPVC and is necessary for survival after birth.

This chapter concerns TAPVC in hearts with concordant atrioventricular and ventriculoarterial connections without other major cardiac anomalies except patent ductus arteriosus. TAPVC can occur in hearts with a wide range of other cardiac anomalies, ranging from ventricular septal defect to tetralogy of Fallot to functional single ventricle. TAPVC in hearts with atrial isomerism is considered in Chapter 58.

Historical Note
TAPVC was apparently first described by Wilson in 1798.1184 In 1951, Muller, while at the University of California Medical Center in Los Angeles, reported the first successful surgical approach.1186 His correction was partial, achieved by anastomosing the common pulmonary venous sinus to the left atrial appendage using a closed technique. In 1956, Lewis, Varco, and colleagues1185 at the University of Minnesota reported successful open repair of TAPVC using moderate hypothermia induced by surface cooling and temporary occlusion of venous inflow to the heart. The same year, Burroughs and Kirklin reported successful repair of TAPVC using cardiopulmonary bypass (CPB).1189 Their report also described a successful operation several years earlier using the atrial well technique of Gross and colleagues.1189 Subsequently, it became apparent that mortality in infants following repair of TAPVC...
using CPB was strikingly higher than in older patients, but attempts to improve results by staged operation or palliative measures were generally unsuccessful.\textsuperscript{6,8,9,10,11} Success was reported from time to time, however, even for critically ill infants with infracardiac connection.\textsuperscript{12} Eventually, improvements in intraoperative techniques substantially improved results in infants. In 1967, Dillard and colleagues achieved good results using hypothermic circulatory arrest without CPB.\textsuperscript{13} and in 1971, Malm, Gersony, and colleagues reported success in a small group of young infants using standard normothermic CPB. Hypothermic circulatory arrest and limited CPB were used in 1969 with strikingly improved results.\textsuperscript{8,9} However, refinements in intraoperative techniques developed over the last 2 decades now allow excellent outcomes using continuous CPB.

**MORPHOLOGY**

**Pulmonary Venous Anatomy**

TAPVC is supracardiac in about 45% of cases, cardiac in about 25%, infracardiac in about 25%, and mixed in about 5% to 10% (Fig. 31-1).\textsuperscript{3,11} The connection in supracardiac TAPVC is usually to a left vertical vein draining into the left brachiocephalic vein, less often to the superior vena cava, usually at its junction with the right atrium, and rarely to theazygos vein. In cardiac TAPVC, the connection is usually to the coronary sinus and less often to the right atrium directly. Connection to the supradiaphragmatic infraventricular vena cava also has been reported.\textsuperscript{3} The most common sites of connection in patients with infracardiac (infraadiaphragmatic) TAPVC are the portal vein (65% of cases, according to Duff and colleagues\textsuperscript{11,12}) and ductus venosus; less common are the gastric vein, right or left hepatic vein, and inferior vena cava. Uncommonly, the pulmonary venous drainage may be through two connections.\textsuperscript{13} Also, part of the pulmonary venous drainage may be to one site and part to another in what is termed mixed TAPVC. At least 15 different morphologic mixed variants have been identified. In the most common form, the left upper lobe of the lung drains to a left vertical vein, and the remainder of both lungs drains to theazygos vein.\textsuperscript{14} Chowdhury and colleagues have categorized this wide assortment of mixed TAPVC into three general groups: the 2+2 pattern, the 3+1 pattern, and thebizarre pattern.\textsuperscript{15}

No matter what the final connection or termination may be, individual right and left pulmonary veins usually converge to form a common pulmonary venous sinus, which in turn connects to the systemic venous system in one of the ways noted earlier. It is usually posterior to the pericardium. Its long axis is usually oriented transversely, with the pulmonary veins of the left lung converging to form its left extremity and those from the right lung to form its right extremity. When the drainage is infracardiac, the right and left pulmonary veins slope downward to converge into a vertical sinus, with the entire arrangement having a Y, T, or treeshape.\textsuperscript{16,17} Rarely, there are two vertical veins that are not confluent until below the diaphragm.\textsuperscript{18} Two vertical veins have also been identified in supracardiac TAPVC.\textsuperscript{19}

A common pulmonary venous sinus may be absent in some cases with cardiac or mixed connections. Its apparent absence in some patients may be an illusion attributable to a defect in the anterior wall of the sinus. That defect is the orifice connecting it to the coronary sinus or right atrium. Pulmonary venous obstruction is a severe associated condition usually resulting from a stenosis involving the vein connecting the common pulmonary venous sinus to the systemic venous system. A localized stenosis may occur at the junction of the left vertical vein with either the left brachiocephalic vein or the common pulmonary venous sinus, or at the junction of a connecting vein that joins the superior vena cava. Severe obstruction may be due to the so-called vascular vice, in which the left vertical vein passes posterior rather than anterior to the left pulmonary artery and is compressed between it and the left main bronchus.\textsuperscript{20}

When TAPVC is to the coronary sinus, a stenosis may occur where the common pulmonary venous sinus joins the coronary sinus or (rarely) at the coronary sinus ostium.\textsuperscript{21} In infracardiac connection, the connecting vein may be similarly narrowed at its junction with the portal vein or ductus venosus, or it may be compressed where it penetrates the diaphragm. In those varieties of infracardiac connection in which the ductus venosus is not available to bypass the liver, the portal sinusoids offer additional important obstruction to venous return. Finally, pulmonary venous obstruction may result simply from the length of a comparatively narrow connecting vein. Rarely, associated cor triatriatum is present and serves as the cause of obstruction.\textsuperscript{22}

Important pulmonary venous obstruction of these various types exists in nearly all patients with infracardiac connection and in almost all with connections to theazygos vein, in 65% of those with connections to the superior vena cava, in 40% of those with connections to theleft brachiocephalic vein, and in 40% with connections of the mixed type.\textsuperscript{23} It is less common in patients with a cardiac connection, although it has been found in 20% of patients in whom the connection is to the coronary sinus. Rarely, pulmonary venous obstruction is the result of stenoses of individual pulmonary veins at or close to their connections to the common pulmonary venous sinus.\textsuperscript{24} Functional pulmonary venous obstruction arguably occurs in patients having a patent foramen ovale rather than an atrial septal defect, although this occurrence may be limited to those with a small orifice at the foramen ovale.

**Cardiac Chamber and Septal Anatomy**

For survival after birth, a communication between systemic and pulmonary circulations must exist. Nearly always, an atrial septal defect or patent foramen ovale is present. However, in the review of Delisle and colleagues, one of 93 autopsy cases was an 11-year-old with an intact atrial septum and multiple ventricular septal defects, and Hastreiter and colleagues reported a 6-week-old patient with TAPVC to the ductus venosus, a patent ductus, and a closed foramen ovale.\textsuperscript{25} Atrial communication in TAPVC is usually of adequate size and not obstructive,\textsuperscript{26,27} although the GLH group reported that the defect was small in about half the infants operated on.\textsuperscript{28} There is frequently no pressure gradient between the two atria even when the defect is small.\textsuperscript{28,29}

The right atrium is enlarged and thick walled in patients with TAPVC, and the left atrium is abnormally small.\textsuperscript{30} Cineangiographic studies by Mathew and colleagues have shown left atrial volume to be 53% of predicted normal.\textsuperscript{31}
Figure 31-1  Classification of total anomalous pulmonary venous connection. A, Supracardiac type (45% of cases), in which the common pulmonary venous sinus connects by a vertical vein on the left side to left brachiocephalic vein. B, Cardiac type (25% of cases), in which the common pulmonary venous sinus connects to the coronary sinus in right atrium. C, Infracardiac type (25% of cases), in which the common pulmonary venous sinus connects to the portal vein or ductus venosus below the diaphragm. D, Mixed type (5%-10% of cases), in which there is no common pulmonary venous sinus, and pulmonary veins connect randomly to the heart.

These investigators noted that the left atrial appendage was normal in size and believed that left atrial smallness could be explained by absence of the pulmonary vein component. In addition, in patients with TAPVC to the right atrium, the posterior attachment of the atrial septum is shifted to the left, so the septum lies nearer to the sagittal than the usual coronal plane. Anatomic studies have shown that the left ventricle (LV) is usually normal in size. Haworth and Reid's quantitative study showed that inflow measurements of the LV were normal in eight of nine infants dying with TAPVC.
In one infant, however, LV inflow measurements were abnormally small, and weight of the free LV wall plus the septum was less than that of a normal fetus at full term. In all nine infants, LV free-wall thickness was normal. In a quantitative autopsy study of infants with TAPVC, Bove and colleagues found LV mass to be normal as well. However, they found the LV cavity was small because of leftward displacement of the septum secondary to right ventricular (RV) pressure-volume overload (see “Mitra Prolapse” under Mor). Correspondingly, Nakazawa and colleagues reported small LVEDV in infants with TAPVC. When both values were measured in the same patient, symbols are connected by solid lines, with two short vertical parallel lines indicating time of repair. X represents values in normal patients. Key: CoS, Coronary sinus total anomalous pulmonary venous connection (TAPVC); Infra, infracardiac TAPVC; RA, right atrial cardiac TAPVC; Supra, supracardiac TAPVC. (From Whight and colleagues.)

The RV varies in size, depending on the magnitude of pulmonary blood flow, presence or absence of pulmonary venous stenosis, and the point at which anomalous pulmonary veins connect. When connection was infracardiac, Haworth and Reid found that the RV was neither hypertrophied nor dilated. When venous connection was supradiaphragmatic, the septum and RV were hypertrophied and the RV dilated.

Pulmonary Vasculature

Because most infants with TAPVC have marked pulmonary hypertension, structural changes are usually found in the lungs of even the youngest infants dying with the malformation. Haworth and Reid demonstrated increased pulmonary arterial muscularity in all infants dying with TAPVC, including an 8-day-old neonate, as shown by increased arterial wall thickness and extension of muscle into

Associated Conditions

Except for an atrial communication, most infants presenting with severe symptoms from TAPVC have either no associated condition or a small or large patent ductus arteriosus. Patent ductus arteriosus is present in nearly all infants coming to operation in the first few weeks of life with pulmonary venous obstruction and, overall, in about 15% of cases. Ventricular septal defects occasionally occur. However, more than one third of cases coming to autopsy, few of which are infants, have other major associated cardiac anomalies. These include tetralogy of Fallot, double-outlet RV, interrupted aortic arch, and other lesions. The combination of TAPVC and other major cardiac anomalies is especially likely to occur when there is atrial isomerism (see Chapter 58). Other associations have been identified. Esophageal varices can occur in obstructed TAPVC, and these are likely caused by obstructed veins. Hypoplasia of the small pulmonary arteries has recently been identified in obstructive TAPVC.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Presentation

Patients with TAPVC present as seriously and often critically ill neonates, especially when a component of obstruction is present. The diagnosis can be missed when obstruction is absent, because of lack of florid signs and symptoms. TAPVC must be suspected in any neonate who has unexplained tachypnea, the cardinal sign of this anomaly. During the first 2 weeks of life, there are other causes of tachypnea that may be impossible to distinguish clinically from TAPVC, particularly a diffuse pneumonic process and retention of fetal lung fluid. Meconium aspiration and myocarditis may also confound the diagnosis. Respiratory distress syndrome should not be difficult to differentiate, because of its classic radiologic features, prematurity, and intercostal and sternal indrawing. Cyanosis is usually unimpressive in TAPVC unless there is marked pulmonary venous obstruction or a widely open ductus arteriosus that permits right-to-left shunting. Both LV and RV functions are depressed compared with normal (P < .001 in both instances) in infants presenting with seriously ill with obstructed TAPVC and marked pulmonary hypertension. Severe metabolic acidosis develops soon after birth when pulmonary venous obstruction is severe, rapidly leading to myocardial necrosis. Some neonates are so critically ill that they require intubation immediately upon hospital admission and before evaluation is begun.

Examination

In neonates and infants, the heart is not particularly overactive on examination. There may be an unimpressive precordial systolic murmur and gallop sound (the latter often proves to be a tricuspid flow murmur). The second heart sound is usually single or narrowly split. In older children, the signs are those of a large atrial septal defect unless there is increased pulmonary vascular resistance.
When the connection is to a left vertical vein, the common pulmonary venous sinus and vertical vein can usually be demonstrated (Fig. 31-5, A). When the anomalous connection is to the coronary sinus, it appears as an ovoid opacification over the left side of the spine within the right atrial contour. When it is infracardiac, the descending vein can usually be demonstrated, although its precise infradiaphragmatic connection may not be seen (Fig. 31-5, B).

Tynan and colleagues have pointed out that in neonates, umbilical vein catheterization permits direct injection of contrast medium into the anomalously connecting infradiaphragmatic vein and an accurate diagnosis of its connections.

Presence of pulmonary venous obstruction is established by demonstrating a gradient between left atrial and pulmonary venous pressure.

**Chest Radiography**

On chest radiography, heart size is usually near normal if there is pulmonary venous obstruction, but it may be large when there is increased pulmonary blood flow. The latter is associated with plethora (Fig. 31-3, A), but the more common pulmonary venous obstruction is evident as a diffuse haziness or, in its severe forms, a “ground glass” appearance. This sign is reduced when the pulmonary circuit can decompress via a patent ductus arteriosus. Older infants with TAPVC to the left brachiocephalic vein have a characteristic “figure-of-eight” or “snowman” configuration on the chest radiograph. A similar chest radiographic appearance is evident in neonates (see previous discussion). When the connection is to a left vertical vein, the common pulmonary venous sinus and vertical vein can usually be demonstrated (Fig. 31-5, A). When the anomalous connection is to the coronary sinus, it appears as an ovoid opacification over the left side of the spine within the right atrial contour. When it is infracardiac, the descending vein can usually be demonstrated, although its precise infradiaphragmatic connection may not be seen (Fig. 31-5, B).

**Echocardiography**

Two-dimensional (2D) echocardiography is remarkably accurate in assessing the morphology of TAPVC (Fig. 31-4). Along with Doppler color flow interrogation, it is almost always diagnostic. Echocardiographic features include criteria for RV diastolic overload and an echo-free space posterior to the left atrium. However, a second drainage site might be overlooked. Echocardiography is commonly accepted as a definitive diagnostic procedure in neonates with important pulmonary venous obstruction, because contrast medium is not required. Cardiac catheterization delays operation and exacerbates myocardial failure and pulmonary edema.

**Cardiac Catheterization and Cineangiography**

Angiograms obtained by pulmonary artery or pulmonary vein injections define the malformation, identify the site of drainage, and often localize the site of pulmonary venous obstruction. This procedure is nearly always diagnostic. However, it should not be used in seriously ill neonates (see previous discussion).
artery wedge pressures. Greene and colleagues employ superimposition digital subtraction angiography to define pulmonary venous anatomy, relationship of common pulmonary vein to left atrium, and size of left atrium.\textsuperscript{G7}

Magnetic Resonance Imaging and Computed Tomography

Because of diagnostic limitations of echocardiography in complex cases and morbidity associated with cardiac catheterization in gravely ill patients, both magnetic resonance imaging (MRI) and computed tomography (CT) have become increasingly important in diagnosing TAPVC. Both modalities should be used selectively, primarily in patients in whom echocardiography is not definitive. When compared with both catheterization and echocardiography, numerous studies have demonstrated the accuracy of MRI and CT in diagnosing TAPVC.\textsuperscript{C4,F1,G8,K5,M2,S14,U1} Several demonstrate improved accuracy of diagnosis using both helical CT angiography, with and without three-dimensional (3D) reconstruction,\textsuperscript{K5} and gadolinium-enhanced 3D cardiac magnetic resonance (CMR) angiography.\textsuperscript{F1,G8}

Physiology of Common Mixing Chamber

In TAPVC, the right atrium is theoretically a common mixing chamber.\textsuperscript{B17} This situation is reflected in the frequent finding of close similarity of oxygen content and saturations from the right atrium, left atrium, pulmonary artery, and systemic artery.\textsuperscript{F4} There is considerable deviation from this pattern, however, because of streaming of systemic venous return in the right atrium, directing inferior vena cava blood through the foramen ovale to the mitral valve, and superior vena cava blood through the tricuspid valve. Thus, in infracardiac TAPVC, systemic arterial saturation is typically higher than pulmonary artery saturation.

Because TAPVC has this common mixing chamber, in most patients who live beyond infancy, a direct relationship exists between the magnitude of pulmonary blood flow and arterial oxygen saturation, assuming a constant oxygen consumption and blood hemoglobin level. This relationship was formulated into a nomogram by Burchell.\textsuperscript{B17} (Fig. 31-6). The upper curve is at rest; the lower is at moderate exercise. Systemic blood flow is assumed to be 25 L · min\(^{-1}\). (From Burchell,\textsuperscript{B17})
NATURAL HISTORY

TAPVC is relatively uncommon, accounting for only about 1.5% to 3% of cases of congenital heart disease.\textsuperscript{89} Infants born with TAPVC have a generally unfavorable prognosis, with only about 20% surviving the first year of life.\textsuperscript{81,83} Only about 50% survive beyond 3 months, with death occurring during the first few weeks or months of life in most neonates in whom tachypnea, cyanosis, and clinical evidence of low cardiac output develop. Such infants usually have pulmonary venous obstruction, long pulmonary venous pathways, and a small patent foramen ovale.\textsuperscript{81} Survival past the critical first few weeks and months does not portend a favorable prognosis, because only about half the patients surviving to age 3 months survive to 1 year. Infants who survive the first few weeks of life usually have cardiomegaly and a large pulmonary blood flow, with mild cyanosis. Most have some degree of pulmonary artery hypertension.\textsuperscript{42} Their clinical syndrome includes tachypnea, recurrent episodes of severe pulmonary congestion, failure to thrive, fluid retention, and hepatomegaly.

Those with TAPVC who survive the first year of life without surgical treatment usually have a large atrial septal defect. Characteristically, they exhibit important physical underdevelopment similar to that of patients with other kinds of large left-to-right shunts, mild cyanosis, and mild exercise intolerance (see “Survival” under Natural History in Chapter 30). Like patients with isolated large atrial septal defects, they tend to have a stable hemodynamic state for 10 to 20 years, with little change in pulmonary vascular resistance and thus little change in pulmonary artery pressure, blood flow, and arterial oxygen levels.\textsuperscript{42} In the second decade of life, pulmonary vascular disease develops in some patients, and there is increasing cyanosis as pulmonary blood flow diminishes (Eisenmenger complex).\textsuperscript{45}

To quantify the natural history, Hazelrig and colleagues analyzed data from 183 autopsied cases of surgically untreated TAPVC reported in the literature.\textsuperscript{1188} Median survival was 2 months, with the shortest survival being 1 day and the longest 49 years; 90% of deaths occurred in the first year of life. Obstruction of the pulmonary venous pathway importantly reduced median survival ($P < .0001$) (Fig. 31-7) from 2.5 months in the nonobstructed group to 3 weeks in the obstructed group. Patients with supracardiac and cardiac connections had a similar history, with median survival of 2.5 and 3 months, respectively, whereas those with infracardiac connections had a worse prognosis, with median survival of 3 weeks (Fig. 31-8). Only three patients had mixed connections; two died at 5 months and one at 3.3 months. Presence of an atrial septal defect (rather than a patent foramen ovale) was associated with increased survival, particularly when the connection was not infracardiac (see Fig. 31-8).

TECHNIQUE OF OPERATION

Operation should be undertaken as an emergency immediately after diagnosis by 2D echocardiography in neonates and infants who enter the hospital critically ill. Preoperative preparation and stabilization should be brief. In stable patients, typically non-neonates without obstruction, the operation can be scheduled electively. Approach is via median sternotomy. The CPB technique can vary depending on surgeon preference, ranging from continuous CPB with either moderate or deep hypothermia to limited CPB with deep hypothermic circulatory arrest. Cardiac arrest using cardioplegia is essential for repair (see Chapters 2 and 3 for a detailed discussion of these techniques).

The ductus arteriosus must be dissected and closed routinely in infants, even if not visualized in preoperative studies.\textsuperscript{811,32} This is usually accomplished just after CPB is established and before cooling is begun. Also, at some point in the operation, the foramen ovale or atrial septal defect must be closed. This is usually done after correcting the anomalous veins. Regardless of the type of TAPVC or type of technical repair, anastomosis of the pulmonary venous sinus to the left atrium is performed with a continuous suture technique using fine polypropylene or polydioxanone suture.

Following completion of the operation, regardless of technical approach to the repair, careful consideration should be given to placing fine polyvinyl pressure catheters into the right atrium, left atrium, and RV or pulmonary trunk for appropriate postoperative monitoring.
Total Anomalous Pulmonary Venous Connection to Left Brachiocephalic Vein

After sternotomy and anterior pericardotomy, the common pulmonary venous sinus, lying behind the pericardium, is identified after lifting up the apex of the heart for a moment to visualize the retrocardiac portion of the pericardium. The right pulmonary artery, running parallel and just cephalad to the sinus, is also identified to avoid confusing it with the common pulmonary venous sinus. The vertical vein connecting the common pulmonary venous sinus to the left brachiocephalic vein can sometimes be seen inside the pericardium, but in most cases the pericardium on the left must be retracted toward the patient’s right and the persistent left vertical vein identified beneath the mediastinal pleura. The vein is isolated after carefully freeing the left phrenic nerve. A ligature is tied to the tip of the left atrial appendage for leftward retraction.

CPB and cardiac arrest are established using the techniques described in the previous section. The ductus arteriosus (if patent) and persistent vertical vein are ligated. The common pulmonary venous sinus can be exposed in several ways. One method approaches the common pulmonary venous sinus from the right side of the heart. The posterior pericardial reflection is opened (Fig. 31-9, A), and the common pulmonary venous sinus is mobilized and opened (Fig. 31-9, B-C). The posterior left atrial wall is opened, and the anastomosis is then made between the common pulmonary venous sinus and left atrium (Fig. 31-9, D-F). The continuous suture line must not be pulled up so tightly as to purse-string the anastomosis and narrow it. The right atrium is opened, the foramen ovale closed, and the atrium closed. The remainder of CPB and reestablishment of myocardial perfusion are completed (see Chapters 2 and 3).

A second method of repairing TAPVC is similar to that just described, but the common pulmonary venous sinus is exposed from the left side of the heart by lifting the cardiac mass out of the pericardial sac by retracting the cardiac apex anteriorly and rightward. This is best achieved by placing a retracting suture into the apical myocardium (Fig. 31-10, A).

This avoids the warming effect on the myocardium that occurs when the surgical assistant’s finger or hand is used to directly retract the heart. The pericardial sac is now essentially vacant, and the incision in the common pulmonary venous sinus is made under direct vision (Fig. 31-10, B). The back of the left atrium is also exposed by this maneuver and is incised. The anastomosis is then made in a fashion similar to that described in the preceding text (Fig. 31-10, C).

A third method of repairing TAPVC to the left brachiocephalic vein is via a right atrial approach. This method has the advantage of allowing the anastomosis of the common pulmonary venous sinus to the left atrium to be performed in precise anatomic relationships, because there is no retraction or displacement of critical structures to gain exposure. The right atrium is incised parallel to the atrioventricular groove (Fig. 31-11, A), exposing the atrial septum. The membrane of the foramen ovale is excised to gain entry to the left atrium. The posterior wall of the left atrium is incised transversely (Fig. 31-11, B) into the free pericardial space behind the atrium. The common pulmonary venous sinus is identified lying beneath the pericardium directly behind the incision in the left atrium. An incision is made in the common pulmonary venous sinus, which extends from the bifurcation on the left side to the bifurcation on the right side (see Fig. 31-11, C). A large anastomosis is constructed between the common pulmonary venous sinus and left atrium (Fig. 31-11, D). This anastomosis has little chance for distortion because it is performed without displacing anatomically adjacent structures. Repair is completed by closing the foramen ovale with a pericardial patch (Fig. 31-11, E). The patch serves both to repair the atrial septum and enlarge the left atrial filling capacity.

Total Anomalous Pulmonary Venous Connection to Superior Vena Cava

A common pulmonary venous sinus is usually present in the rare anomaly of TAPVC to the superior vena cava, providing free communication between right and left pulmonary veins. After the presence of this sinus is confirmed by direct
Figure 31-9  Repair of total anomalous pulmonary venous connection (TAPVC) to left brachiocephalic vein, right lateral approach.  

A, Posterior pericardial attachments of heart are cut, allowing cavae and atria to be lifted completely free of common pulmonary venous sinus, which is behind the pericardium. Left vertical vein is exposed, preferably from within the pericardium. If extrapericardial exposure is required, the phrenic nerve is elevated off the pericardium and vein. This dissection must be done sharply and with perfect exposure and visibility, because damage to this vein might necessitate its premature ligation. In this case, the common pulmonary venous sinus would have to be opened immediately to prevent severe pulmonary venous hypertension. Also, the dissection must identify the site of connection of the uppermost left pulmonary vein so that the vertical vein may be ligated superior to that point.  

B, With ventricles in normal position in the pericardium, exposure for repair (and for repair of other types of TAPVC) is obtained by elevating atria up and to the left. Posterior pericardium over common pulmonary venous sinus and anterior wall of the sinus are opened parallel to long axis of the sinus.
C, Incision should be made over full length of sinus. Orifices of left and right pulmonary veins are located and inspected, and care is taken to avoid damaging them. A corresponding incision is made more or less transversely in the back wall of left atrium. The incision may need to be carried onto the base of the left atrial appendage to gain sufficient length. It is carried to the atrial septum on the right, but care is taken not to enter the septum itself. When in doubt about initial placement of the left atrial incision, it is helpful to pass a small curved clamp through an incision in the right atrial wall and through the foramen ovale so that its tip tents the back wall of the left atrium outward. D, Traction sutures of 5-0 polypropylene are placed on inferior and superior lips of the incision into the common pulmonary venous sinus; both the sinus wall and posterior pericardium are caught with these sutures and with the suture line. Anastomosis is begun at the point shown, with the first stitch placed from outside to inside in the atrial wall, allowing suture line to be made from inside the vessels. E, Suture line is carried toward and around the left-sided angle of the incisions and along most of the superior side. The previously held other end of the double-armed 6-0 or 7-0 polypropylene or polydioxanone stitch is then used to approximate, in similar fashion, the inferior edge. Here the stitches are placed from outside to inside on the sinus and from inside to outside on the atrial wall. Suture line is carried nearly to the right-sided angle. F, Suture line is then completed, either with a few interrupted stitches or as a continuous stitch.
Figure 31-10  A, A retraction suture is placed into the myocardium at the apex and is used to retract the cardiac mass, elevating it superiorly and to the right, out of pericardial space, exposing posterior parietal pericardium. This allows visualization of pulmonary venous sinus lying behind pericardium. B, Cardiac mass is raised and lowered in and out of pericardial sac using retraction suture to identify region of left atrial free wall that lies directly against pulmonary venous sinus. Identifying this region of left atrium is necessary to plan the left atrial incision so that there is no distortion of pulmonary veins after anastomosis. Parallel incisions of equal length are made in the left atrial free wall and pulmonary venous sinus. Incisions are made as large as possible, but the pulmonary venous sinus incision does not extend into individual pulmonary veins. C, Anastomosis is performed using a continuous suture technique.
Figure 31-11 Repair of total anomalous pulmonary venous connection to left brachiocephalic vein, right atrial approach. **A**, Right atrium is incised parallel to atrioventricular groove. Membrane of foramen ovale is excised. **B**, Posterior wall of left atrium is incised transversely into pericardial space behind it. **C**, A long incision is made in common pulmonary venous sinus, which extends from the pulmonary vein bifurcation on the left side to the right side. **D**, Common pulmonary venous sinus is anastomosed to left atrium using continuous stitches of 7-0 polypropylene or polydioxanone suture. Suture line is started at apex of pulmonary venous sinus incision on the left side, placing stitches from inside the pulmonary vein. **E**, Foramen ovale is closed with pericardial patch to increase capacity of left atrium.
both the roof of the coronary sinus, so that it communicates freely with the left atrium, and the fossa ovalis (Fig. 31-12, A-B). The resulting large defect, made up of a confluence between the rim of the fossa ovalis and the coronary sinus ostium, is then closed with a pericardial patch (Fig. 32-12, C).

However, occurrence of stenosis at the repair site late after operation has prompted use of the technique described by Van Praagh and colleagues. The foramen ovale is enlarged to obtain an adequate exposure within the left atrium (Fig. 31-13, A). The wall between the coronary sinus and left atrium is incised (Fig. 31-13, B), and the incision is enlarged as much as possible in both directions. The foramen ovale and coronary sinus ostium are closed separately (Fig. 31-13, C). The pulmonary veins then drain into the left atrium through the surgically unroofed coronary sinus (Fig. 31-13, D). The remainder of the operation is completed as described for other types of TAPVC.

Total Anomalous Pulmonary Venous Connection to Coronary Sinus

The right atrial approach described in the preceding text is used. The right atrium is opened by the usual oblique incision. The repair most commonly used includes excising both the roof of the coronary sinus, so that it communicates freely with the left atrium, and the fossa ovalis (Fig. 31-12, A-B). The resulting large defect, made up of a confluence between the rim of the fossa ovalis and the coronary sinus ostium, is then closed with a pericardial patch (Fig. 32-12, C).

However, occurrence of stenosis at the repair site late after operation has prompted use of the technique described by Van Praagh and colleagues. The foramen ovale is enlarged to obtain an adequate exposure within the left atrium (Fig. 31-13, A). The wall between the coronary sinus and left atrium is incised (Fig. 31-13, B), and the incision is enlarged as much as possible in both directions. The foramen ovale and coronary sinus ostium are closed separately (Fig. 31-13, C). The pulmonary veins then drain into the left atrium through the surgically unroofed coronary sinus (Fig. 31-13, D). The remainder of the operation is completed as described for other types of TAPVC.

Obstructed pulmonary venous drainage can occur in patients with TAPVC to the coronary sinus. Thus, the surgeon must be prepared to abandon usual approaches if a stenosis is proximal to the coronary sinus itself, and proceed to anastomose the common pulmonary venous sinus, which
Figure 31-13  Repair of total anomalous pulmonary venous connection to coronary sinus, Van Praagh method. A, After usual preparations, right atrium is opened obliquely and exposure arranged. Foramen ovale is enlarged cephalad and at times caudad to attain adequate visibility within left atrium. B, An opening is made in the common wall between coronary sinus and left atrium after wall has been tented with right-angle forceps. This opening is enlarged downward and to the left; care must be taken not to go outside the heart in the process. (If this occurs, the opening must be closed at this point from within the heart by a few sutures, because the area is difficult to expose from outside the heart.) The incision is carried anteriorly and to the right to within a few millimeters of the ostium of the coronary sinus.

Continued
Foramen ovale and ostium of coronary sinus are closed, usually individually, with interrupted or continuous suture. Suture line should start inferiorly just below the last tiny coronary vein entering the sinus and, as it proceeds superiorly, should be made with shallow bites and preferably kept within the coronary sinus ostium to avoid the atrioventricular (AV) node. Arrow indicates path of blood flow through the coronary sinus to the right atrium before repair. After repair, blood flow from the coronary sinus is to the left atrium above the mitral valve through the unroofed coronary sinus.
is actually the junction of the right and left pulmonary veins, to the back of the left atrium.\textsuperscript{32}

Total Anomalous Pulmonary Venous Connection to Right Atrium

Initial stages of the operation are as described for other types of TAPVC using the right atrial approach. The right atrium is opened obliquely. The anomalous connection into the right atrium is explored with an instrument to verify the presence of a confluent pulmonary venous sinus. The foramen ovale is then enlarged, and working through it, an incision is made in the posterior left atrial wall. The common pulmonary venous sinus is visualized through this incision, and the anterior wall of the sinus is incised. This opening is enlarged and anastomosed to the left atrial incision, still working from within the atria. The enlarged foramen ovale is closed by direct suture. The original connection of the common pulmonary venous sinus to the right atrium is closed with a relatively small pericardial patch; it must be remembered that the pulmonary venous pathway from the right lung is beneath the patch.

Alternatively, as described for the repair of TAPVC to the superior vena cava, the common pulmonary venous sinus can be detached from the right atrium, the opening in the sinus enlarged and used for anastomosis to the left atrium, and the resulting defect in the posterior atrial wall closed. The remainder of the operation is completed as usual.

Total Anomalous Pulmonary Venous Connection to Infra-diaphragmatic Vein

In TAPVC to an infradiaphragmatic vein, the distal (inferior) portion of the common pulmonary venous sinus is vertical, and proximally (superiorly) it forms a Y or T connection with the left and right pulmonary veins. Therefore, after initial stages of the operation have been performed as described for other types of TAPVC, a decision is made about the approach, which may be similar to that for other types, through the opened right atrium, or through the back of the left atrium directly after tilting the apex of the heart up and to the right. Good results have been obtained by all approaches. The approach using retraction of the cardiac mass out of the pericardial sac is described. The heart is freed from its posterior attachments and the back of the left atrium exposed (Fig. 31-14, \textit{A}). The common pulmonary venous sinus and left atrium are incised (Fig. 31-14, \textit{B}). The common pulmonary venous sinus is Anastomosed to the back of the left atrium (Fig. 31-14, \textit{C}) and is ligated (Fig. 31-14, \textit{D}) and may be divided to allow the anastomosis to conform better.\textsuperscript{74}

Miscellaneous Types of Total Anomalous Pulmonary Venous Connection

Some rare types of TAPVC occur, such as connection to the azygos vein or inferior vena cava, or dual connection from the common pulmonary venous sinus.\textsuperscript{51,56,71,\textit{V2}} These connections can usually be sorted out using MRI or CT. In the rare event that the connection cannot readily be found or dissected out at operation, the common pulmonary venous sinus is opened and the connection(s) identified from within it. After the connection is closed, the usual anastomosis is made between the common pulmonary venous sinus and left atrium.

Mixed Total Anomalous Pulmonary Venous Connection

Patients with mixed TAPVC present a diagnostic as well as surgical challenge. MRI or CT is almost always used to supplement echocardiographic imaging and to provide an accurate characterization of the morphologic details.\textsuperscript{\textit{P1,G8,K5,M2,S14,U1}} Chowdhury and colleagues have recently categorized the spectrum of mixed TAPVC into five major groups.\textsuperscript{\textit{E5,C6}} Each group is characterized by a set of similar general morphologic patterns, but many variations occur from case to case.

Management of each patient must be individualized based on analysis of the mixture presented. A variety of techniques must be used, including many of those already described for TAPVC to the left brachiocephalic vein, right atrium, superior vena cava, and structures below the diaphragm. Combining these techniques with others, such as construction of a right atrial intracardiac baffle for isolated veins to the superior vena cava (similar to repair of partial anomalous pulmonary venous connection) or direct anastomosis of isolated left upper pulmonary vein to the left atrial appendage, will usually allow complete repair.\textsuperscript{\textit{R7,C9,N6,J1,S8}} In some small babies in whom an extensive operation would be required for complete one-stage repair, subtotal repair can be successful, leaving unrepaired, for example, anomalous connection of the left upper lobe to the left brachiocephalic vein.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Overall management of patients after correction of TAPVC is accomplished in the usual way (see Chapter 5). The relationship between left and right atrial pressures is of particular importance. Left atrial pressure may be considerably higher than right when pulmonary artery pressure decreases immediately after repair, particularly when a small and noncompliant left atrium acts more like a conduit than a reservoir.\textsuperscript{\textit{P1}} The left atrial pressure pulse after operation is then characterized by a steep y descent (Fig. 31-15). A small or borderline-sized LV contributes to this situation.

In infants, particularly neonates, who present for operation in critical condition with pulmonary venous obstruction, pulmonary artery pressure and resistance may remain high early postoperatively, which in part may reflect the damaging effects of CPB (see Chapter 2), preoperative lung injury, and postoperative acidemia. Because of this, continuous monitoring of pulmonary artery pressure for at least 48 hours after repair is essential.\textsuperscript{\textit{K9}} When pulmonary artery systolic pressure remains elevated to two thirds or more of systemic arterial systolic pressure, right atrial and RV end-diastolic pressures are usually higher than left atrial pressure, and RV stroke volume is likely to be reduced. When this situation is present, acidemia must be vigorously treated; in addition, PaCO\textsubscript{2} should be kept low (25-30 mmHg) by hyperventilation.\textsuperscript{\textit{J9}}

Fentanyl should be continued for at least 36 hours postoperatively, and all features of the regimen to minimize occurrence of paroxysmal pulmonary hypertension employed (see “Pulmonary Hypertensive Crises” under Pulmonary Subsystem in Section I of Chapter 5). Use of inhaled nitric oxide may be particularly helpful in this setting and has essentially replaced other pulmonary vasodilatory drugs that have important side effects such as systemic hypotension.
Figure 31-14  Repair of total anomalous pulmonary venous connection draining infradiaphragmatically. A, Exposure of common pulmonary venous sinus and posterior wall of the left atrium is obtained by tilting the heart superiorly and to the right. Pulmonary venous sinus is identified behind the pericardium posteriorly. B, Posterior wall of left atrium is incised beginning at base of the appendage and somewhat more vertically than for other types of repair of total anomalous pulmonary venous connection (TAPVC). A long incision is made in common pulmonary venous sinus. Alternatively, common pulmonary venous sinus may be ligated and divided (inset).
C. Anastomosis of common pulmonary venous sinus to left atrium is constructed using 6-0 or 7-0 polypropylene or polydioxanone suture. Anastomosis is started at the apex superiorly, working from within the left atrium and pulmonary venous sinus. The technique with the venous sinus divided is also shown (inset).

D. Common pulmonary venous sinus is ligated below the anastomosis, with care taken to place ligature below any pulmonary vein branch. The sinus may be divided to allow the anastomosis to conform better (inset).
Table 31-1  Incremental Risk Factors for Mortality after Repair of Mixed TAPVC

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio (CL, %)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤2 months</td>
<td>5.2 (1.2-22)</td>
<td>.02</td>
</tr>
<tr>
<td>Obstructive TAPVC</td>
<td>13 (2.5-75)</td>
<td>.01</td>
</tr>
<tr>
<td>Pulmonary hypertensive crises</td>
<td>10 (1.5-57)</td>
<td>.02</td>
</tr>
<tr>
<td>Complex anatomy</td>
<td>5.8 (1.5-36)</td>
<td>.02</td>
</tr>
</tbody>
</table>

Data from Chowdhury and colleagues.\textsuperscript{c5}  
Key: CL, 95% confidence limits; TAPVC, total anomalous pulmonary venous connection.

and colleagues reported similar findings.\textsuperscript{a2} Other studies indicate a slight drop in survival at mid- to late follow-up. The study by Hancock Friesen and colleagues shows 1-month survival of 90% and 3-year survival of 87%.\textsuperscript{k1} Karamlou and colleagues reported that most deaths occurring outside the perioperative period occurred within a few months of surgery, with essentially no late events.\textsuperscript{k1} In patients with mixed TAPVC, Chowdhury and colleagues demonstrated late mortality of 4.3%, with follow-up of 42 months (median).\textsuperscript{c5}

Modes of Death

The most common modes of hospital death after repair are cardiac failure and hypertensive pulmonary artery crises. Postoperative pulmonary hypertensive crisis can occur in neonates and infants who go into surgery with severe cardiopulmonary instability, even though an adequate vein repair has been achieved, or in patients with postoperative pulmonary venous obstruction. In the modern era, most early and late deaths are associated with some combination of pulmonary venous obstruction, complex mixed TAPVC morphology, and low birth weight.\textsuperscript{a2,c3,k2,k1,k1,k1,k1,k1}

Incremental Risk Factors for Death

Risk factors for early death have been identified. These include earlier year of operation, single-ventricle intracardiac morphology, mixed TAPVC morphology, infradiaphragmatic TAPVC morphology, pulmonary venous obstruction, poor preoperative physiologic state, and lower weight at operation.\textsuperscript{b2,b11,c3,d5,d9,d6,d11,d2,d7,k1,k1,m4,m4} Importantly, many studies cited here are not uniform in identifying all these risk factors. This variability reflects variations in analysis from study to study and also acknowledges that many or most of these risk factors are mutable. For example, Bove and colleagues found severe acidosis on admission to be the most important risk factor for hospital death after repair of infracardiac TAPVC.\textsuperscript{b11} Other studies indicate that preoperative pulmonary venous obstruction is not a risk factor unless accompanied by single-ventricle intracardiac morphology.\textsuperscript{k11} Studies by Bando and colleagues\textsuperscript{b9} and Hyde and colleagues\textsuperscript{c5} argue that preoperative pulmonary venous obstruction and infradiaphragmatic connection have been neutralized as risk factors for death. Risk factors for death in mixed TAPVC have been defined\textsuperscript{c5} (Table 31-1).

Risk factors for late death are difficult to define because late deaths occur so infrequently. Most deaths outside the perioperative period involve recurrent or persistent pulmonary venous obstruction. Possibly, preoperatively small
pulmonary veins predispose patients to develop the lethal postoperative complication of pulmonary vein stenosis. Therefore, this finding may also be a risk factor for death after repair, as may small size of the coronary sinus in cardiac TAPVC.

In older patients presenting for surgical correction, a mild or moderate increase in pulmonary vascular resistance increases the risk of operation, and severe elevation makes older patients inoperable. The situation in these older patients is analogous to that in patients with atrial septal defect (see Indications for Operation in Chapter 30). There may be a few patients with TAPVC in which the LV is so small that it per se represents an incremental risk factor. However, this is rare. More commonly, preoperative LV volume calculations are falsely reduced because of the ventricular septal shift that occurs with pulmonary hypertension. Fortunately, major associated cardiac anomalies in this condition are rare as well.

Functional Status

McBride and colleagues have shown that compared with healthy children, peak oxygen consumption (88% ± 16% of predicted) and ventilatory anaerobic threshold (91% ± 21% of predicted) were mildly reduced in a group of 27 patients with a mean age of 11 years. Chronotropic impairment was observed in seven patients (32%). Neurodevelopmental outcome has been evaluated. Kirshbom and colleagues assessed 30 patients, mean age 11 years, who had undergone TAPVC repair in the neonatal period or infancy. All patients underwent repair using hypothermic circulatory arrest. Microcephaly was present in 28%, and abnormal neuromuscular examination in 27%. Performance IQ, motor skills, and attention were below normal, while full and verbal IQ and memory were normal. In another study of 34 patients at 18 to 24 months of age, all of whom underwent repair using hypothermic circulatory arrest, Mental Developmental Index (87 ± 16) and Psychomotor Developmental Index (89 ± 13) were at the low end of normal.

Hemodynamic Result

Pulmonary artery pressure is normal in patients recatheterized after repair unless there is abnormal cardiac rhythm, and cardiac index is normal, ranging from 2.9 to 5.2 L · min⁻¹ · m⁻² (average 3.7 L · min⁻¹ · m⁻²) in the study of Whight, Barratt-Boyes, and colleagues.

Postoperative cineangiographic studies of infants have shown that left atrial volumes are mostly within normal range, with the exceptions more often large than small. Incorporation of the pulmonary venous sinus, and the coronary sinus in some types of TAPVC, probably increases left atrial size (which was small before repair) to normal for age postoperatively. Some functional left atrial abnormality is present early and late postoperatively, perhaps based on abnormally low compliance of part of the atrium, because left atrial pressure tracings are often abnormal both early and late postoperatively.

RV volume, variable but often increased preoperatively, is normal or only mildly enlarged late postoperatively. LVEDV, abnormally small preoperatively, increases to normal late postoperatively. LV systolic function, often markedly depressed before operation, returns to normal late postoperatively (Fig. 31-16). Part of the explanation for this may be the improved LV geometry resulting from reduction in RV size (see “Ventricular Function” under Results in Chapter 30).

Cardiac Rhythm

Normal sinus rhythm is present in nearly all patients unless there is rhythm abnormality preoperatively. However, at least some of the preferential pathways of conduction from the sinus node to the atrioventricular node (see “Midostral Pathways” under Conduction System in Chapter 1) could be damaged by the repair. Holter monitoring after repair demonstrates that asymptomatic ectopic atrial pacemaker activity and other abnormalities are present in most patients. To date, these conditions appear not to have handicapped patients. McBride and colleagues reported that of 22 patients achieving peak aerobic capacity during late evaluation, 7 (32%) had an attenuated heart rate response (168 ± 14 beats · min⁻¹).

Reoperation and Development of Postoperative Pulmonary Venous Obstruction

Reoperations are performed for two reasons: severe anastomotic stenosis and pulmonary vein stenosis. They have been necessary in every experience. In an early unpublished study by Kirklin, essentially all patients with restenosis required reoperation within the first 6 to 12 months of repair (Fig. 31-17). Karamlou and colleagues, who reviewed 377 cases over a 60-year span, confirmed this
finding. However, other studies imply that need for reoperation may develop later. An analysis from Great Ormond Street Hospital showed that only one third of reoperations (7/20) occurred within 6 months of initial repair.

Patients usually become symptomatic with development of recurrent dyspnea and signs of pulmonary venous congestion, but ideally the diagnosis should be made before that stage. Risk factors for developing recurrent pulmonary venous obstruction include an original diagnosis of infracardiac TAPVC, and obstructed TAPVC. Despite theoretical considerations favoring use of interrupted sutures, there is no correlation between stricture formation and method of suturing. It is likely, however, that the open technique of anastomosis is preferable to use of clamps. Suture material may influence formation of anastomotic stricture. Absorbable polydioxanone suture as a continuous stitch technique of anastomosis is preferable to use of clamps. Absorbable polydioxanone suture compared with nonabsorbable suture.

A powerful tool for evaluating patients after repair of pulmonary venous obstruction but before hospital discharge is 2D pulsed Doppler echocardiography. Ideally, it should be repeated on several occasions during the first postoperative year. High-velocity turbulent flow at either the anastomosis or the pulmonary vein orifices suggests stenosis. Prompt angiographic restudy may further clarify the anatomic point of stenosis. The pulmonary veins are entered retrogradely from the left atrium to make a direct pulmonary vein angiogram and to determine pressure gradient across the anatomic site.

MRI and CT are also useful imaging modalities for defining morphology of the obstruction. According to Ricci and colleagues, about half (10/20) of all cases of recurrence are due to anastomotic stenosis, about one third to combined anastomotic and ostial (6/20) stenosis, and a minority (3/20) to ostial stenosis alone. Risk factors for death following reoperation are earlier age at recurrence and persistence of pulmonary hypertension after reoperation.

Anastomotic Stenosis
In up to 10% of patients, strictures appear to develop at the anastomosis (Table 31-2), usually within a few months of repair. However, results of reoperation are occasionally disappointing, with an important chance of a subsequent restenosis, as reported by Brekenridge and colleagues. Despite theoretical considerations favoring use of interrupted sutures, there is no correlation between stricture formation and method of suturing. It is likely, however, that the open technique of anastomosis is preferable to use of clamps. Suture material may influence formation of anastomotic stricture. Absorbable polydioxanone suture as a continuous stitch has been recommended by Hawkins and colleagues for constructing the left atrium–to–common pulmonary venous sinus anastomosis. Late anastomotic stenosis occurred in 1 (3.2%; CL 0.4%-10%) of 32 survivors having anastomosis with polydioxanone compared with 4 (17%; CL 9%-29%) of 23 patients having anastomosis with nonabsorbable suture. However, groups compared in this series were not concurrent. Based on complete absence of this complication late postoperatively, it is likely that anastomoses grow appropriately as patients grow.

Table 31-2 Prevalence of Anastomotic Strictures after Repair of Total Anomalous Pulmonary Venous Connection

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wight et al., 1969-1977</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0.0-21</td>
</tr>
<tr>
<td>Applebaum et al. and Katz et al.</td>
<td>32</td>
<td>3</td>
<td>9</td>
<td>4.18</td>
</tr>
<tr>
<td>Behrendt et al., 1963-January 1970</td>
<td>11</td>
<td>1</td>
<td>9</td>
<td>1.33</td>
</tr>
<tr>
<td>Brekenridge et al.</td>
<td>11</td>
<td>2</td>
<td>18</td>
<td>6.38</td>
</tr>
<tr>
<td>Cooley et al., 1995-1964</td>
<td>16</td>
<td>1</td>
<td>6</td>
<td>1.20</td>
</tr>
<tr>
<td>Hawkins et al., 1982-1988</td>
<td>23</td>
<td>4</td>
<td>17</td>
<td>9.29</td>
</tr>
<tr>
<td>Hawkins et al., 1989-1994</td>
<td>32</td>
<td>1</td>
<td>3</td>
<td>0.4-10</td>
</tr>
<tr>
<td>Hancock Freisen et al., 1989-2000</td>
<td>84</td>
<td>5</td>
<td>6</td>
<td>3.10</td>
</tr>
<tr>
<td>TOTAL</td>
<td>217</td>
<td>17</td>
<td>9</td>
<td>6.10</td>
</tr>
</tbody>
</table>

*The variable n refers to number of hospital survivors. Except in the GHE (Whight et al.) patients, in whom routine postoperative cardiac catheterization was performed, the data concern patients dying or requiring reoperation for stricture formation. The 70% confidence limits of the individual proportions all overlap; this overlap and the P value make institutional differences in prevalence unlikely.

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wight et al., 1969-1977</td>
<td>8</td>
<td>0</td>
<td>0</td>
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</tr>
<tr>
<td>Behrendt et al., 1963-January 1970</td>
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<td>Brekenridge et al.</td>
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<td>17</td>
<td>9</td>
<td>6.10</td>
</tr>
</tbody>
</table>

P(χ²) .4

Pulmonary Vein Stenosis
Compared with anastomotic stenosis, pulmonary vein stenosis tends to occur later and is less common. In most instances, the stenosis is due to diffuse fibrosis and thickening of the vein wall and often to localized narrowing at the vein–left atrial junction. Pulmonary vein stenosis may or may not be accompanied by anastomotic stenosis.
5.7% of 377 patients undergoing TAPVC repair but do not make a distinction between anastomotic and pulmonary vein stenosis.\textsuperscript{81}

Pulmonary vein stenosis is usually lethal, even with reoperation and extensive attempts at revision or repair. This lack of success has led to alternative treatment such as balloon dilatation and stenting, but these do not appear to provide additional benefit. In 1996, Lacour-Gayet and colleagues described the sutureless repair technique, using in situ autologous pericardium, for recurrent pulmonary vein stenosis following initial TAPVC repair.\textsuperscript{N1} Subsequent reports emphasize the utility of this technique in selected cases.\textsuperscript{1,2,3,7} Following their initial description of the sutureless technique, Lacour-Gayet and colleagues reported that of 178 patients undergoing correction of TAPVC, progressive obstruction developed in 16 (9%) within a median interval of 4 months (range 5 weeks to 12 years) after operation.\textsuperscript{1,2,7} Only 4 of these 16 had isolated pulmonary vein stenosis, with the remaining 12 having either isolated anastomotic stenosis or combined anastomotic and pulmonary vein stenosis. The obstruction was bilateral in 7 patients. Fifteen of the 16 patients underwent reoperation, and 4 (27%) died afterward. The authors used the in situ pericardial patch technique to relieve the stenosis in 7 of the 16 patients.

Despite interest in the sutureless technique, there is little firm evidence that it provides a benefit over conventional techniques. Yun and colleagues\textsuperscript{7,2} used a retrospective analysis to compare the outcomes of death and restenosis after conventional and sutureless techniques. Patients in this series were heterogeneous, and only 17 of the 60 had a history of previous TAPVC repair. By multivariable analysis, there was no statistically significant difference between the conventional and sutureless techniques, although a trend for better outcome using the sutureless technique was observed when all 60 patients were considered.

Development of pulmonary vein stenosis many years after repair is exceedingly rare but has been reported. Kveselis and colleagues reported successful repair of infracardiac TAPVC in a 17-day-old infant who had a demonstrated absence of pulmonary vein obstruction when recatheterized 3.7 years after operation. This patient continued to be healthy without limitations until 12 years of age, at which time he became symptomatic, and important obstruction was demonstrated at the anastomosis.\textsuperscript{8,12} Reoperation successfully corrected the problem.

**INDICATIONS FOR OPERATION**

Investigation must be undertaken promptly in any neonate or infant, no matter how young, who develops signs and symptoms suggestive of TAPVC. Procrastination leads to death in babies with obstructive TAPVC (and in some without it) or to hospital admission in a semimoribund state, which importantly increases operative mortality.

Once the diagnosis is made, operation should be undertaken immediately in any neonate or infant importantly ill with TAPVC. This policy should lead to surgical intervention during the first few days or week of life, frequently in the first month of life, and usually before 6 months of age. In infants in whom the diagnosis is made between 6 and 12 months of age, operation should be undertaken promptly because risk of operation is low, and even infants who appear to be doing well are at risk of dying before age 1 year.\textsuperscript{8,10,34}

Rarely, individuals survive into childhood or early adult life with TAPVC and are first seen for surgical consideration at that time. Operation is advisable if severe pulmonary vascular disease has not developed; the criteria for operability are the same as for patients with atrial and ventricular septal defects (see Indications for Operation in Chapters 30 and 35. In TAPVC, degree of cyanosis is not helpful because of the common mixing chamber, nor is height of mean pulmonary artery pressure relative to systemic pressure, because the shunt is not at systemic level.

When pulmonary vascular disease is suspected clinically, measurement of pulmonary vascular resistance is required at preoperative cardiac catheterization. Using the Fick principle, the patient’s response to 100% oxygen and to inhaled nitric oxide is determined. If pulmonary vascular resistance is less than 8 U - m\textsuperscript{2} using these maneuvers, operation is undertaken. If resistance is higher than 8 U - m\textsuperscript{2}, chronic pulmonary vasodilatory therapy, both pre- and postoperatively, can be considered in an attempt to increase operability.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Pulmonary Vein Stenosis**

Pulmonary vein stenosis may be either a postoperative complication (as discussed previously) or a primary congenital anomaly.\textsuperscript{87} Congenital lesions are classified as (1) diffuse hypoplasia, (2) long-segment (tubular) focal stenosis, and (3) ostial (discrete) stenosis. Diffusely hypoplastic pulmonary veins extending into the lung parenchyma usually require heart-lung or lung transplantation, and prognosis is poor. Long-segment tubular stenoses of pulmonary veins with normal-caliber intraparenchymal pulmonary veins may be treated, but prognosis is also poor.

Treatment includes operative patch venoplasty, the sutureless technique, catheter dilatation and stent placement, or a combination of therapies. Currently, balloon dilatation and stent placement are not considered effective therapies, because rapid restenosis is the rule. Short-segment discrete stenoses located at or near the left atrial ostium of the pulmonary vein have the best chance for success following surgery. In general, congenital pulmonary vein stenosis has a poor prognosis because of development of pulmonary venous hypertension, followed by pulmonary arterial hypertension.

**Delayed Operation**

In critically ill neonates and young infants whose obstruction is primarily at the atrial level (an unusual situation), balloon atrial septostomy (with a blade if necessary) and delay of operation for 1 to 2 days are reasonable approaches.\textsuperscript{82} Preoperative preparation of the critically ill neonate by infusion of prostaglandin E\textsubscript{1} combined with low-dose dopamine for a few hours has been advised by Serraf and colleagues.\textsuperscript{59} However, such treatment may shunt blood away from the lungs and increase cyanosis in neonates with severe pulmonary venous obstruction and pulmonary venous hypertension.

**Operative Exposure**

Tucker and colleagues described exposing the structures for anastomosis of the common pulmonary venous sinus to the left atrium through the transverse sinus between the aorta...
and superior vena cava. This approach can occasionally be helpful if the pulmonary venous sinus is positioned superiorly.

**Surgical Enlargement of Left Atrium**

Trusler and colleagues found that in dogs, a decrease in atrial volume of more than 50% resulted in an important reduction in cardiac output. Brighton and colleagues, using a mechanical model, obtained substantial improvement in cardiac output by adding a flexible atrium to the inlet of their artificial heart. In studying the effect of atrial compliance on cardiac performance with a mathematical electrical analog, Suga found that cardiac performance was markedly improved by increasing atrial compliance while maintaining constant ventricular contractility. Analysis suggested that increased atrial compliance facilitated the reservoir function of the atrium and maintenance of a relatively high mean atrial pressure during ventricular filling. These facts, combined with the preoperatively observed small left atrium in patients with TAPVC, have made its enlargement by shifting the atrial septum to the right attractive.

Katz and colleagues, on the other hand, found similar survival with and without left atrial enlargement. This may be because surgical efforts to improve left atrial size are not effective, or because adequate left atrial enlargement may result from incorporating the common pulmonary venous sinus into the left atrium. Also, lack of left atrial reservoir function may rarely be critical early or late postoperatively if other aspects of the situation favor survival. Nonetheless, the repair must be done in a manner that does not decrease size of the left atrium.

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A


B

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E

F

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J
PART VII Congenital Heart Disease

K


L


M


S

U

Y
**DEFINITION**

Classic (or typical) cor triatriatum, or *cor triatriatum sinister*, is a rare congenital cardiac anomaly in which the pulmonary veins typically enter a “proximal” left atrial chamber separated from the “distal” left atrial chamber by a partition in which there are one or more restrictive ostia. In the Congenital Heart Surgery Nomenclature and Database Project, cor triatriatum is classified as a pulmonary venous anomaly, with subclassifications as described in Box 32-1.

**HISTORICAL NOTE**

Cor triatriatum was apparently first described in 1868 by Church. The name *cor triatriatum* was applied to the malformation by Borst in 1905. The angiographic diagnosis seems first to have been made at Mayo Clinic and described by Miller and colleagues in 1964. Echocardiographic diagnosis of this cardiac anomaly was described by Ostman-Smith and colleagues in 1984 and by Wolf in 1986. The first surgical correction is believed to have been performed by Vineberg and Gialloreto in 1956; the second by Lewis and colleagues followed shortly thereafter.

**MORPHOLOGY**

It is unfortunate that cor triatriatum was first defined as “an abnormal septum in the left auricle” and has been described as resulting in a “subdivided left atrium,” because these terms obscure surgically important concepts about cor triatriatum.

**Morphology of Classic Cor Triatriatum**

Typically, the proximal (common pulmonary venous) chamber is somewhat larger than the distal (left atrial) chamber. The common wall partitioning them (“diaphragm” or “membrane”), which may have one or more openings (apertures), is usually thick and fibromuscular (Fig. 32-1). The aperture is typically two dimensional, meaning it has no length, but occasionally it is three dimensional, exhibiting a tubular or tunnel-like configuration.

The proximal chamber contains all pulmonary vein connections and is usually thick-walled, whereas the distal chamber always contains the left atrial appendage and leads into the mitral valve, and is thin-walled (Fig. 32-2). Despite high pressure in the proximal chamber, the pulmonary veins are not dilated. Entry of the right pulmonary veins into the proximal chamber usually bears the same relationship to the right atrium and superior vena cava as in the normal heart (Fig. 32-3).

The right ventricle is usually enlarged, but this enlargement depends on the presence and degree of left-to-right shunting at the atrial level. The left ventricle is usually normal in size or small. The fossa ovalis may be in the septum between the proximal chamber and right atrium, but occasionally it is in the septum between the distal chamber and right atrium. The foramen ovale is usually patent and stretched.

**Relationship of Cor Triatriatum to Partial and Total Anomalous Pulmonary Venous Connection**

In classic cor triatriatum, the right and left pulmonary veins can be considered as not joining the left atrium but rather as entering a chamber, generally posterior and a little superior or medial to the left atrium, that is analogous to the common pulmonary venous sinus found in many patients with total anomalous pulmonary venous connection (TAPVC, see...
Chapter 32 Cor Triatriatum

Box 32-1 Proposed Classification of Pulmonary Venous Anomalies

I. Primary Anomalies of Pulmonary Venous Connection

A. Partially (or partial) anomalous pulmonary venous connection (or return or drainage) (PAPVC, PAPVR)
   1. Non-scimitar
   2. Scimitar (right pulmonary vein[s] draining to inferior vena cava)
B. Totally (or total) anomalous pulmonary venous connection (or return or drainage) (TAPVC, TAPVC)
   1. Supracardiac (supradiaphragmatic, type I)
   2. Cardiac (supradiaphragmatic, type II)
   3. Infracardiac (infradiaphragmatic, type III)
   4. Mixed (type IV)

II. Atresia of the Common Pulmonary Vein

III. Cor Triatriatum (Stenosis of the Common Pulmonary Vein, Triatrial Heart, Cor Triatriatum Sinister)

A. Accessory atrial chamber receives all pulmonary veins and communicates with left atrium
   1. No other connections (classic cor triatriatum)
   2. Other anomalous connections
      a. To right atrium directly
      b. With TAPVC
B. Accessory atrial chamber receives all pulmonary veins and does not communicate with left atrium
   1. Anomalous connection to right atrium directly (cardiac TAPVC with all pulmonary veins first draining to a venous confluence)
   2. With TAPVC (supracardiac or infracardiac TAPVC)
C. Subtotal cor triatriatum
   1. Accessory atrial chamber receives part of the pulmonary veins and connects to left atrium
      a. Remaining pulmonary veins connect normally
      b. Remaining pulmonary veins connect anomalously (partial cor triatriatum with PAPVC)
   2. Accessory atrial chamber receives part of the pulmonary veins and connects to right atrium
      a. Remaining pulmonary veins connect normally (PAPVC with anomalously connected pulmonary veins first draining to a venous confluence)
      b. Remaining pulmonary veins connect anomalously (mixed TAPVC)

IV. Stenosis of Individual Pulmonary Veins

A. Congenital
B. Acquired
   1. Postoperative
   2. Other

From Herlong and colleagues.\(^{11}\)

Chapter 31). Indeed, Van Praagh and Corsini did not use the term proximal left atrial chamber, but called it the common pulmonary vein chamber of cor triatriatum.\(^{12}\) Marin-Garcia and colleagues used similar terminology.\(^{11}\)

From an embryologic standpoint, the confluence of the pulmonary veins is completely incorporated into the left atrium in a normal heart, is not incorporated into the left atrium in TAPVC, and is partially incorporated into the left atrium in cor triatriatum. Just as TAPVC does not always involve all pulmonary veins connecting to a single pulmonary venous sinus (i.e., mixed TAPVC), cor triatriatum does not always involve all pulmonary veins draining to the proximal chamber. There are several examples of cor triatriatum in which some of the pulmonary veins drain to the
proximal chamber, and the remainder have classic anomalous drainage.

Partial anomalous left pulmonary venous connection (from left upper lobe only or from entire left lung) may connect to a left vertical vein that connects to the left brachiocephalic vein, with all other pulmonary veins entering the proximal chamber.\(^{1,2,3}\) Partial anomalous venous connection may consist of all left pulmonary veins connecting to the coronary sinus, with the proximal chamber receiving only the right pulmonary veins and connecting through the usual small orifice into the distal left atrial chamber.\(^2\) Comparisons to partial anomalous pulmonary venous connection (PAPVC)
also exist. In these examples, some pulmonary veins connect to the proximal chamber, and the remainder connect normally to the left atrium.

In “partial” cor triatriatum, the right pulmonary veins alone may connect to the proximal chamber, with the left pulmonary veins connecting normally to the left atrium.\textsuperscript{51} Other unusual variants have been documented. The proximal chamber, receiving all pulmonary veins, may have an imperforate portion between it and a typical distal chamber and instead connect to the right atrium, whereas the right and left atria are in communication through a coronary sinus atrial septal defect, with the coronary sinus itself being completely unroofed (see Chapter 33). In another example, all pulmonary veins may fail to join an otherwise typical proximal chamber separated from the distal chamber by a perforated partition, and instead connect to a common pulmonary venous sinus behind the heart that may connect to the coronary sinus, superior vena cava, or infradiaphragmatically.\textsuperscript{52,56}

**Relationship of Cor Triatriatum to a Left Superior Vena Cava**

A left superior vena cava coexists with cor triatriatum considerably more frequently than with other types of congenital heart disease.\textsuperscript{55,61,62} One proposed pathogenesis of cor triatriatum is impingement of a left superior vena cava on the developing left atrium.\textsuperscript{62} Ascuito and colleagues reported cases in which a persistent left superior vena cava joining a dilated coronary sinus impinged on the posterior wall of the left atrium and divided it into two chambers, both of which had defects that communicated with the right atrium.\textsuperscript{56} It seems clear that a relationship exists between these two anomalies, at least in some patients.

**Associated Anomalies**

In addition to PAPVC and unroofed coronary sinus with a left superior vena cava joining the left atrium, other associated anomalies include ventricular septal defect, coarctation of the aorta, atrioventricular septal defect, tetralogy of Fallot, and (rarely) asplenia and polysplenia.\textsuperscript{51}

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Infants with classic cor triatriatum, with a small aperture between the proximal and distal chambers, usually present with evidence of low cardiac output, including pallor, tachypnea, poor peripheral pulses, and growth failure.\textsuperscript{51} When there is associated left-to-right shunting due to connection of the proximal chamber to the right atrium or because of associated PAPVC, evidence of pulmonary overcirculation and venous obstruction may be present in the chest radiograph, and right ventricular enlargement is prominent. In children and young adults, the classic presentation is with signs and symptoms of pulmonary venous hypertension. However, like mitral stenosis, cor triatriatum may present with less classic symptoms.\textsuperscript{52}

Diagnosis is usually made by echocardiography\textsuperscript{53,52} (Fig. 32-4). Transesophageal echocardiography has also proven useful in selected cases.\textsuperscript{64} Recently, three-dimensional echocardiography has been used to identify complex morphology in cor triatriatum.\textsuperscript{53,61} Magnetic resonance imaging with three-dimensional reconstruction provides excellent delineation of both simple and complex morphology in cor triatriatum and is the imaging study of choice if standard two-dimensional echocardiography is not definitive.\textsuperscript{12} Cardiac catheterization and cineangiographic studies are no longer considered necessary unless major associated cardiac anomalies are suspected. However, further evidence may be obtained from selective cineangiographic studies and pressure measurements in the proximal and distal chambers. If the catheter cannot be manipulated into the proximal and distal chambers from the right atrium, sometimes an arterial catheter can be advanced into the left ventricle and retrogradely catheter into the mitral valve and into the distal and then proximal chamber.\textsuperscript{51} Gradients of 20 to 25 mmHg have been demonstrated between the two chambers.\textsuperscript{51}

**NATURAL HISTORY**

Natural history depends on the effective size of the aperture in the partition between the proximal and distal chambers. When it is small, the infant becomes critically ill during the early months of life, with signs of pulmonary venous obstruction (Fig. 32-5, A). Without surgical treatment, such patients die at that young age.\textsuperscript{51,61,63,51} If the aperture is larger, the patient presents in childhood or young adulthood with the signs, symptoms, and prognosis of mitral stenosis.\textsuperscript{52}

In most patients, the aperture is severely restrictive, and approximately 75% of persons born with classic cor triatriatum die in infancy. However, when the proximal chamber communicates with the right atrium through a fossa ovalis atrial septal defect, the prognosis is better because the proximal chamber decompresses into the right atrium (Fig. 32-5, B). These patients present with signs of a large left-to-right shunt and generally survive longer than those with an obstructive aperture. Rarely, cor triatriatum may be discovered in an adult.\textsuperscript{2,61,62,63} Delay in diagnosis may be accounted for by a lesser degree of obstruction by the partition or by a unilateral pulmonary venous obstruction.\textsuperscript{51}

**TECHNIQUE OF OPERATION**

**Classic Cor Triatriatum**

Treatment of cor triatriatum is primarily by operation. In small infants, approach through the right atrium is preferable. In older patients, especially when the proximal chamber is
enlarged and no other cardiac anomalies exist, approach through an incision in the right side of this chamber is recommended.

After usual preparations, moderately hypothermic cardiopulmonary bypass (CPB) using two venous cannulae is established (see Section III of Chapter 2). Alternatively, hypothermic circulatory arrest may be employed according to surgeon preference. Cold cardioplegia is established as usual after clamping the aorta (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).

When the approach is through the proximal chamber, a vertical incision is made in the chamber anterior to the right pulmonary veins (Fig. 32-6, A) exactly as for mitral valve surgery (see Technique of Operation in Chapter 11). After insertion of an appropriately sized Richardson retractor or similar instrument, the diaphragm is exposed and apertures in it identified. A preliminary incision out from the apertures improves exposure for the definitive excision (Fig. 32-6, B). Orifices of the pulmonary veins on both sides are located. Position of the atrial septum is also identified, if necessary, by opening the right atrium and inserting a curved clamp to displace the atrial septum into either the distal or proximal chamber. Most of the partition between these chambers is then excised to make as large an opening as possible (Fig. 32-6, C). This procedure is usually easily and quickly done.

When an approach through the right atrium is used, its free wall is incised as in atrial septal defect closure. The right side of the atrial septum is examined and the fossa ovalis identified. If a foramen ovale or atrial septal defect is present, this is enlarged by incision to gain access into the left-sided chamber with which it communicates, either proximal or distal. If there is no atrial septal defect, the septum primum within the fossa ovalis is incised. The partition between the proximal and distal chambers is then identified. In Fig. 32-7, the exposure provided by an atrial septal incision leading into the proximal chamber is shown (Fig. 32-7, A). The partition is easy to identify and expose by this approach (Fig. 32-7, B). The procedure described for the left-side approach is carried out and the opening in the atrial septum closed with a pericardial patch (Fig. 32-7, C). The cardiotomy is closed, the heart having been filled with blood or saline solution before the last few sutures were placed. The remainder of the operation is completed in the usual fashion (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

In the rare case in which there is a specific contraindication to CPB, percutaneous balloon dilatation is possible using a double balloon technique similar to that proposed for mitral valve stenosis. Relief of symptoms is good, but follow-up is too short (3 months) to establish confidence in this treatment.

Atypical Cor Triatriatum
As noted earlier under Morphology, patients occasionally present for treatment with atypical forms of cor triatriatum, or other important cardiac anomalies may coexist. A persistent left superior vena cava may be present, connecting to the coronary sinus or directly to the upper left atrium, with “unroofing” of the coronary sinus. Because almost any number of specific combinations may be encountered, the general surgical approach is described rather than a detailed description of each possible combination.

Before operation, the surgeon must determine with reasonable certainty the connections and drainage of all pulmonary and systemic veins, including the possible presence and connection of a left superior vena cava. The possible presence

---

**Figure 32-5** Morphology of cor triatriatum. A, Cor triatriatum with patent foramen ovale below obstructing partition. Proximal chamber is separated from distal chamber by an obstructing partition. Partition is attached to the atrial septum medially and immediately below left inferior pulmonary vein laterally. The lateral attachment is also closely related to the mitral valve. Left atrial appendage is in the distal chamber. Clinical presentation is that of pulmonary venous obstruction (like mitral valve stenosis) when the aperture in the partition is small. Distal chamber communicates with right atrium through foramen ovale, but left-to-right shunt is small. B, Cor triatriatum with patent foramen ovale above obstructing partition, through which the proximal chamber may communicate with the right atrium. Clinical presentation in this situation is that of a large left-to-right shunt or may mimic total anomalous pulmonary venous connection. Right ventricle may be enlarged.
RESULTS

Early (Hospital) Death

Hospital deaths are uncommon after repair of classic cor triatriatum. Those that occur are in critically ill infants and should be considered to be related to inadequate myocardial management. Seven separate single-institution retrospective studies constitute a combined total of 96 surgical cases of classic cor triatriatum with six early deaths (6.2%; CL 4.1%-9.4%) (Table 32-1).

Atypical cor triatriatum can also be successfully repaired. Many of the studies documented in Table 32-1 report successful repairs in patients in this more complex subset but also emphasize that mortality is higher than for classic cor triatriatum.

Time-Related Survival and Functional Status

Life expectancy after repair of classic cor triatriatum approaches that of the general population, especially when the operation is done in infancy. Richardson and colleagues

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is as usual (see Chapter 5), with special attention given to support of the respiratory system, which may be compromised by pulmonary venous obstruction existing before operation.
survival was 96% at 5 years and 88% at 15 years. The association of pulmonary vein stenosis with cor triatriatum reinforces the interrelationship between cor triatriatum and TAPVC (see “Pulmonary Vein Stenosis” under Reoperation and the Development of Pulmonary Venous Obstruction in Chapter 31). Another unfavorable late event is restenosis of the orifice between the proximal chamber and left atrium. This may be the result of an inadequate original operation in which the common wall between the two chambers was incompletely resected. Most follow-up studies suggest that essentially all patients are either described as asymptomatic or are documented to be in New York Heart Association functional class I. 

Table 32-1 Hospital Mortality after Repair of Classic Cor Triatriatum

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
</tr>
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<tr>
<td>Van Son et al.</td>
<td>1993</td>
<td>11</td>
<td>1</td>
<td>9.0</td>
<td></td>
</tr>
<tr>
<td>Gheissari et al.</td>
<td>1992</td>
<td>7</td>
<td>1</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Rodefeld et al.</td>
<td>1990</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Carpena et al.</td>
<td>1974</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Alphonso et al.</td>
<td>2005</td>
<td>28</td>
<td>1</td>
<td>3.6</td>
<td></td>
</tr>
<tr>
<td>Al Qethamy et al.</td>
<td>2006</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Salomone et al.</td>
<td>1991</td>
<td>15</td>
<td>3</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>96</td>
<td>6</td>
<td>6.2</td>
<td>4.1-9.4</td>
</tr>
</tbody>
</table>

reported one late death attributed to pulmonary vein stenosis in their group of eight hospital survivors. Qethamy and colleagues reported no late deaths in 20 patients with a mean follow-up of 31 months. Alphonso and colleagues reported 27 patients with a mean follow-up of 98 months; survival was 96% at 5 years and 88% at 15 years. The association of pulmonary vein stenosis with cor triatriatum reinforces the interrelationship between cor triatriatum and TAPVC (see “Pulmonary Vein Stenosis” under Reoperation and the Development of Pulmonary Venous Obstruction in Chapter 31). Another unfavorable late event is restenosis of the orifice between the proximal chamber and left atrium. This may be the result of an inadequate original operation in which the common wall between the two chambers was incompletely resected. Most follow-up studies suggest that essentially all patients are either described as asymptomatic or are documented to be in New York Heart Association functional class I.

INDICATIONS FOR OPERATION

Classic cor triatriatum with a restrictive aperture in the partition between the proximal and distal chambers is an urgent indication for operation, because 75% of patients with such malformations die in infancy. When older patients present with chronic symptoms, operation is also urgently indicated.
In atypical cor triatriatum, when the proximal chamber opens into the right atrium, a restrictive opening or no opening is present between the proximal and distal chambers, and only a small patent foramen oval exists between the right atrium and distal chamber, physiologic instability will be present. A large left-to-right shunt combined with restricted left atrial and left ventricular inflow produces severe symptoms during the early months of life, and operation is urgently indicated.

REFERENCES

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<th>1217</th>
</tr>
</thead>
<tbody>
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<td>1218</td>
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<tr>
<td>Partially Unroofed Terminal Portion of Coronary Sinus</td>
<td>1218</td>
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<tr>
<td>Relationship of Unroofed Coronary Sinus Syndrome to Cor Triatriatum and Atrioventricular Septal Defect</td>
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**Definition**

Unroofed coronary sinus syndrome is a spectrum of cardiac anomalies in which part or all of the common wall between the coronary sinus and left atrium is absent. Hearts with atrial isomerism and a left-sided superior vena cava (LSVC) entering a left-sided atrium are included in this chapter, despite the controversy concerning proper classification of such anomalies (see “Atrial Isomerism” under Morphology later in this chapter; see also Chapter 58).

**Historical Note**

Unroofed coronary sinus syndrome was unknown to cardiac pathologists before the era of cardiac catheterization and cardiac surgery. In 1954, Campbell and Deuchar referred to instances of LSVC attached to the left atrium. Although they did not have such an example in their own series of LSVC, they appreciated that in such cases there was no true coronary sinus. That same year, Winter, a radiologist at Hahnemann Hospital in Philadelphia, published a report that identified persistent LSVC attached to the left atrium, and 2 years later, Friedlich and colleagues identified by cardiac catheterization LSVC entering the left atrium in four patients. An isolated case was also reported by Tuchman and colleagues in 1956. However, true understanding of the morphology of the syndrome awaited the classic paper by Raghib, Edwards, and colleagues in 1965. The descriptive phrase “unroofed coronary sinus” was first used by Helseth and Peterson in 1974.

In cyanotic patients with a communication between the left and right SVC, the LSVC was first ligated (appropriately) by Hurwitt and colleagues in 1955 and then by Davis and colleagues in 1959. In 1965, Taybi and colleagues reported a ligation and mentioned “transferring the left SVC to the right atrium,” but presumably this was unsuccessful, because no further details were given. The first report of successful repair was from the Mayo Clinic in 1963. In this case, a tunnel was constructed from the posterior wall of the left atrium. In a second case, a large pericardial atrial baffle was constructed that corrected the anomalous connection of both the SVC and the inferior vena cava (IVC) to a left-sided atrium. This procedure was also described by Helseth and Peterson in 1974.

**Morphology**

Completely Unroofed Coronary Sinus with Persistent Left Superior Vena Cava

In one form of unroofed coronary sinus syndrome, the coronary sinus does not exist, because the common wall between it and the left atrium is absent. A persistent LSVC, which usually becomes continuous with the coronary sinus, connects to the left upper corner of the left atrium. The site of connection of the LSVC to the left atrium appears to be constant and lies between the opening of the left atrial appendage anteriorly and slightly superiorly, and the opening of the left pulmonary veins posteriorly and inferiorly. The
pulmonary veins may enter the left atrium more superiorly than usual in this form of the syndrome.

A coronary sinus atrial septal defect (ASD) is present in the posteroinferior region of the atrial septum in the usual position of the ostium of the coronary sinus (see Chapter 20, Fig. 30-5). The ASD is separated from the atrioventricular (AV) valve ring by a remnant of atrial septum (in contrast to an ostium primum ASD), and its posterior margin is formed by the atrial wall where it joins the IVC. There may be a separate foramen ovale ASD or a single large ASD formed by the confluence of both defects. The coronary sinus ASD may be confluent with an ostium primum ASD, or there may be a common atrium. Because the coronary sinus does not exist, individual coronary veins connect separately to the inferior aspect of the left atrium. Some also connect to the right atrium.

Of considerable surgical importance is the fact that the left brachiocephalic vein is absent in 80% to 90% of cases of unroofed coronary sinus syndrome and LSVC. The right SVC is frequently small and may be absent. The IVC not infrequently crosses to the left side below the diaphragm to enter the left hemiazygos vein, which joins the LSVC. The hepatic veins usually enter the inferior aspect of the right atrium, but they too may enter the inferior wall of the left atrium. When all the systemic veins enter a morphologically left atrium, total anomalous systemic venous connection is present (see Chapter 31).

**Completely Unroofed Coronary Sinus without Persistent Left Superior Vena Cava**

In some cases, the syndrome is characterized by a completely unroofed coronary sinus without a persistent LSVC. Such cases consist of a coronary sinus type of ASD and total absence of the coronary sinus because of absence of the partition between it and the left atrium.

**Partially Unroofed Midportion of Coronary Sinus**

Another form of the syndrome is characterized by a partially unroofed midportion of the coronary sinus (also called biatrial opening of coronary sinus or coronary sinus to left atrial window or fenestration). In this anomaly, an aperture is present in the midportion of the wall between the coronary sinus and left atrium. Through this aperture, a left-to-right or right-to-left shunt occurs, depending on whether obstruction is present to left atrial or right atrial outflow. When this rare form of unroofed coronary sinus syndrome occurs as an isolated lesion, there may be a large left-to-right shunt. It has also been reported as a major cardiac anomaly associated with tricuspid atresia, recognized only after the Fontan repair has elevated the right atrial pressure and produced a right-to-left shunt.

When midportion unroofing occurs in the presence of LSVC, there is a right-to-left shunt into the left atrium.

**Partially Unroofed Terminal Portion of Coronary Sinus**

Particularly in the presence of an atrioventricular septal defect (see “Completely Unroofed Coronary Sinus with Left Superior Vena Cava” under Morphology in Chapter 34), the coronary sinus ostium may open into the left atrium rather than the right. Also, a localized unroofing of the sinus may occur just before it enters the ostium of the coronary sinus, resulting in a coronary sinus ASD with preservation of the coronary sinus (see “Coronary Sinus Defect” under Morphology in Chapter 30). Such anomalies can be considered to be unroofing (or absence) of the terminal portion of the coronary sinus.

**Relationship of Unroofed Coronary Sinus Syndrome to Cor Triatriatum and Atrioventricular Septal Defect**

As indicated, when a completely unroofed coronary sinus with persistent LSVC is present, both the left and right pulmonary veins may enter the left atrium more superiority than usual. Sometimes this condition is accompanied by a mild or moderate narrowing between the portion of the left atrium to which the pulmonary veins are attached (the common pulmonary venous chamber) and that to which the LSVC, left atrial appendage, and mitral valve are attached (see “Relationship of Cor Triatriatum to a Left Superior Vena Cava” under Morphology in Chapter 32).

Unroofed coronary sinus syndrome has as its most common major associated cardiac anomaly an atrioventricular septal defect, not infrequently with a common atrium (see Chapter 34). Interestingly, atrioventricular septal defects are more commonly associated with persistent LSVC than are other types of ASD.

**Atrial Isomerism**

Many patients with an LSVC connecting to a left-sided atrium have atrial isomerism (see Chapter 58), and the majority of such patients have an atrioventricular septal defect. In an unpublished autopsy series from GLH of 26 hearts with the LSVC connecting to the left-sided atrium, only 3 were examples of classic unroofed coronary sinus syndrome; 23 hearts had atrial isomerism, 17 with bilateral morphologically right atria (most with asplenia) and 6 with bilateral morphologically left atria (most with polysplenia). Of the 23, 20 had an atrioventricular septal defect in addition to numerous other cardiac anomalies. When bilateral morphologically right atria are present, the LSVC enters the left-sided right atrium behind a typical crista terminalis and is not therefore an example of unroofed coronary sinus, even though the coronary sinus is usually absent. When bilateral morphologically left atria are present, the LSVC may or may not be part of an unroofed coronary sinus syndrome. In such cases, however, the coronary sinus is frequently absent.

**Clinical Features and Diagnostic Criteria**

In most cases, diagnosis of unroofed coronary sinus syndrome is made by two-dimensional echocardiography and confirmed at operation (Fig. 33-1). Demonstration of an LSVC by catheter passage into the vein or by cineangiography suggests the diagnosis, which is confirmed at operation if the LSVC can also be shown to drain into the left atrium. Diagnosis of a partially unroofed midportion of the coronary sinus can be made by cineangiography after injection into the right atrium, when right atrial pressure is higher than left (e.g., after the Fontan operation). Konstam and colleagues have pointed out that radionuclide angiography can be diagnostic, because intravenous injections into the left arm show much larger right-to-left shunting than those into the right arm. Diagnosis sometimes can be made by cross-sectional, contrast, and
transesophageal echocardiography.\textsuperscript{2,3} Contrast-enhanced gated multidetector computed tomography is also useful for diagnosis (Fig. 33-2). Often, however, the diagnosis is made by the surgeon viewing external and internal morphology of the heart at operation.

**NATURAL HISTORY**

Cyanosis from right-to-left shunting dominates the clinical picture of isolated completely unroofed coronary sinus with persistent LSVC and determines its natural history. In the series of Quaegebeur and colleagues, cyanosis was mild (all patients were younger than 17 years), but it was severe in some older patients in other series.\textsuperscript{91}

Cerebral embolization manifested by transient ischemic attacks or stroke and brain abscess complicate the life history in 10% to 25% of patients\textsuperscript{91} (Table 19-1). This situation is similar to that in other types of right-to-left shunting. Presumably, life expectancy is considerably reduced by these complications and by other problems associated with increasing cyanosis and polycythemia.

**TECHNIQUE OF OPERATION**

Isolated Completely Unroofed Coronary Sinus with Persistent Left Superior Vena Cava

Anesthesia and preparation of the patient for repair of isolated completely unroofed coronary sinus with persistent LSVC are as described in Section III of Chapter 2. When the diagnosis is known preoperatively, the anesthesiologist inserts a pressure-monitoring line into the left external or, preferably, internal jugular vein.

Operation may be done with cardiopulmonary bypass (CPB) at 25°C and the usual direct caval cannulation (see “Clinical Methodology of Cardiopulmonary Bypass” in Section III of Chapter 2); venous blood from the LSVC is collected with a sump sucker connected to the pump oxygenator. Alternatively in infants, a single venous cannula and repair during hypothermic circulatory arrest may be used. Myocardial management is conducted as for other cardiac operations (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3).

**Intracardiac Repair**

After sternotomy, a large piece of pericardium is excised and set aside (see Chapter 30). Following aortic clamping and infusion of cardioplegic solution, the right atrium is opened through the usual oblique incision. Orifices of the three vena cavae are identified with certainty. Repair can be accomplished satisfactorily using one of two methods (the original method of “reroofing the coronary sinus”\textsuperscript{Q1,R2,S3} is no longer used because of its technical difficulty and because the left pulmonary veins are at risk of obstruction by the baffle). One method consists of excising the entire atrial septum except for the anterior limbus, which is preserved to protect the AV node and bundle of His.\textsuperscript{C3,M2} A pericardial patch is sutured into place as a repositioned atrial septum, and all three caval orifices are positioned on the right side of this septum (Figs. 33-3 and 33-4). This method is particularly useful when a common atrium is part of the cardiac anomaly.

A second method, described by Sand and colleagues, consists of “rerouting the coronary sinus”\textsuperscript{S1} to the roof of the left atrium (Fig. 33-5) and then reconstructing the atrial septum.\textsuperscript{51}

After the right atriotomy is closed, the caval tapes are released and aortic clamp removed. Usual de-airing maneuvers are performed (see “De-airing the Heart” in Section III of Chapter 2), and the operation is completed.

**Extracardiac Repair**

A third method involves extracardiac correction of the unroofed coronary sinus in combination with the associated intracardiac repair. If the brachiocephalic vein is absent, the LSVC is divided at its junction with the left atrium, and the...
A continuous 6-0 or 7-0 absorbable monofilament suture is used for these anastomoses.

If the brachiocephalic vein is present but restrictive, it can be enlarged with a patch of autologous pericardium.\textsuperscript{V2} The LSVC is then divided at its junction with the left atrium, and both ends are oversewn.

These extracardiac techniques eliminate the need for constructing an intraatrial baffle or tunnel. They can be performed during the period of rewarming after correction of opening in the left atrium is oversewn. The divided end of the LSVC is anastomosed to the side of the right SVC either anterior or posterior to the aorta.\textsuperscript{R3,V3} Alternatively, the LSVC can be anastomosed to the right atrial appendage or left pulmonary artery as a bidirectional superior cavopulmonary shunt.\textsuperscript{F1,R3,S4,T1,V4}
Chapter 33 Unroofed Coronary Sinus Syndrome

1221

Patch used to close the interventricular communication (complete atrioventricular septal defect) (see Fig. 33-4; see also Chapter 58 and Fig. 58-6).

Completely Unroofed Coronary Sinus Associated with Other Complex Cardiac Anomalies

No simple description can be given of repairing complex anomalies in which unroofed coronary sinus syndrome is but a part. Such cases are often unique, and the surgeon must study the malformation in detail and plan the repair according to the findings. General comments concerning atypical cor triatriatum may be applicable (see Chapter 32). The types of procedures performed in two large surgical series of uncomplicated unroofed coronary sinus are shown in Tables 33-1 and 33-2.

RESULTS

Early (Hospital) Death

Risk associated with repair of simple unroofed coronary sinus syndrome is low. No deaths occurred among 18 patients (0%; CL 0%-10%) reported by Quaegebeur and colleagues (Table 33-3). In two subsequent series reported by Ootaki and colleagues and Attenhofer Jost and colleagues, early mortality was 0% (0 of 11 patients; CL 0%-16%) and 4.3% (1 of 23 patients; CL 0.7%-14%), respectively.

When the syndrome is part of a complex anomaly associated with atrial isomerism, risk has been much higher. Three of six patients (50%; CL 24%-76%) reported by Quaegebeur and colleagues died (see Table 33-3). A similar experience was reported by Cherian and Rao. Better understanding of morphology and improved operative methods, including avoidance of intracardiac repair, should result in improved outcomes (for further details, see Chapter 58).
Figure 33-4  Autopsy specimen showing a pericardial baffle that corrects an unroofed coronary sinus syndrome (left superior vena cava [LSVC] to left atrium) in association with a common atrium and partial atrioventricular septal defect. Operation was performed on a patient 20 months of age; the child died at 13 years of age, probably from arrhythmia. In both views, the pericardial baffle suture line is identified by a dashed line. A, Exposure from opened right atrium and right ventricle. Baffle suture line passes behind the LSVC ostium to reach the ventricular septal crest between right and left atrioventricular valves and then behind inferior vena caval ostium. There is no right superior vena cava in this heart. B, Viewed from opened left atrium. Key: A, Anterior leaflet of right atrioventricular valve; CoV, opening of large coronary vein into atrium; IVC, inferior vena cava; LA, left atrium; LPV, left pulmonary veins; LSL, left superior atrioventricular valve leaflet; RA, right atrium; RIL, right inferior atrioventricular valve leaflet; RPV, right pulmonary veins; RV, right ventricle.
Time-Related Survival and Functional Status

No late deaths occurred after repair of simple unroofed coronary sinus syndrome in the series of Quaegebeur and colleagues, but one patient required reoperation after 8 years because of tunnel obstruction. No late deaths occurred among the patients reported by Ootaki and colleagues (mean duration of follow-up, 85.5 months), and one late death occurred among 22 hospital survivors (mean duration of follow-up, 85 months) in the series of Attenhofer Jost and colleagues. In the series of Cherian and Rao, one of eight hospital survivors required reoperation for closure of a coronary sinus ASD. At the time of the reports, surviving patients in all series were without symptoms, including the ones who required reoperation.

INDICATIONS FOR OPERATION

When diagnosis of isolated completely unroofed coronary sinus with persistent LSVC is made, operation is advisable because of arterial desaturation, risk of cerebral emboli, and satisfactory results of operation. Indications for repair of the rare isolated completely unroofed coronary sinus without persistent LSVC (coronary sinus ASD) are the same as for other
Figure 33-5, cont’d  
C. Elliptical contoured patch (of pericardium, polyester, or polytetrafluoroethylene) is sutured into place posteriorly to begin creating a pathway for diverting blood from LSVC to right atrium. Care is taken to avoid encroachment of suture line or patch on orifice of left superior pulmonary vein. D, Atrial flap has been laid back into position. Posteriorly and inferiorly, it is resutured to remnant of atrial septum to close the coronary sinus atrial septal defect. Superiorly, the flap is sewn to the other edge of contoured patch; before this, the patch is trimmed to be as narrow as possible to avoid any encroachment on pulmonary veins. Note free access of all three caval orifices to the right atrium. Key: IVC, Inferior vena cava; SVC, superior vena cava.

SPECIAL SITUATIONS AND CONTROVERSIES
Ligation of Left Superior Vena Cava

When the brachiocephalic vein is absent or restrictive, some surgeons ligate the LSVC in this and other conditions even when the jugular venous pressure goes as high as 30 mmHg after temporary occlusion of the LSVC. No ill effects have been reported late postoperatively, although venous engorgement, facial edema, and chylothorax may be early complications.\textsuperscript{12}

We do not recommend ligation in this circumstance, because the other methods described are safe and widely applicable. An alternative practice, when correction of unroofed coronary sinus may complicate intracardiac repair of a coexisting condition and extracardiac repair is not possible, involves temporarily occluding the LSVC and ligating it if the increase in left jugular venous pressure does not types of ASD\textsuperscript{11} (see Chapter 30). When unroofed coronary sinus is associated with complex cardiac anomalies, the associated anomaly usually presents a clear indication for operation.
Table 33-1 Some Details of Eight Patients with Isolated Completely Unroofed Coronary Sinus with Left Superior Vena Cava

<table>
<thead>
<tr>
<th>Data</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1-11 years: 8</td>
</tr>
<tr>
<td></td>
<td>History</td>
</tr>
<tr>
<td></td>
<td>Brain abscess or TIA: 2</td>
</tr>
<tr>
<td></td>
<td>Mild arterial desaturation: 8</td>
</tr>
<tr>
<td></td>
<td>Anatomy</td>
</tr>
<tr>
<td></td>
<td>LSVC to upper corner of left atrium: 8</td>
</tr>
<tr>
<td></td>
<td>LSVC to brachiocephalic vein: 1</td>
</tr>
<tr>
<td></td>
<td>Coronary sinus–type ASD:</td>
</tr>
<tr>
<td></td>
<td>Isolated: 4</td>
</tr>
<tr>
<td></td>
<td>With foramen ovale: 2</td>
</tr>
<tr>
<td></td>
<td>Confluent ASD (coronary sinus plus fossa ovalis type): 4</td>
</tr>
<tr>
<td></td>
<td>Management</td>
</tr>
<tr>
<td></td>
<td>Ligation of LSVC and closure of ASD: 1</td>
</tr>
<tr>
<td></td>
<td>Roofing of coronary sinus:</td>
</tr>
<tr>
<td></td>
<td>With posterior wall of left atrium: 4</td>
</tr>
<tr>
<td></td>
<td>With pericardium: 2</td>
</tr>
<tr>
<td></td>
<td>With opened polyester tube: 1</td>
</tr>
</tbody>
</table>

Data from Quaegebeur and colleagues. Numbers are not cumulative.

Key: ASD, atrial septal defect; LSVC, left superior vena cava; TIA, transient ischemic attack.

Table 33-2 Methods of Repair for Partially Unroofed Coronary Sinus and Persistent Superior Caval Vein in 23 Patients

<table>
<thead>
<tr>
<th>Type of Procedure</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Intraatrial Baffle (n = 7)</em></td>
<td></td>
</tr>
<tr>
<td>CS drainage:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>To left atrium: 6</td>
</tr>
<tr>
<td></td>
<td>To right atrium: 1</td>
</tr>
<tr>
<td><em>Repair of CS Fenestration (n = 6)</em></td>
<td></td>
</tr>
<tr>
<td>Suture closure:</td>
<td>5</td>
</tr>
<tr>
<td>Patch closure:</td>
<td>1</td>
</tr>
<tr>
<td><em>CS Ostium Closure (n = 10)</em></td>
<td></td>
</tr>
<tr>
<td>Suture closure:</td>
<td>6</td>
</tr>
<tr>
<td>Patch closure:</td>
<td>4</td>
</tr>
<tr>
<td><strong>TOTAL</strong>: 23</td>
<td></td>
</tr>
</tbody>
</table>

Modified from Attenhofer Jost and colleagues. PSVC ligated in 5 patients (4 left, 1 right) and anastomosed to LPA in 1 patient.

Key: CS, coronary sinus; LPA, left pulmonary artery; PSVC, persistent superior caval vein.

exceed 15 to 20 mmHg. Even in this setting, however, creating an LSVC–to–left pulmonary artery anastomosis (bidirectional Glenn) would seem preferable to ligating the LSVC. This procedure is technically simple and is feasible in essentially all circumstances except in the presence of pulmonary hypertension. Increasing experience with the bidirectional pulmonary shunt as part of a two-ventricle repair (the “one-and-a-half ventricle repair”) has shown that this physiologic arrangement is well tolerated when applied to a variety of morphologic conditions (see Chapters 34, 40, 41, and 55).

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A

C

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F

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**DEFINITION**

Atrioventricular (AV) septal defects are characterized by a deficiency or absence of septal tissue immediately above and below the normal level of the AV valves, including the region normally occupied by the AV septum, in hearts with two ventricles. The AV valves are abnormal to a varying degree.

These defects have also been called AV canal defects, AV defects, endocardial cushion defects, ostium primum atrial septal defects (when there is no interventricular communication), and common AV orifice (when there is only a single AV valve orifice).  

**HISTORICAL NOTE**

**Morphology**

Abbott apparently recognized ostium primum atrial septal defect (ASD) and common AV canal defect, but it was Rogers and Edwards who in 1948 recognized their morphologic similarity. This concept was further elaborated by Wakai and Edwards in 1956 and 1958. The terms partial and complete atrioventricular canal defects were introduced by these investigators, who realized nonetheless that not all cases fit their definitions. During this period, Lev was formulating his concepts of ostium primum ASD (or partial AV canal) and common AV orifice (or complete AV canal), and he described the position of the AV node and bundle of His in these malformations.  

Wakai and Edwards and later Bharati and Lev became dissatisfied with trying to compress all cases into two categories and added the term transitional. During this period, Van Mierop’s scholarship added a great deal of knowledge about the overall anatomic features of AV septal defects.

By the early 1960s, surgical treatment of these defects provided a stimulus to further morphologic studies. In 1966, Rastelli and colleagues at the Mayo Clinic described in more detail the morphology of AV valve leaflets in cases with common AV orifice. The error made in this study was to compress into the designation common anterior leaflet a leaflet that was in fact divided in two by a commissure (i.e., the divided common anterior leaflet of type A). The description of AV valve leaflets by Rastelli and colleagues was accepted for some years, but in 1976 a publication by Ugarbe and colleagues emphasized the idea of leaflets bridging the ventricular septum, a concept also held by Lev. Meanwhile, based on anatomic and cineangiographic studies and in accordance with the description of Baron and colleagues and Van Mierop and colleagues, it was recognized in the late 1960s that the basic defect in these malformations was absence of the AV septum. This concept is particularly important because the AV septum can be imaged by echocardiography and in the left ventriculogram in the right anterior oblique projection. These concepts were further expanded by Piccoli and colleagues under the direction of Anderson, who further emphasized that all the variations of the defect were part of a spectrum (Fig. 34-1).

**Surgical Treatment**

In 1952 at the University of Minnesota Hospital in Minneapolis, after a long period of laboratory investigation, Dennis and Varco attempted for the first time a cardiac operation in a human using a pump-oxygenator. The preoperative diagnosis was ASD, and at operation the defect was thought to be closed. The patient died, and autopsy showed the true diagnosis to be partial AV septal defect (Edwards JE: personal communication, 1980). The first successful repair of a complete AV septal defect was performed by Lillehei and colleagues in 1954, using cross-circulation and direct suture of the atrial rim of the septal defect to the crest of the ventricular septum. In 1954, Kirklin and colleagues successfully repaired a partial AV septal defect through the atrial well of Watkins and Gross, and in 1955 began repairing AV septal defects by open cardiotomy and use of the pump-oxygenator.

Early experiences with complete AV septal defects were all associated with a high hospital mortality, often related to complete heart block, postrepair left AV valve regurgitation, or creation of subaortic stenosis. Interestingly, in many of these early operations, a two-patch technique was used (see “Two-Patch Technique” under Technique of Operation later in this chapter). In 1958, Lev’s description of the location of the bundle of His provided the basis for repair techniques that avoid heart block. In 1959, Dubost and Blondeau reported their early experience and emphasized that the “cleft” in the “mitral leaflet” need not be sutured in repairing partial AV septal defects, a concept currently challenged. In 1962, Maloney and colleagues described two cases in which a single patch was used to close both
defects and with the valve tissue suspended from the patch. This technique was again described by Gerbode in 1962 and was associated with decreased in-hospital mortality. McGoon recognized the importance of “taking from the tricuspid valve” to leave sufficient tissue from which to create an adequate left AV valve. These technical advances allowed repair of even the more complex variants of the defect. Subsequently, good results were obtained in patients older than about 2 years of age, but results in infants remained relatively poor. Between 1968 and 1971, Barratt-Boyes successfully repaired this anomaly in four severely ill infants; subsequently, improved results in infants were reported by many others.

In 1978, Carpentier again emphasized (as did Dubost and Blondeau) that generally, the left AV valve functions best when repaired as a three-leaflet valve. As a result of these advances, risks of operation for nearly all types of AV septal defect are now low.

**MORPHOLOGY**

**General Morphologic Characteristics**

AV septal defects have as defining characteristics a deficiency or absence of the AV septum, resulting in an ostium primum defect immediately above the AV valves and a deficiency (or scooped-out area) in the inlet (basal) portion of the ventricular septum immediately below the AV valves. Patients with partial AV septal defects have a normal length of atrial septum, and the ostium primum ASD is the result of absence of the relatively small AV septum plus some deficiency in the inlet portion of the ventricular septum. The deficiency in the inlet portion of the ventricular septum is variable, but on average is greater in patients with complete AV septal defects than in those with partial defects.

These septal deficiencies may or may not result in interatrial or interventricular communications, depending on configuration and attachments of the AV valves (Tables 34-1 and 34-2). Whereas the basic defect in these malformations is absence of the AV septum, whether the ventricular septal or atrial septal deficiency or the AV valve abnormality is the result only of AV septal absence is still debated.

Five or more AV valve leaflets of variable size are usually present (see Fig. 34-1), but there is often variability in completeness of commissures and prominent crenations in the leaflets (Fig. 34-2). For example, among the 43 hearts with all types of AV septal defects and 2 ventricles in the GLH autopsy series in which the number of leaflets could be accurately assessed, 10 (23%) had 4 leaflets, 18 (42%) had 5 leaflets, 14 (33%) had 6 leaflets, and 1 (2%) had 7 leaflets. When a large interventricular communication was present (complete AV septal defect), the most common number of leaflets was 5 (16 of 28, or 57%).
The left superior leaflet (LSL) and left inferior leaflet (LIL) are particularly variable in size, connections one to another (Table 34-5), and degree of bridging across the crest of the ventricular septum (Table 34-4; see Figs. 34-1 and 34-2). There may be one or two AV valve orifices (Table 34-5).

Hearts with AV septal defects are also characterized by absence of the usual wedged position of the aortic valve above the AV valves. Instead, it is elevated and deviated anteriorly.\textsuperscript{53,63,73,74} Details of the aortic-mitral fibrous continuity often differ from those in the normal heart. Thus, continuity was abnormal in more than half of 21 specimens with normally related great arteries in the GLH autopsy series; continuity was to the base of the noncoronary cusp in only 5 (24%) and to both the noncoronary and right coronary cusps in 7 (33%). In addition, the left ventricular (LV) inflow tract is shortened in length to the outflow portion, and there is a related reduction in length of the diaphragmatic wall of the LV.\textsuperscript{3,16} The LV outflow tract is also narrowed, although rarely is the narrowing sufficient to be of hemodynamic importance in the unrepaired heart.\textsuperscript{57}

AV septal defects include a spectrum of malformations. At one end is the simplest type, in which there is an interatrial communication but no interventricular communication and a connection of variable width between the LSL and LIL; this is called a partial AV septal defect or ostium primum defect. At the other end of the spectrum is the most extreme form, with large deficiencies in atrial and ventricular septa, a common AV valve orifice, and large interatrial and interventricular communications; this is called a complete AV septal defect. Because a continuous spectrum of gradations lies between these extremes, some anomalies have been grouped.

### Table 34-1 Size of Interventricular Communication in Atrioventricular Septal Defects\textsuperscript{a}

<table>
<thead>
<tr>
<th>Size</th>
<th>Prevalence</th>
<th>% of 310</th>
</tr>
</thead>
<tbody>
<tr>
<td>0\textsuperscript{b}</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>2</td>
<td>27</td>
<td>8.7</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>11.3</td>
</tr>
<tr>
<td>4</td>
<td>223</td>
<td>71.9</td>
</tr>
<tr>
<td>5\textsuperscript{c}</td>
<td>21</td>
<td>6.8</td>
</tr>
</tbody>
</table>

Data from Studer and colleagues.\textsuperscript{515}  
\textsuperscript{a}Study is based on data from 310 surgical patients.  
\textsuperscript{b}Condition in which the characteristic atrioventricular (AV) septal deficiency is present, but the AV valves are adherent on their atrial side to the edge of the defect, resulting in no interatrial communication.  
\textsuperscript{c}Common atrium.

### Table 34-2 Size of Interventricular Communication in Atrioventricular Septal Defects

<table>
<thead>
<tr>
<th>Degree of LSL-LIL Connection\textsuperscript{a}</th>
<th>Interventricular Communication (n = 154)</th>
<th>Interventricular Communication (n = 156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>% of 154</td>
<td>No.</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>1</td>
<td>55</td>
<td>36</td>
</tr>
<tr>
<td>2</td>
<td>82</td>
<td>53</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>0.6</td>
</tr>
<tr>
<td>Connected, unknown degree</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data from Studer and colleagues.\textsuperscript{515}  
\textsuperscript{a}0, Separate LSL and LIL, such as in common AV orifice; 1 and 2, narrow connections (deep cleft in “anterior mitral leaflet”); 3 and 4, broad connection (shallow cleft or notch); 5, no cleft, anterior mitral leaflet.

### Table 34-3 Left Superior and Left Inferior Leaflet Connections in Atrioventricular Septal Defects

<table>
<thead>
<tr>
<th>Degree of LSL Bridging</th>
<th>Without Interventricular Communication (n = 154)</th>
<th>With Interventricular Communication (n = 156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>% of 153\textsuperscript{b}</td>
<td>No.</td>
</tr>
<tr>
<td>0</td>
<td>150</td>
<td>98</td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>2.0</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>5.2</td>
</tr>
</tbody>
</table>

Data from Studer and colleagues.\textsuperscript{515}  
\textsuperscript{b}Data not available for one patient.  
\textsuperscript{c}Data not available for two patients.  
Key: LIL, Left inferior leaflet; LSL, left superior leaflet.

### Table 34-4 Left Superior Leaflet Bridging in Atrioventricular Septal Defects

Data from Studer and colleagues.\textsuperscript{515}  
\textsuperscript{b}Data not available for one patient.  
\textsuperscript{c}Data not available for two patients.  
Key: LSL, Left superior leaflet.

---

\textsuperscript{a}Prevalence
Figure 34-2  Atrioventricular (AV) valves in AV septal defects viewed from atrial aspect in a series of fixed specimens. A, Specimen with partial AV septal defect in which left superior (LS) and left inferior (LI) leaflets are adherent to crest of ventricular septum and there is no interventricular communication. Arrow marks line of closure between LS and LI leaflets, formerly called the “cleft in the anterior mitral leaflet.” Note that as usual, LS leaflet does not bridge septum (there is no leaflet tissue in the position of the superior portion of the normal tricuspid septal leaflet). In this heart, as is not uncommon, there are two left lateral and two right lateral leaflets. B, Specimen with complete AV septal defect in which there are interventricular communications beneath LS and LI leaflets. LS leaflet does not bridge crest of septum. Right superior (RS) leaflet is characteristically large. LI leaflet is bridging (grade 2) and very distinct from right inferior (RI) leaflet. C, Specimen of a complete AV septal defect in which LS leaflet markedly bridges crest of septum. Correspondingly, RS leaflet is small. LS leaflet is characteristically larger than LI leaflet. Key: LA, Left atrium; RA, right atrium.
as intermediate or transitional AV septal defects. Definitions of these intermediate types have varied but usually include presence of two AV valve orifices and a restrictive inlet ventricular septal defect (VSD), with dense chordal attachments to the ventricular septum (see “Unusual Atrioventricular Combinations” under Morphology). Added complexity is provided by occurrence of a large variety of major and minor associated cardiac anomalies (Tables 34-6 and 34-7). In addition, Down syndrome is common, particularly in patients with an interventricular communication.

Because it is virtually impossible to subdivide the spectrum of AV septal defects into satisfactory noncontroversial subgroups, this chapter describes cases based on morphologic and functional variables rather than categorizing them into subgroups. The older imprecise terms continue to be useful as shorthand, and in this chapter, partial AV septal defect refers to a malformation with two AV valve orifices and no interventricular communication, whereas complete AV septal defect refers to a malformation with a common AV valve orifice and large (grade 2 or more) nonrestrictive interventricular communication.

### Table 34-5 Type of Atrioventricular Valve Orifices in Atrioventricular Septal Defects

<table>
<thead>
<tr>
<th>Type</th>
<th>No.</th>
<th>% of 310</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two AV valves</td>
<td>171</td>
<td>55</td>
</tr>
<tr>
<td>Common AV valve</td>
<td>139</td>
<td>45</td>
</tr>
</tbody>
</table>

Data from Studer and colleagues.

*Includes the 154 patients without interventricular communications; 11 with small interventricular communications beneath the left superior (LSL) and/or inferior leaflets (UIL); four with connected but free-floating and connected LSL and UIL (see Table 34-3); and two with no interatrial communication but large interventricular communication (not inlet atrioventricular septal-type ventricular septal defects).

### Table 34-6 Major Associated Cardiac Anomalies in Atrioventricular Septal Defects

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>No.</th>
<th>% of 310</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>237</td>
<td>76</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>31</td>
<td>10.0</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>20</td>
<td>6.5</td>
</tr>
<tr>
<td>Completely unroofed coronary sinus</td>
<td>9</td>
<td>2.9</td>
</tr>
<tr>
<td>with left SVC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Situs ambiguus</td>
<td>7</td>
<td>2.3</td>
</tr>
<tr>
<td>DORV without PS</td>
<td>6</td>
<td>1.9</td>
</tr>
<tr>
<td>Additional VSDs</td>
<td>5</td>
<td>1.6</td>
</tr>
<tr>
<td>DORV + PS</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>Situs inversus totalis</td>
<td>3</td>
<td>1.0</td>
</tr>
<tr>
<td>TAPVC</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Left ventricular outflow obstruction</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Transposition of the great arteries</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>PS, supravalvar mitral stenosis,</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>Ebstein malformation, coarctation,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>isolated dextrocardia</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data from Studer and colleagues.

### Table 34-7 Minor Associated Cardiac Anomalies in Atrioventricular Septal Defects

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Without Interventricular Communication (n = 154)</th>
<th>With Interventricular Communication (n = 156)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Sizable) ASD</td>
<td>17</td>
<td>11</td>
</tr>
<tr>
<td>Left SVC without unroofed coronary sinus</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Partially unroofed coronary sinus</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Azygos extension of IVC</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>IVC to lower left common atrium</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Bilateral IVCs</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>TASVC to common atrium</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right PVs to RA</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anomalous origin LAD from RCA (TF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Origin stenosis LPA (not TF)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Wolff-Parkinson-White syndrome</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Spontaneous heart block</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Coronary artery disease requiring CABG</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Data from Studer and colleagues.

*Does not include patent foramen ovale.

Key: ASD, Atrial septal defect; CABG, coronary artery bypass grafting; CL, 70% confidence limits; IVC, inferior vena cava; LAD, left anterior descending coronary artery; LPA, left pulmonary artery; PV, pulmonary vein; RA, right atrium; RCA, right coronary artery; SVC, superior vena cava; TASVC, total anomalous systemic venous connection; TF, tetralogy of Fallot.
Chapter 34  Atrioventricular Septal Defect

Common Atrium
Deficiencies in the anterior limbus or fossa ovalis may be associated with AV septal defects, resulting in a larger interatrial communication. Occasionally the entire limbus and fossa ovalis are absent, along with the AV septum. The condition is then termed common atrium (see Table 34-1).

Absence of Interatrial Communication
Rarely, AV valve tissue is attached completely to the edge of the atrial septum, and no interatrial communication exists despite the deficiency in the septum (see Table 34-1). In this unusual variant, the characteristic deficiency of the inlet (basal) portion of the ventricular septum is also present and associated with a large interventricular communication beneath the leaflets. The functionally left AV valve, consisting only of those portions of the LSL and LIL on the left side of their attachment to the atrial septum, tends to be competent. As seen from a right atrial approach, part of the right AV valve may have chordal attachments across the ventricular defect to the left side of the septum—that is, it is straddling. When viewed from the ventricular side, the appearance is typical of a complete AV septal defect. It is distinct from an inlet type of perimembranous VSD that is sometimes called inlet septal, AV septal, or AV canal type of VSD, which is unrelated to deficiency of the AV septum (see “Inlet Septal Ventricular Septal Defect” under Morphology in Chapter 35.

Atrial Septal Deficiency and Interatrial Communications

Partial Atrioventricular Septal Defect
Usually there is an interatrial communication related to deficiency of the AV septum, the so-called ostium primum ASD (Fig. 34-3). The defect is bounded below by the inferiorly displaced AV valve leaflets and above by a crescentic ridge of atrial septum that fuses with the AV valve anulus only at its extremities.

Generally, there is little atrial septal tissue at the superior point of fusion of the atrial septum with the valve anulus adjacent to the aorta, but more tissue is usually present inferiorty adjacent to the coronary sinus (Fig. 34-4). The distance between the crescentic atrial margin of the defect and the AV valves (and thus the size of the interatrial communication) is variable. In most cases, the fossa ovalis is normally formed and there is a patent foramen ovale or an associated fossa ovalis ASD. Usually the interatrial communication through the ostium primum defect is moderate in size. When the interatrial communication is small, the atrial septal deficiency is restricted to the area normally occupied by the AV septum (26). The communication may be still smaller due to fusion of the base of the LSL or LIL to the edge of the adjacent portion of the atrial septum. Rarely, there may be an accessory “parachute” of fibrous tissue that narrows or obstructs the defect. Under such circumstances, a pressure difference exists between the two atria.

Figure 34-3  Partial atrioventricular (AV) septal defect. A, View from right atrium and right ventricle. Large ostium primum atrial septal defect is seen above AV valve leaflets. No interventricular communication is present beneath the leaflets. However, deficiency of basal (inlet) portion of ventricular septum is apparent. Left superior (LS) leaflet is attached firmly by fibrous tissue to crest of septum (dashed line) and does not bridge onto right ventricular side. There is thus a bare area on right side of superior aspect of ventricular septum (arrow). Left inferior (LI) leaflet bridges on right ventricular side. Right superior (RS) leaflet is clearly visible, but right lateral and inferior leaflets are not in photograph. B, Left ventricular outflow view. LS and LI leaflets are firmly attached to crest of ventricular septum. Narrowing and elongation of left ventricular outflow tract are apparent. This figure makes clear why, in describing position of the two leaflets attached to the ventricular crest, the terms superior and inferior are preferable to anterior and posterior, terms that lead to confusion with normal mitral leaflets. (Courtesy Dr. Maurice Lev.)
and “Inlet Septal Type of Ventricular Septal Defect” in text that follows).

Ventricular Septal Deficiency and Interventricular Communications

Partial Atrioventricular Septal Defect
Some degree of deficiency of the inlet portion of the ventricular septum immediately beneath the AV valves is a constant finding. Thus, the inlet portion of the ventricular septum is shortened. There is usually no interventricular communication when the LSL and LIL are connected and attached to the downwardly displaced crest of the septum throughout its length (Fig. 34-5; see also Fig. 34-3), the situation described as a partial AV septal defect. Occasionally, one or several small interventricular communications are present beneath the attachment of the AV valve to the septum (Fig. 34-5, B).

Complete Atrioventricular Septal Defect
With ventricular septal deficiency generally greater than that in a partial AV septal defect, a moderate or large interventricular communication may be present, and usually the LSL and LIL are separate. This anomaly is described as a complete AV septal defect (Fig. 34-5, C). Deficiency of the inlet portion of the ventricular septum (the “scoop”) is generally deeper in hearts with complete AV septal defects than in those with partial AV septal defects.\(^{A10,B1,F2}\) Often the communication is particularly large beneath the LSL and smaller beneath the LIL (see Table 34-2), whereas in about 5% of cases there is a larger interventricular communication beneath the LSL and none beneath the LIL. Rarely, there is no VSD beneath the LSL and a large one beneath the LIL.

A remnant of the membranous ventricular septum may be present (see Fig. 34-5, B). This was the case in 8 of 27 (30%) GLH autopsy specimens of AV septal defect with normally related great arteries; in 19 specimens the membranous septum could not be identified.

Atrioventricular Valves
Attachments of the AV valves to the crest of the ventricular septum in partial AV septal defects, as well as their chordal attachments in complete AV septal defects, are displaced toward the apex of the heart because of deficiency of the inlet (basal) portion of the septum. This alters orientation of the AV orifices relative to the aortic orifice (i.e., the aortic valve is no longer wedged between the AV valves) and provides an important diagnostic imaging criterion of this malformation.\(^{E5,E6,F2}\)

Two Atrioventricular Valve Orifices
Typically when two AV valve orifices are present, as in partial AV septal defects, the LSL and LIL are joined together to a variable extent anteriorly by leaflet tissue near the crest of the ventricular septum (see Figs. 34-1 and 34-3). Together they resemble an anterior (septal) mitral leaflet with a cleft, but in fact the left AV valve is tricuspid and oriented differently from the normal valve (see Figs. 34-1 and 34-2). The connection between the LSL and LIL may be only a thin strand of tissue (complete cleft), but more commonly it is 2 to 4 mm or more deep (see Table 34-3). This connection, too, is usually fused to the crest of the ventricular septum in partial AV septal defects. Occasionally, chordae pass from opposing edges of the LSL and LIL to the muscular ventricular septum beneath.\(^{E5}\) Yilmaz and colleagues identify a difference in this area of separation and distinguish between a commissure supported by chordal apparatus on either side of the gap and a cleft that is relatively unsupported and bereft of chordae at its edges.\(^{F2}\) In addition, the chordae that originate from the central edges of the LSL and LIL attach to different papillary muscles, which can cause a distracting force on the leaflets during closure. This contrasts with the normal commissure in which the chordae from adjacent leaflet edges attach to a single papillary muscle, encouraging coaptation. Rarely, separation into LSL and LIL is represented only by a notch in the center of the free edge of a nearly normal “anterior mitral leaflet.” The left lateral leaflet (LLL) is usually smaller than the other two leaflets and is triangular.

In aggregate, these left AV valve leaflet anomalies may make the valve regurgitant to a variable degree, sometimes severely (Table 34-8). When LSL and LIL are nearly completely separated (connection grades 1 and 2; see Table 34-3), an appreciable gap may occur during systole, producing regurgitation. When there is failure of valve coaptation at this site, leaflet tissue forming the margin usually becomes thickened and rolled. In other cases, regurgitation appears to be due to deficiency of leaflet tissue, particularly in the LIL.\(^{B16,M10}\) The mechanism of severe left AV valve regurgitation is, however, not evident in some cases. The jet of regurgitation is usually directed into the right atrium. Rarely, the left AV valve is stenotic, but this usually is associated with hypoplasia of the LV.\(^{B18}\)

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**Figure 34-4** Right atrial view of a specimen of a partial atrioventricular (AV) septal defect. Coronary sinus ostium (CoS) is seen inferior and posterior to ostium primum (P) defect in atrial septum. Approximate position of AV node and bundle of His is shown as a dashed line. Placement of inferior part of patch suture line is shown by the line of x’s. Key: EV, Eustachian valve of inferior vena cava; FO, fossa ovalis; SVC, superior vena cava.
Figure 34-5  Left ventricular aspect of atrioventricular (AV) septal defects.  
A, Partial AV septal defect viewed from opened left ventricle.  
Left superior (LS) and left inferior (LI) leaflets are completely attached to crest of a deficient ventricular septum (VS).  
Area of contact or closure between left superior and left inferior leaflets is indicated by arrow.  
In this specimen, only the anterior papillary muscle (APM) is present (“parachute” mitral valve).  
B, Intermediate type of AV septal defect from left ventricular view.  
Numerous small interventricular communications are present between thick, short chordae that tether both LS and LI leaflets to ventricular crest.  
Fibrous tissue extending from superior leaflet to below right coronary aortic cusp (RC) represents remnant of membranous septum.  
C, Complete AV septal defect viewed from left ventricular aspect.  
LS and LI bridging leaflets are free floating, and there is a large interventricular communication between them and the underlying crest of the ventricular septum.  
This specimen also has double outlet right ventricle.  
Key: AoV, Aortic valve; LI, left lateral leaflet; NC, noncoronary aortic cusp.
The right AV valve is also abnormal when there are two AV orifices, although less attention has been paid to it. It may consist of three leaflets—right superior leaflet (RSL), right lateral leaflet (RLL), and right inferior leaflet (RIL)—or of two or four leaflets (see Figs. 34-1 and 34-2). Leaflet tissue attached directly or by chordae to the crest or right side of the crest of the septum, and thus contributing to closure of the right AV valves, is considered to represent bridging of the LSL or LIL (see Fig. 34-1).

Usually in cases without an interventricular communication, the LSL does not bridge at all (previously, this finding was interpreted as absence or hypoplasia of the superior part of the tricuspid septal leaflet) and the LIL bridges moderately (see Fig. 34-2, A). Even with abnormalities of the right AV valve, regurgitation is rare (unless right heart failure develops).

**Common Atrioventricular Orifice**

When the AV valve orifice is a common one and the interventricular communication is large (complete AV septal defect), the LSL and LIL are separate, and a bare area is exposed on the crest of the ventricular septum (Fig. 34-6; see Figs. 34-1 and 34-5, C). The LSL may be entirely on the LV side of the septum or may, to a variable degree, bridge the septum and extend onto the right ventricular side (see Fig. 34-2, B-C and Table 34-4). This variability formed the basis for the classification by Rastelli and colleagues into types A, B, and C.\(^2\) Chordal attachments of the right ventricular extremity of the LSL vary according to degree of bridging (Fig. 34-7). When there is no bridging, chordal attachments are to the ventricular crest (Fig. 34-7, A). With mild bridging, they are to the medial papillary muscle in the right ventricle; with moderate bridging, to an accessory (often large) apical papillary muscle (Fig. 34-7, B); and with marked bridging, to the normally positioned (although often bifid) anterolateral papillary muscle of the right ventricle (Fig. 34-7, C). When the LSL bridges the septum moderately or markedly and extends into the right ventricle, it is usually unattached to the underlying ventricular crest (free-floating), but it may occasionally be attached by chordae (tethered). Length of the chordal or fibrous attachments to the right side or crest of the ventricular septum varies according to size of the interventricular communication or the position of the leaflet.

![Figure 34-6](image)

**Table 34-8** Preoperative Atrioventricular Valve Regurgitation in Patients with Atrioventricular Septal Defect without Major Associated Cardiac Anomalies

<table>
<thead>
<tr>
<th>Magnitude of AV Valve Regurgitation</th>
<th>Total</th>
<th>Without Interventricular Communication</th>
<th>With Interventricular Communication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>% of 305(^a)</td>
<td>No.</td>
</tr>
<tr>
<td>0</td>
<td>29</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>1</td>
<td>39</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>85</td>
<td>28</td>
<td>48</td>
</tr>
<tr>
<td>3</td>
<td>98</td>
<td>32</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>43</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>305</td>
<td>154</td>
<td>151</td>
</tr>
</tbody>
</table>

Data from Studer and colleagues.\(^11\)

\(^a\) No information on five patients.

\(^b\) \(\chi^2\) for difference = .007.

![Image](image)

The LIL typically bridges moderately, but it too varies in this respect. It is not uncommon for a bridging LIL to be attached to the underlying ventricular crest either completely or by short, thick chordae with interchordal spaces.

Chordal attachments of the leftward components of the common AV valve in the LV are usually relatively normal, although the posterior papillary muscle is displaced more laterally than normal and a third papillary muscle may be present.\(^2\) There may be only one papillary muscle, producing a parachute-type valve that is difficult to repair.\(^2\) This was true in 7 of 53 (13%) cases in the GLH autopsy series, in 14% of the specimens described by David and colleagues, and in 4% of 155 surgical cases reported by Ilbawi and colleagues.\(^12\)
The right ventricular portion of the common AV valve has superior, lateral, and inferior leaflets, but as in partial AV septal defects, they vary considerably in number and size (see Fig. 34-2). When bridging of the LSL is absent or mild, the RSL is large, whereas with more extensive bridging, it is smaller.78

When leaflets of the common AV valve close appropriately during ventricular systole, AV valve regurgitation is absent or mild. However, important left AV valve regurgitation may be present (see Table 34-8). The mechanism of the regurgitation is often not clearly understood.

Anatomic studies by Kanani and colleagues have emphasized the marked valvar abnormalities in this malformation, not only of the anular component but also of the subvalvar apparatus (with deficiency of chordal arrangement) and leaflet tissue (which is often deficient in coaptation surface and pliability following repair).75
Accessory Orifice

An accessory orifice (double left AV valve orifice) is present in the commissure on one side, usually the inferior side, of the LLL in about 5% of cases. A ring of chordae surrounds the orifice, and a very small papillary muscle is usually beneath it. The accessory orifice may be conceptualized as an incomplete commissure, and the fibrous tissue “bridge” between the accessory orifice and main orifice

Unusual Atrioventricular Combinations

Other unusual combinations of size, connections, attachments, and degree of bridging of AV valve leaflets in the spectrum of AV septal defects prompted Wakai and Edwards, Bharati and colleagues, and others to use a transitional or intermediate category. Rarely in patients with two AV valve orifices with no interventricular communication beneath the LSL and LIL, these leaflets are connected only by a fibrous strand adherent to the ventricular septal crest, forming what Bharati and colleagues have called a “pseudomitral leaflet,” rather than an “anterior mitral leaflet with a complete cleft.”

In such patients, deficiency of LIL tissue and severe left AV valve regurgitation are common. Occasionally when the LSL and LIL are connected (and thus two AV valve orifices are present), one or multiple small interchordal interventricular communications are present beneath the leaflets (see Tables 34-2 and 34-5), and occasionally one or two larger holes may be present (Fig. 34-8; see Fig. 34-5, B). In about 1% of cases, the connected LSL and LIL have large interventricular communications beneath them; in these patients, the connection is a thin strand of valve tissue beneath which there is also a large interventricular communication (Fig. 34-9), but two AV valve orifices can be said to be present (see Table 34-5). Bharati and colleagues have referred to this as intermediate type C.

### Accessory Orifice

An accessory orifice (double left AV valve orifice) is present in the commissure on one side, usually the inferior side, of the LLL in about 5% of cases. A ring of chordae surrounds the orifice, and a very small papillary muscle is usually beneath it. The accessory orifice may be conceptualized as an incomplete commissure, and the fibrous tissue “bridge” between the accessory orifice and main orifice

### Table 34-9

<table>
<thead>
<tr>
<th>Left AV Valve Orifice</th>
<th>Without Interventricular Communication</th>
<th>With Interventricular Communication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 154)</td>
<td>(n = 156)</td>
</tr>
<tr>
<td>No.</td>
<td>% of 154</td>
<td>No.</td>
</tr>
<tr>
<td>Single</td>
<td>149</td>
<td>147</td>
</tr>
<tr>
<td>Double</td>
<td>5</td>
<td>9</td>
</tr>
</tbody>
</table>

Data from Studer and colleagues. $^{115} \chi^2$ for difference = .3.
which case it overrides the left AV valve to a varying degree and may be associated with hypoplasia of the left atrium. This variant is therefore sometimes included in “hypoplastic left heart physiology” (see Chapter 49).

The right ventricle has no specific anomalies, but is usually enlarged secondary to the left-to-right shunt. Its size is also variable, and occasionally it is importantly hypoplastic.

S15

Ventricles

The LV outflow tract is characteristically elongated and narrowed (Fig. 34-10) in all types of AV septal defect (see “General Morphologic Characteristics” under Morphology earlier in this chapter).

In AV septal defect with large interventricular communications, the LV may be abnormally large, but its size is variable, both absolutely and in relation to the right ventricle. In the severely right-dominant type of AV septal defect, the LV is severely hypoplastic (Fig. 34-11). In such cases, the atrial septum may be displaced leftward in relation to the plane of the ventricular septum, in which case it overrides the left AV valve to a varying degree and may be associated with hypoplasia of the left atrium. This variant is therefore sometimes included in “hypoplastic left heart physiology” (see Chapter 49).

The right ventricle has no specific anomalies, but is usually enlarged secondary to the left-to-right shunt. Its size is also variable, and occasionally it is importantly hypoplastic.

The LV or right ventricle is severely hypoplastic in about 7% of patients born with complete AV septal defect. Prevalence of the two types is similar. Presence of severe ventricular hypoplasia can increase risk of surgical correction and may demand a Fontan-type repair, alone or with a technique for correcting the hypoplastic left heart physiology (see Special Situations and Controversies later in this chapter and Chapter 41).

Septal Malalignment

Usually the two AV valves or common AV valve orifice lies in proper proportion over the two ventricles. When one ventricle is hypoplastic, the ventricular septum is malaligned and lies more to the side of the hypoplastic ventricle (see Fig. 34-11).
Less commonly, the atrial septal remnant is malaligned, and then usually leftward. When this is severe, both AV valves (or common AV valve orifice) are accessible only from the right atrium, and blood exists from the left atrium only through the ostium primum defect (so-called double outlet right atrium).66,15,51

Left Ventricular Outflow or Inflow Obstruction

Important LV outflow tract obstruction occurs rarely in unoperated hearts (about 1% of cases) in all types of AV septal defect.8,11,31,11 It more often becomes apparent as a postoperative complication. It is surprising that it is not more frequent, in view of the elongation and narrowing of this area in affected hearts.66,64

Part of the elongation and narrowing is due to the more extensive area of direct fibrous continuity between the aortic valve and the LSL than is present normally between the aortic and mitral valves.53 This is caused in part by the short, thick chordae that often anchor the LSL to the crest of the ventricular septum.34,35 Also, the anterolateral muscle bundle of the LV (muscle of Moulaert) bulges more into the LV outflow tract in hearts with AV septal defects than in normal hearts, contributing to the tendency to outflow obstruction after repair.36 In addition to these basic arrangements tending to narrow the LV outflow tract, LV obstruction may be contributed to by morphologically discrete subaortic stenosis or by excrescences of AV valve tissue heaped up in the LV outflow tract.51,61,77,73 It may also result from abnormally positioned papillary muscles.87 Occasionally, its presence is overlooked preoperatively, and it becomes apparent or develops only after operation.

Important LV inflow obstruction may occur rarely.87 This may be from simple narrowing of the AV valve entrance into the LV, usually associated with marked right ventricular dominance. It may be related to presence of an accessory AV valve orifice on the left side, or it may result from cor triatriatum (see Chapter 32) or a supravalvar fibrous ring.76 These associated cardiac anomalies appear to be more prevalent in patients without Down syndrome.33,65

Conduction System

The defect in the AV septum often displaces the coronary sinus ostium inferiorly, which may appear to lie in the left atrium, especially when the ostium primum atrial defect is particularly large. The AV node is also displaced inferiorly (caudally) and lies in the posterior right atrial wall between the orifice of the coronary sinus and ventricular crest.15 (Fig. 34-12) in what has been termed the nodal triangle.75 The bundle of His passes forward and superiorly from the node to the ventricular crest, reaching it where the crest fuses posteriorly with the AV valve anulus.81 It then courses along the top of the ventricular septum beneath the bridging portion of the LIL, giving off the left bundle branches. As it reaches the midpoint of the crest of the ventricular septum, it becomes the right bundle branch, which continues along the crest a little farther before it descends toward the muscle of Lanclusi and moderator band. These anatomic find- ings have been supported by electrophysiologic studies at operation.14,11 This morphology of the conduction system is a determinant of the electrocardiographic pattern usually seen in AV septal defects.1,75

Major Associated Cardiac Anomalies

Table 34-6 presents the prevalence of the major cardiac anomalies associated with AV septal defects.

Patent Ductus Arteriosus

A patent ductus arteriosus is present in about 10% of patients with AV septal defects. It is particularly common in those with an interventricular communication.

Tetralogy of Fallot

Typical tetralogy of Fallot is present in about 5% of patients with complete AV septal defects, and about 1% of patients with tetralogy of Fallot have associated complete AV septal defects.81,8,71 The LSL bridges markedly and is free-floating over the crest of the ventricular septum, and the interventricular communication beneath it is large and juxtaaortic.81,64 An interventricular communication beneath the LIL is present in only about half of cases.79 Rarely the LSL and LIL are connected by a fibrous (or valvar) band, beneath which also is a large interventricular communication. The right ventricular outflow tract has typical tetralogy morphology (see Chapter 38) that may be so severe that pulmonary atresia is present. Localized narrowing occasionally occurring in that portion of the LV outflow tract just upstream from the recess formed by the subaortic deficiency of the ventricular septum further complicates the situation in rare cases.

Double Outlet Right Ventricle

Double outlet right ventricle (DORV) without pulmonary stenosis complicates complete AV septal defect in about 2% of cases.86,8,11,11,51,72 As in tetralogy of Fallot, usually...
deficiency of the ventricular septum is large and juxtaaortic beneath the extensively bridging and free-floating LSL. However, occasionally the interventricular communication is far from the aortic and pulmonary valves and is “non-committed.” Rarely, Taussig-Bing type of DORV is present.\textsuperscript{8,13,12} DORV combined with severe pulmonary stenosis coexists with complete AV septal defects in about 1% of cases.\textsuperscript{315} These combinations of DORV and AV septal defect with large interventricular communication frequently also have atrial isomerism or situs inversus, common atrium, completely unroofed coronary sinus with left superior vena cava, azygos extension of the inferior vena cava, or total anomalous pulmonary venous connection.\textsuperscript{2,312}

**Transposition of the Great Arteries**

Very rarely, transposition of the great arteries (discordant ventriculoarterial connection) is associated.\textsuperscript{313}

**Completely UnroofedCoronary Sinus with Left Superior Vena Cava**

Completely unroofed coronary sinus with persistent left superior vena cava (see Chapter 33) attached to left atrium occurs in about 3% of patients with an interventricular communication and in about 3% without, and is more frequent when common atrium is present.\textsuperscript{91} A partially unroofed distal end of the coronary sinus resulting in drainage of the coronary sinus into the left atrium occasionally occurs, but is a minor and unimportant associated anomaly.\textsuperscript{15} When complete AV septal defect is associated with persistent left superior vena cava and unroofed coronary sinus, atrial isomerism is also frequent (see Chapter 58).\textsuperscript{34}

**Minor Associated Cardiac Anomalies**

Table 34-7 lists minor cardiac anomalies associated with AV septal defects.

**Pulmonary Vascular Disease**

In partial AV septal defects, as in other types of ASDs, pulmonary vascular disease is uncommon, whereas in complete AV septal defects, as with large VSDs, pulmonary vascular disease usually appears early in life and progresses.\textsuperscript{313}

Morphologically, pulmonary vascular disease associated with complete AV septal defects is similar to that associated with large VSDs (see “Pulmonary Vascular Disease” under Morphology in Section I of Chapter 35). However, it tends to progress more rapidly in patients with complete AV septal defects. Correlation between histologic findings and pulmonary vascular resistance is similar in the two conditions.\textsuperscript{315} The pulmonary vascular changes probably are more frequent and occur at an earlier age in patients with Down syndrome with complete AV septal defects compared with patients without Down syndrome.\textsuperscript{19,31}

**Down Syndrome**

Down syndrome is rare in patients with partial AV septal defects but common (about 75%) in those with complete AV septal defects.\textsuperscript{199} Left-sided obstructive lesions are 10 times less common in Down syndrome patients\textsuperscript{2,31,35} whereas advanced pulmonary vascular disease may be more frequent.\textsuperscript{31}

Inlet Septal Type of Ventricular Septal Defect

It is important to note that an isolated inlet (AV septal) type of VSD (see Morphology in Section I of Chapter 35) occurs without any of the features of an AV septal defect as defined in this chapter, except that it involves the inflow portion of the ventricular septum beneath the septal tricuspid valve leaflet and usually also the area of the membranous ventricular septum. The AV septum, however, is intact, and the mitral and tricuspid annuli and aortic orifice lie in normal positions. This feature allows these VSDs to be readily differentiated echocardiographically and angiographically from AV septal defects. Interestingly, in isolated inlet VSD, the anterior mitral leaflet is occasionally cleft.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Pathophysiology

Left-to-right shunting is present in AV septal defects unless severe pulmonary vascular disease has developed or important right ventricular outflow tract obstruction or pulmonary valve stenosis coexists. When there is no interventricular communication, the shunt is at atrial level and usually large, but it may be small or moderate; in such cases, a pressure gradient can be demonstrated between left and right atria. When the shunt is large and left AV valve regurgitation is mild or absent, the hemodynamic state of the patient is identical to that in isolated ASD (see Clinical Features and Diagnostic Criteria in Chapter 30); only right ventricular stroke volume is increased. When important left AV valve regurgitation is present, the left-to-right shunt becomes much larger; in fact, the regurgitation jet usually goes directly from LV to right atrium. Left as well as right ventricular stroke volume is increased, and marked cardiomegaly and heart failure develop early in life.

When a large interventricular communication is also present (complete AV septal defect), the left-to-right shunt is large, and right ventricular and pulmonary artery pressures approach or equal systemic pressures (Table 34-10). Pulmonary vascular resistance rises rapidly and is usually importantly elevated after age 6 to 12 months and sometimes before.\textsuperscript{31}

<table>
<thead>
<tr>
<th>Table 34-10</th>
<th>Preoperative Pulmonary Artery–Aortic Pressure Ratios in Patients without Major Associated Cardiac Anomalies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ratio</strong></td>
<td><strong>No. % of 97\textsuperscript{a)</strong></td>
</tr>
<tr>
<td>PPA/PAO</td>
<td>Without Interventricular Communication (n = 140)</td>
</tr>
<tr>
<td>≤  .03</td>
<td>65</td>
</tr>
<tr>
<td>.03–.05</td>
<td>20</td>
</tr>
<tr>
<td>.05–.07</td>
<td>5</td>
</tr>
<tr>
<td>.07–.09</td>
<td>6</td>
</tr>
<tr>
<td>.09–.14</td>
<td>1</td>
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</tbody>
</table>

Data from Studer and colleagues.\textsuperscript{315}

\textsuperscript{a}Data not available for 43 patients.

\textsuperscript{b}Data not available for 23 patients.

Key: AO, Aortic; PA, pulmonary artery.
When present, AV valve regurgitation adds greatly to ventricular volume overload. For some reason, however, the overload usually seems to enlarge the right ventricle more than the left.

**Atrioventricular Valve Regurgitation**

Prevalence of regurgitation at the left AV valve or common AV valve is considered to be less than before echocardiographic studies were available. Probably 10% to 15% of patients with partial AV septal defect have important regurgitation, not 40% as was estimated earlier (see Table 34-8). Moderate AV valve regurgitation is present in about 20% of infants with complete AV septal defects and severe regurgitation in only about 15%. AV valve regurgitation may be considerably more common in older patients with complete AV septal defects.

A not-uncommon site of regurgitation is through the gap between the LSL and LIL, particularly near the leaflet hinge or base; partly for this reason, regurgitant flow frequently goes directly into the right atrium. Under such circumstances, the left atrium remains small and the right becomes large; but when the interatrial communication is smaller or the regurgitation is sited elsewhere, regurgitation may enter the left atrium, which enlarges.

Although the precise mechanism of AV valve regurgitation is often unclear, it apparently varies considerably, as would be expected from variations in the number, size, and configuration of the leaflets and their chordal attachments. In patients with partial AV septal defects and important left AV valve regurgitation, the LIL is commonly severely hypoplastic.

**Symptoms and Physical Findings**

Patients without an interventricular communication (partial AV septal defect) and with absent or mild left AV valve regurgitation often present in the first decade of life but may remain asymptomatic well beyond that age. Their clinical presentation is virtually identical to that of patients with the more common fossa ovalis ASD (see “Fossa Ovalis Defect” under Morphology in Chapter 30), except that they may have an apical systolic murmur when mild left AV valve regurgitation is present, and left axis deviation and a counterclockwise frontal plane loop.

Moderate or severe (grade 3, 4, or 5) left AV valve regurgitation in patients with partial AV septal defects may produce symptoms earlier, and progressive severe heart failure may require treatment in infancy. In addition to the usual signs of ASD, the heart is more active in association with a loud apical pansystolic murmur, and the apex of the LV may be palpable. Tachypnea and hepatomegaly are often evident.

In patients with complete AV septal defect, presentation is usually in the first year of life, frequently during the first months, as a result of progressive severe heart failure, which may not be controllable medically. There is associated tachypnea, poor peripheral perfusion, and failure to thrive. Occasionally, heart failure is minimal early in life, and presentation may be delayed until some years later, by which time there is almost always severe hypertensive pulmonary vascular disease and Eisenmenger complex (see “Clinical Findings” under Clinical Features and Diagnostic Criteria in Section I of Chapter 35). On physical examination, cardiomegaly with increased ventricular activity is apparent. The second heart sound at the base is split and usually fixed, with accentuation of the second component caused by elevated pulmonary artery pressure. A systolic murmur is audible over the left precordium from the shunt at ventricular level and is increased in intensity and nearer the apex when there is important AV valve regurgitation. A mid-diastolic flow murmur is characteristically widely heard both over the lower left precordium and at the apex secondary to the large diastolic flow across the malformed AV valve leaflets (depending on both the left-right shunt and any AV valve regurgitation).

In those patients with morphology intermediate between the partial and complete AV septal defects, clinical features depend on size of the interventricular communication and severity of left AV valve regurgitation.

**Chest Radiograph**

In patients without an interventricular communication or important left AV valve regurgitation, the chest radiograph is the same as in other large ASDs. When moderate or severe left AV valve regurgitation is present, the radiograph usually shows marked cardiomegaly with evidence of LV, right ventricular, and right atrial enlargement and marked pulmonary plethora. Left atrial enlargement is not apparent unless the ostium primum defect is restrictive.

In complete AV septal defect, cardiomegaly and pulmonary plethora are evident in infants and young children presenting with heart failure. In patients who survive beyond this age, severely increased pulmonary vascular resistance usually dominates, and the heart is less enlarged, central pulmonary arteries are large, and lung fields are clear.

**Electrocardiogram**

Electrocardiographic findings are rather specific. They usually indicate marked right ventricular hypertrophy and may show LV hypertrophy as well. The PR interval is frequently prolonged. Of considerable diagnostic importance is the vectorcardiogram. Ongley and colleagues conclude that a counterclockwise frontal plane loop anterior and to the right strongly suggests, but does not prove, the diagnosis.

**Two-Dimensional Echocardiogram**

In AV septal defects without an interventricular communication or important left AV valve regurgitation, two-dimensional echocardiography, together with clinical presentation, chest radiograph, and electrocardiogram, is diagnostic, and cardiac catheterization with cineangiography is not necessary. Two-dimensional echocardiography, particularly with Doppler color flow imaging and, when possible, with a transthoracic window, can also provide full information for complete AV septal defects.

The common AV orifice is easily seen in the four-chamber view (Fig. 34-13). Characteristically, left and right AV valves (separated or common) exist at the same level, in contrast to the cephalad displacement of the normal mitral valve. The elongated outflow septum and unwedged position of the aortic valve are also identifiable. Chordal attachment and degree of leaflet bridging can also be assessed. Finally, the degree of AV valve regurgitation is assessed with color flow.
Figure 34-13  Echocardiograms of atrioventricular (AV) septal defects. **A**, Apical four-chamber view of a heart with an unbalanced AV septal defect. In this figure, the common AV valve (arrow) is positioned such that there is malalignment between interatrial septum and interventricular septum and a disproportionate size of the ventricles. Smaller arrow shows primum atrial septal defect. **B**, Apical four-chamber view showing common AV valve (arrows) with virtual absence of interatrial septum. **C**, Parasternal long axis view showing a “gooseneck” appearance of left ventricular outflow tract caused by displacement of left-sided portion of a common AV valve (arrow). **D**, Coronal image of heart as viewed from apex (apical four-chamber view). This heart has a complete AV septal defect. There are both primum and secundum atrial septal defects. **E**, Coronal image of a heart with a complete AV septal defect as viewed from the apex (apical four-chamber view). Arrows point to the common AV valve. There are both primum and secundum atrial septal defects. **F**, Coronal image of a heart with a partial AV septal defect as viewed from the apex (apical four-chamber view). Thin arrows point to common AV valve. Thick arrow points to tissue occluding the inlet ventricular septal defect right AV valve pouch formation. Key: Ao, Aorta; IVS, interventricular septum; LA, left atrium; LV, left ventricle; RA, right atrium, RV, right ventricle; V, inlet ventricular septal defect; 1°, primum; 2°, secundum.
With subcostal views, the degree of balance in the commitment of the common AV orifice to right and left ventricles can be ascertained (see “Unbalanced Atroventricular Septal Defects” under Special Situations and Controversies).

Limitations of echocardiography include lack of sensitivity for double orifice left AV valve and inability to assess quantitatively pulmonary vascular resistance and reactivity.

Cardiac Catheterization and Cineangiogram

Direction and magnitude of shunting; pulmonary and systemic pressures, resistances, and flows; and right and left ventricular pressures can be measured and calculated from data obtained at cardiac catheterization (see “Cardiac Catheterization” under Clinical Features and Diagnostic Criteria in Section I of Chapter 35). P4 However, these studies are now required only when major cardiac anomalies coexist and when operability is questioned because of evidence of pulmonary vascular disease.

Angiocardiographic features of AV septal defects were well described by Baron and colleagues in 1964 and further refined by the work of Brandt and colleagues, Bargeron and colleagues, and Macartney and colleagues. B3,B4,B20,M1,S10 Both oblique and axial views are used. B3,R20 They demonstrate absence of the AV septum and deficiency of the inlet portion of the ventricular septum, elongation of the LV outflow tract in relationship to the inflow tract, elevation and anterior displacement of the aortic valve vis-à-vis the AV valves, and the anomalous relationship of anterior components of the left AV valve to the aorta. These are well portrayed by the line drawings of Baron and colleagues and representative cineangiograms (Figs. 34-14 through 34-16). The anomalous left AV valve’s relationship to the aorta results in change in direction of left AV valve movement. Interaltrial and interventricular shunting can also be demonstrated, as can presence of one or two AV valve orifices. With high-quality studies, leaflets of the left AV valve often can be visualized in motion to delineate the degree, location, and mechanism of valvar regurgitation.

The relative size of the two ventricles and of AV orifices must be determined by whatever technique—echocardiography or angiography—is preferred. Severe hypoplasia of one or the other ventricle must be identified preoperatively, because such hypoplasia makes it less likely anatomic correction will be successful. C8,M1

Special Situations and Associated Defects

Presence of common atrium generally can be identified preoperatively by echocardiography or a cineangiogram, which show nearly complete absence of both atrial and AV septum (see Fig. 34-13). Finding mild arterial desaturation in a patient with clinical findings of an AV septal defect, but without an interventricular communication or pulmonary artery hypertension, suggests presence of common atrium. C9,M18,R2,R5 Presence of a left superior vena cava in such a setting suggests both unroofed coronary sinus syndrome and common atrium, because they frequently coexist. Q1,R5 In patients with common atrium and atrial isomerism, even more complex associations occur, including DORV, partial or total anomalous pulmonary venous connection, and azygos extension of the inferior vena cava D7,K16,P2,S13,T1 (see Morphology in Chapter 58).

A patent ductus arteriosus can be identified on aortography. Likewise, associated malformations such as tetralogy of Fallot, DORV, transposition of the great arteries, and additional VSDs are identified by a combination of echocardiography and cineangiography.

It is essential to recognize functionally important LV outflow tract obstruction. Narrowing of this tract is inherent in AV septal defects but rarely results in a systolic pressure gradient. Distortion results from the shortened inflow axis of the LV and anterior displacement of the left AV valve complex (Fig. 34-17). Thus, LV outflow obstruction is most prevalent in patients with Rastelli type A valve morphology. P7,S17 This distortion is rarely evident preoperatively as LV outflow obstruction. More frequently, important obstruction becomes evident postoperatively, both early and later. Usually it takes the form of subaortic discrete membranous stenosis, but the process may be relatively diffuse along the outflow tract. Infrequently, it occurs as a result of the ventricular patch component pulling the left AV valve apically and anteriorly such that the new “mitral” valve apparatus narrows the outflow tract. Thus, the initial AV septal repair must place the left AV valve at the appropriate level: caudad toward the apex may result in LV outflow tract obstruction; cephalad toward the atria may result in left AV valve regurgitation.

NATURAL HISTORY

The life history of patients with surgically untreated AV septal defects depends on morphologic and functional details of their malformation. When there is a partial AV septal defect, only mild left AV valve regurgitation, and no major associated cardiac anomaly, life history without surgical treatment is similar to that of patients with large fossa ovalis ASDs (see Natural History in Chapter 30). Important pulmonary vascular disease develops in a small number of patients in their 20s, 30s, and 40s. P4 As in other types of large ASD, symptomatic deterioration of patients in adult life often coincides with development of atrial fibrillation (Fig. 34-18).

Patients with a partial AV septal defect and moderate or severe left AV valve regurgitation have a different natural history. Because of a nonrestrictive interatrial communication, severe left atrial and pulmonary venous hypertension are absent, but the left-to-right shunt is large and pulmonary artery pressure usually at least moderately elevated. Probably at least 20% of such individuals are severely symptomatic in infancy, and without surgical treatment, many would die in the first decade of life.

Patients with a complete AV septal defect have a still more unfavorable natural history. Because no group of infants known to have this malformation has been followed from birth without surgical intervention, the ideal database for delineation of their natural history does not exist. The closest approach is the prospective study of 56,109 live births by Mitchell and colleagues that included 10 infants judged to have isolated complex AV septal defect (excluding four stillbirths with the malformation), 4 of whom died within the first 3 years of life. M15 This information is inconclusive, however, because of the small number of patients involved; failure to obtain a positive diagnosis by surgery, autopsy, or cardiac catheterization in all patients in the study; use of surgical intervention in some cases; and nonreporting of specific ages of the six survivors.
Figure 34-14  Diagrams of altered attachment of left atrioventricular (AV) valve leaflets in AV septal defect compared with normal heart. Heart is shown in its in vivo position as seen in a frontal angiogram. Right ventricle (RV) and most of the ventricular septum and right atrium have been removed. Dashed line indicates portion of line of attachment of left AV valve hidden by other structures. A, Normal heart. Attachment of anterior mitral leaflet (A) begins at anterolateral commissure (AL) and runs anteriorly for a short distance along free wall of left ventricle (LV). It is then continuous with root of aorta in relation to adjacent portion of left coronary (L) and noncoronary (N) aortic cusps. Line of attachment proceeds downward along AV septum to posteromedial commissure (PM). Attachment of mitral valve to AV septum is profiled in right anterior oblique view (see Fig. 34-15). B-C, Partial AV septal defect shown in diastole (B) and systole (C). Scooped-out crest of basal portion of ventricular septum is shown considerably thinner than it actually is. Right AV valve leaflets are shown only at their sites of attachment. Diastolic figure (B) depicts left superior and left inferior leaflets as open; their line of attachment to aortic root is nearly normal, but it then passes along the superior rim of the scooped-out ventricular septal crest. Left superior leaflet is displaced upward into the left ventricular outflow tract, narrowing it. Left inferior leaflet is folded back against left ventricular aspect of sinus septum. In systolic figure (C), left superior and inferior leaflets are closed. Increased left ventricular pressure balloons them toward the atria. Arrow marks their point of coaptation. Key: AP, Anterior papillary muscle; AV, atrioventricular septum; L, left inferior leaflet of atrioventricular valve; LA, left atrium; MS, muscular ventricular septum; P, posterior mitral leaflet; PP, posterior papillary muscle; R, right aortic cusp; S, left superior leaflet of atrioventricular valve; T, tricuspid valve. (From Baron and colleagues.13)
Figure 34-15  Diagrammatic representations of cineangiograms of a normal heart and hearts with atrioventricular (AV) septal defects, in oblique and axial views. A, Mitral valve orifice and leaflet attachments (interrupted line) in right anterior oblique (RAO) and left anterior oblique (LAO) projections. (1) Normal mitral orifice is approximately profiled in 40-degree RAO projection, but is overlapped by left ventricular (LV) outflow tract. Rightward posterior border of normal LV outflow tract is formed by AV septal tissue, not mitral valve. (2) In 50-degree LAO projections, the rightward anterior margin of the normal outflow tract consists of the basal ventricular sinus (inlet) septum: membranous above, muscular below. Mitral valve attachments do not reach the septal margin. (3, 4) In AV septal defects, absence of AV septum and adjacent deficiency of basal (inlet) ventricular septum modify left AV valve attachments and position and shape of left AV orifice and LV outflow tract. B, LV cineangiograms in 40-degree RAO projections. (1, 2) Normal features can be compared with those of typical partial (3, 4) and complete (5, 6) AV septal defect in systole and diastole. In the normal heart, mitral (left AV valve) leaflets contribute only to the lowest portion of rightward posterior LV outflow margin in systole, the relatively immobile AV septum forming the remainder of this margin throughout cardiac cycle in diastole. Line of attachment (m) of mural (posterior) leaflet of mitral valve can be identified, because contrast is trapped between leaflet and adjacent LV wall. In AV septal defects, rightward posterior margin of LV outflow tract consists of mobile leaflet tissue: left superior leaflet (s) above and left inferior leaflet (i) below. AV septum is absent. Mural leaflet attachment lies in relatively normal position. When there is complete attachment of left superior and inferior leaflets to septal crest (dashed line), LV outflow tract deformity is well marked in systole, and position of septal crest can be identified in diastole, with contrast being trapped between open leaflets and septum. When there is a large interventricular communication with superior and inferior leaflets free-floating or attached to septal crest by thin chordae only (5, 6), systolic deformity may be less marked and septal crest may be invisible, because contrast is washed away by non-radiopaque inflow. RAO view separates an AV regurgitant stream (AVR) from an interventricular shunt (VS).
Figure 34-15, cont’d  C, Left ventricular (LV) cineangiograms in 50-degree left anterior oblique (LAO) projection. (1, 2) In normal heart, septal margin of LV outflow tract is uninterrupted in systole and diastole. In AV septal defect (3-8), septal margin is interrupted by defect in basal (inlet) ventricular septum, the defect being continuous with left AV orifice. (3, 4) When left superior (s) and inferior (i) leaflets are completely attached to septal crest, as in partial AV septal defect, leaflet tissue bulges into defect in systole, and position of septal crest (c) can be identified in diastole. (7, 8) When there is a large interventricular communication, systolic flow into right ventricle can be observed passing beneath left superior (upper arrow) or left inferior (lower arrow) leaflets. In diastole, a common AV orifice is identified. (5, 6) In some cases, attachments to septal crest are present but leave smaller interventricular communications. AV valve regurgitation tends to obscure valve detail as overlying atria opacify.

D, LV or left atrial cineangiograms of AV septal defect in 50-degree LAO with cranial angulation (axial, hepatoclavicular, or four-chamber view). (1) Arrows in 40-degree RAO view illustrate why conventional LAO (part C) shows full height of the AV orifice, providing the best separation of left superior from left inferior leaflets. Cranially tilted version of LAO (CR LAO) foreshortens AV orifice and tends to superimpose these leaflets. (2, 3) However, the characteristic deformity of septal and AV orifice anatomy seen in conventional LAO view can be appreciated in axial LAO views, which are shown in both systole and diastole. In addition, midmuscular and apical parts of the sinus septum are better separated from basal defect so that additional muscular defects in cross-hatched area (e.g., at x) may be identified. AV valve regurgitation obscures detail, but partial separation of atria from ventricles improves differentiation of regurgitation from interventricular shunting. With a left atrial or right upper pulmonary venous injection in 50-degree LAO with cranial angulation (4), contrast flow (arrows) early in the sequence shows position of atrial septal defect adjacent to AV valves. Contrast enters right atrium, right ventricle, and left ventricle. Cranial angulation rarely achieves a perfect profile of AV anulus, and ventricular opacification obscures detail later in the sequence. Key: AV, Atrioventricular septum; AVR, atrioventricular regurgitant stream; bs, basal (inlet) portion of ventricular septum; c, septal crest; CR LAO, cranial left anterior oblique; i, left inferior leaflet; l, left coronary sinus of aortic root; LA, left atrium; LAO, left anterior oblique; LV, left ventricle; m, line of attachment of posterior mitral leaflet; N, noncoronary sinus of aortic root; R, right coronary sinus of aortic root; RA, right atrium; RUPV, right upper pulmonary venous injection; RV, right ventricle; s, left superior leaflet; VS, ventricular shunt.
An important event in the natural history is development of severe pulmonary vascular disease. This complication becomes apparent at 7 to 12 months of age in up to 30% of patients with complete AV septal defect and is probably present in 90% of such patients by age 3 to 5 years.\textsuperscript{F3,N2} Thus, its prevalence in early life is higher in patients with complete AV septal defect than in those with large VSD.

In the absence of a definitive prospective study, approximation of natural history of complete AV septal defect has been constructed from 39 patients in two reports of

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**Figure 34-16** Cineangiograms of atrioventricular (AV) septal defects. A, Partial AV septal defect shown by left ventriculogram in four-chamber position: diastolic frame (left) and systolic frame (right). Loss of straight line contour from aortic valve to crux cordis indicates absence of major part of AV septum. B, AV septal defect with two AV valve orifices and an interventricular communication.
This analysis indicates that about 80% of patients who do not undergo operation die by age 2 years (Fig. 34-19). A child surviving to age 1 year has only about a 15% chance of living to age 5. Those who die in the first 1 to 2 years of life usually do so with heart failure, with or without recurrent pulmonary infections, as a result of the large left-to-right shunt and moderate-to-severe AV valve regurgitation present in 60%. The high incidence of death in the first year of life has been confirmed by Samanek. Thereafter, valve regurgitation and increasing pulmonary vascular disease become dominant factors in the natural history. Newfeld and colleagues showed histologically that advanced pulmonary vascular disease (Heath-Edwards grade 3 and 4; see “Pulmonary Vascular Disease” under Morphology in Section I of Chapter 35) is occasionally present in such infants, even in the first year of life. However, it is...
uncertainty as to the appropriateness of analyses underlying their inferences, however.\textsuperscript{K8,W9}

Another aspect of the natural history of patients with AV septal defects is the tendency of their offspring to have similar defects or other congenital cardiac malformations. Emanuel and colleagues found that 14% of children of mothers with AV septal defects have congenital heart disease; half have tetralogy of Fallot, and half have AV septal defects. This prevalence is much higher than the 2% to 4% among children of parents with other types of congenital heart disease.\textsuperscript{N4}

**TECHNIQUE OF OPERATION**

Surgical treatment of AV septal defects is directed toward (1) closing the interatrial communication, which is virtually always present; (2) closing the interventricular communication if one is present; (3) avoiding damage to the AV node and bundle of His; and (4) maintaining or creating two competent, nonstenotic AV valves.

Repair techniques vary considerably, but when used properly, all appear to provide good results.\textsuperscript{B1,L1} For example:

- One or two patches may be used to repair the malformation when there is large interventricular communication.\textsuperscript{R3}
- A markedly bridging LSL may be divided to facilitate the repair, or it may be left intact.\textsuperscript{B17,R4,S15}

![Figure 34-17 Anatomic specimens (above) and drawings of them (below) contrasting outflow angle in a normal heart compared with that in atrioventricular (AV) septal defect. A, Wide angle between plane of outlet septum and plane of septal crest (outflow angle) in a normal heart. B, Narrow angle in a heart with AV septal defect. Septal crest is scooped out, shortened, and anteriorly displaced; outflow axis is elongated. (From Van Arsdell and colleagues.\textsuperscript{V1})](image)

![Figure 34-18 Cardiac arrhythmias in surgically untreated patients with a partial atrioventricular septal defect according to age. Increased prevalence in older patients is striking. (From Somerville.\textsuperscript{S9})](image) present in nearly 90% of patients older than age 1 year (7 of their 8 specimens).

Bull and colleagues dispute these inferences and deduce a more favorable prognosis for infants with complete AV septal defects based on a study of patients with Down syndrome and this anomaly.\textsuperscript{B21} Careful study of their report generates
in this regard the results are imperfect, particularly in patients without interventricular communications. The same improvements have been obtained while retaining the single-patch technique. Addition of intraoperative transesophageal echocardiography (TEE) to assess completeness of repair provides a further safeguard against an imperfect anatomic and functional result.

**Figure 34-19** Life expectancy without surgery of patients with complete atrioventricular septal defects. A, Plus signs represent nonparametric survival estimates; solid line, with its 70% confidence limits (dotted lines), represents parametric survival estimates. Note that probability of surviving beyond 6 months is 50%, and beyond a year is only 30%. B, Hazard function according to age. Note that risk of dying is highest in the first few months of life. (From Berger and colleagues.)

Methods described in this chapter are the product of experiences in several centers and have improved surgical results. They avoid functionally important damage to the conduction system, provide complete and permanent closure of interatrial and interventricular communications, and are suitable for the many variations across the spectrum of AV septal defects. They are well adapted to cases with major associated cardiac anomalies. They retain AV valve competence when it is present, minimize occurrence of valve repair dehiscence, and generally abolish or lessen AV valve regurgitation, although

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- The AV node and bundle of His may be avoided by staying on the LV and left atrial side (McGoon DC: personal communication, 1978) or by staying on the right side of the septum.
- Contiguous surfaces of the LSL and LIL may be sutured together, or the left AV valve may be left as a tricuspid structure.
- The patch may be attached to leaflet tissue by simple sutures or by pledgeted mattress sutures with some sort of sandwich method, with assortment of techniques employed to establish AV valve competence.

Methods described in this chapter are the product of experiences in several centers and have improved surgical results. They avoid functionally important damage to the conduction system, provide complete and permanent closure of interatrial and interventricular communications, and are suitable for the many variations across the spectrum of AV septal defects. They are well adapted to cases with major associated cardiac anomalies. They retain AV valve competence when it is present, minimize occurrence of valve repair dehiscence, and generally abolish or lessen AV valve regurgitation, although

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**Repair of Complete Atrioventricular Septal Defect with Little or No Bridging of Left Superior and Left Inferior Leaflets: Rastelli Type A**

**Two-Patch Technique**

After the usual preparations, a median sternotomy is made, a large piece of pericardium is removed and set aside, and pericardial stay sutures are applied. External cardiac anatomy is evaluated and a left superior vena cava sought. If one is present, there is a 50% chance of associated unroofed coronary sinus syndrome. Purse-string sutures are placed.

In patients weighing less than 5 kg, repair may be performed with limited cardiopulmonary bypass (CPB) with a single venous cannula and hypothermic circulatory arrest; in larger patients, standard CPB is used. Alternatively, in both infants and older children, hypothermic CPB at 20°C and cold cardioplegia may be used. In this method, the cavae are cannulated directly with thin-walled, right-angled metal cannulas (see “Venous Cannulation” in Section III of Chapter 2). CPB flow is reduced to about 1.2 L · min⁻¹ · m⁻² when the patient’s temperature reaches 20°C. Short periods of circulatory arrest or low flow perfusion are occasionally used if visibility is not excellent. As cooling proceeds, the aorta is clamped, and cold cardioplegic solution is injected. The right atrium is opened widely, and a sump sucker is passed through the foramen ovale into the left atrium. Stay sutures are applied.

The malformation is examined and each morphologic detail noted (Fig. 34-20). Morphology of the LSL and LIL is noted carefully with the leaflets in both the closed and open positions. Cold saline solution is injected once or twice through the valve and the closure pattern and any regurgitant leaks studied (Fig. 34-21, A-C). The most anterior point of LSL-LIL opposing edges is found, and a double-armed 6-0 or 7-0 polypropylene suture is placed through it. Leaflet stay and marking sutures are placed, measurements are made, and the polyester interventricular patch is trimmed.

The patch is sutured to the right side of the crest of the ventricular septum with continuous polypropylene suture (Fig. 34-21, D and E). Chordae of the RSL and RIL stay on the right ventricular side of the patch; those of the LSL and LIL stay on the LV side, and some may be cut if they interfere with the suturing, because the anterior edges of these leaflets will be sutured to the polyester patch.

When this phase is completed, the marking suture on the anterior edges of the coapting surfaces of the LSL-LIL complex is passed through the appropriate point of the edge of the polyester ventricular defect patch. The pericardial interatrial patch is then trimmed to appropriate shape and size, and the first part of its insertion is accomplished (Fig. 34-21, F). For this, interrupted mattress sutures of 5-0 or 6-0 polyester are placed to enclose anterior edges of the LSL and LIL between the polyester patch below and pericardial patch above. Alternatively, left-sided leaflet tissue is anchored as a separate maneuver to the polyester patch; the pericardial atrial
The interventricular patch is in place to study its closure pattern and competence. A few additional “tailoring sutures” are placed without tension along the coapting surfaces of the LSL and LIL near the patch, if needed, to prevent systolic eversion or prolapse; usually they are not required. If a central leak (at the point of junction of LSL, LIL, and LLL) persists, an additional septal patch is then sewn to the leaflet-patch line of attachment. Great care is taken to ensure alignment of left AV valve leaflets is perfect and without distortion during this process.

Saline solution is again injected through the left-sided portion of the AV valves (two orifices are present once the interventricular patch is in place) to study its closure pattern and competence. A few additional “tailoring sutures” are placed without tension along the coapting surfaces of the LSL and LIL near the patch, if needed, to prevent systolic eversion or prolapse; usually they are not required. If a central leak (at the point of junction of LSL, LIL, and LLL) persists, an

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**Figure 34-20** Repair of complete atroventricular (AV) septal defect; right atrial view, showing two variations of bridging. **A**, Bridging grade 1. **B**, Bridging grade 4. In both there is a common AV orifice and interventricular communication. AV node lies on right side of inferior (caudal) atrial septal remnant at its junction with floor of right atrium over crux cordis. Node pierces abnormally formed central fibrous body to become the short penetrating portion of bundle of His. This structure immediately becomes the branching bundle, which gives off left bundle branches earlier than normal as it travels along crest of ventricular septum. **C**, Cross-section through AV septal defect with common AV valve orifice showing mild bridging of left inferior leaflet (LIL) and scooped-out crest of ventricular septum. View is anterior to posterior. Key: **CS**, Coronary sinus; **LSL**, left superior leaflet; **RSL**, right superior leaflet.
Figure 34-21  Repair of complete atrioventricular (AV) septal defect. A, After right atrium is opened, valve leaflets are often closed exactly as they are in systole. If, instead, they are open, saline is injected into left ventricle to close them. At this point, morphology of the leaflets, particularly their closure pattern, is studied and information obtained is used to plan repair of any regurgitation present or accommodate any lack of left AV valve tissue. B, A fine polypropylene suture is placed between left superior leaflet (LSL) and left inferior leaflet (LIL) in position shown (anterior aspect) and left loose. C, Leaflets are allowed to open, and details of atrial and ventricular septal deficiencies and of interatrial and interventricular communications are studied. Position of coronary sinus (CS) is noted, and course of the unseen AV node and bundle of His is conceptualized by surgeon from knowledge of the anatomy. Leaflets are retracted as much as possible and projected width (shown here) and depth of AV patch estimated. Planned suture line of interventricular patch to ventricular septum and free wall is thus visualized by surgeon. D, Polyester ventricular patch is trimmed to a flat, rectangular-pyramidal shape. Suture line may begin anywhere along ventricular septum, but it must be on the right ventricular side of all chordae from left-sided leaflets, including those from any bridging components of the LIL. Retractor in right inferior aspect of the common valve marks position in which base of right inferior leaflet (RIL) is sandwiched between ventricular and atrial patches. Suture line here stays well back from crest of interventricular septum and catches some of the base of the RIL to avoid the bundle of His.

Continued
E. Suture line for interventricular patch is completed anteriorly, retracting defect posteriorly and elevating the RSL to expose the aspect of the defect closest to left ventricular outflow tract. Width of patch at the valve level will be less than its width deeper on ventricular septum level. 

F. Left superior leaflet (LSL) and left inferior leaflet (LIL) are precisely anchored to ventricular septal patch using fine interrupted simple or mattress sutures. It is here that care is taken to ensure that the left-sided valve apparatus at the patch is appropriately narrow so as not to create regurgitation and at the correct height so as not to produce left ventricular outflow tract narrowing (too low) or left AV valve regurgitation (too high). To provide accuracy, the previously placed fine stay suture joining LSL and LIL is positioned approximately at midpoint of the suture line. 

G. Pericardial patch for closure of the atrial defect is trimmed to size and a new suture line is begun with bites incorporating pericardial patch, left AV valve tissue (at its junction with the top of the polyester patch), and polyester patch, sandwiching delicate left AV valve tissue between pericardium and fabric. Initial suturing at crest of polyester patch can be done with the pericardial patch folded leftward toward left AV valve. Conduction system is avoided by extending the pericardium to the right of the coronary sinus, leaving its drainage to left atrium. Competence of left (and right) AV valve is next tested with saline injection. If necessary, small anuloplasty sutures can be placed between LSL and left lateral leaflet (LLL) and between LIL and LLL. 

H. Remainder of pericardial patch is sutured inferiorly and then superiorly to rim of atrial defect, often also incorporating closure of foramen ovale defect. 

Key: RLL, Right lateral leaflet; RSL, right superior leaflet.
acceptable if within 2 SD of normal for the size of the patient (z value is −2 or greater; see Chapter 1, Appendix 1D, Table 1D-2).

Repair is completed by suturing the rest of the pericardial interatrial patch in place, with the suture line passing around the AV node and bundle of His and not across them (Fig. 34-21, G and H). The right-sided leaflets are usually not sutured to the patch because they close competently without this. If any commissural tissue between the LSL and RSL or LIL and RIL is cut, the right side of this (as well as the left side) is sutured to the patch.

Rewarming of the patient is begun (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). A few sutures are placed, but not pulled up or tied, for closure of the foramen ovale. Air is evacuated through the foramen ovale, and the aortic clamp is removed with suction on the needle vent.

The first stitch for closure of the right atriotomy is placed at its inferior angle, and closure of the right atriotomy is continued up to the midportion. Usually, cardiac action has begun by then, so the pump sump-sucker is removed from the right atrium and sutures closing the foramen ovale are tied, with care taken to avoid trapping air in the left atrium. The remainder of the right atrium is closed and caval tapes released. Assessment at this stage of the morphologic and functional result by two-dimensional color flow Doppler TEE is useful.37 If important abnormalities are present, CPB and cardioplegia are reestablished and corrections made. Otherwise, the remainder of the operation is completed in the usual manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2 and “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Left and right atrial and pulmonary artery pressure-monitoring catheters are placed.

Alternatively, when hypothermic circulatory arrest is used in infants, circulatory arrest is continued until the right atrium is closed, provided the procedure can be completed within 45 minutes (which is usually possible). The single venous cannula is then reinserted, the heart is de-aired, CPB for rewarming is begun, and the remainder of the procedure continues as usual. (For repair that requires more than 45 minutes, the sequence described in Chapter 2, Section IV, is adopted.)

Repair of Complete Atrioventricular Septal Defect with Bridging of Left Superior Leaflet: Rastelli Type B or C

Repair is similar to that just described, but special consideration is given to the LSL. Whether bridging is moderate (Rastelli type B) or marked (Rastelli type C), the commissure between it and the RSL is generally only slightly on the right ventricular side of the intersection of the atrial (and ventricular) septum with the anulus. This location is critically important because, again, suturing for insertion of the interventricular polyester patch usually begins in the anulus at the level of this commissural tissue. If suturing in the anulus is too far anterior—that is, too far on the right ventricular side of the junction of anulus with atrial septum—either by error or because the LSL-RSL commissure is far anterior, the right AV valve orifice will be too narrow. Narrowing of its orifice can also be produced by attaching the interventricular polyester patch too far to the right of the crest of the septum with the first few superior (cephalad) stitches. Compensation too far leftward narrows the LV outflow tract.

The interventricular patch is slid beneath the chordae going from the right extremity of the LSL to right ventricular papillary muscles. The interventricular patch must have appropriate dimensions and configuration (Fig. 34-22). If the patch is excessively wide (in a superior-inferior direction), there is greater likelihood of postoperative LV outflow tract obstruction. If the patch is excessively long (deep, in a caudad-cephalad direction), there is a greater likelihood of left AV valve regurgitation.

Incising the LSL from its free edge to the anulus is rarely necessary, although in extreme cases in which a small right AV valve would otherwise result, it may be done, with both divided edges later sutured onto the interventricular polyester patch.

Repair of Complete Atrioventricular Septal Defect with Single-Patch Technique

Repair using a single patch differs from the two-patch technique in the following ways: (1) the single patch is almost always pericardium, (2) tailoring the waist of the patch (at the level of the AV valves) is critical, and (3) both the LSL and RSL and the LIL and RIL are sutured to the patch. Setup using bicaval cannulation is the same as for the two-patch technique, making sure that the inferior vena cava cannula is placed well caudad at the cavoatrial junction. CPB is established at 20°C to 24°C, and antegrade cardioplegia is infused after aortic clamping. The right atrial incision is made and atrial exposure is arranged as for the two-patch technique. The most anterior point of LSL-LIL apposing edges is identified, and a 6-0 polypropylene suture is placed to retain that apposing relationship. Bridging leaflets superiorly and occasionally inferiorly are incised laterally to the valve anulus (Fig. 34-23, A). This maneuver allows easy later exposure for closing the intraventricular portion of the defect and accommodating the waist of the patch.

The patch for the ventricular septal closure is inserted using continuous polypropylene or interrupted synthetic braided mattress sutures. Generally the initial suture is placed at the midpoint of the ventricular defect and is continued upward anteriorly (Fig. 34-23, B). Posteriorly, the suture line stays behind the rim of the defect to avoid conduction fibers. Both left and right AV valve leaflets are then anchored to the waist of the patch using double-pledgeted horizontal mattress sutures (Fig. 34-23, C). Pledgets are
Figure 34-23 Complete atrioventricular (AV) septal defect repair, single-patch technique. A, Right atriotomy is made as for two-patch technique and AV valves are inspected. Saline is infused into ventricles as for two-patch technique, and apposition point of left superior leaflet (LSL) and left inferior leaflet (LIL) is identified as the leaflets float up to their systolic position. A fine guy suture is placed for alignment and left loose. Frequently, the bridging LSL or LIL is incised to gain access to the anterior portion of interventricular defect. Later, each cut edge of the superior leaflet will be attached to pericardial patch at its waist. B, Fresh or glutaraldehyde-treated pericardial patch is trimmed partially after measuring height and width of interventricular communication. Generally, ventricular portion of patch is attached to right side of crest of ventricular septum using a continuous suture initiated at the deepest aspect (midpoint) of the rim of the ventricular septal defect (VSD). Usual precautions are taken as in the two-patch technique to avoid the bundle of His at posterior-inferior aspect of ventricular defect. C, AV leaflets, both left and right, are attached to pericardial patch at appropriate level. As in the two-patch technique, the central guy suture, which approximates the gap between LSL and LIL, helps position the AV valves at correct height and midpoint on the single pericardial patch. Interrupted horizontal mattress sutures incorporate bites of right-sided valve tissue, pass through pericardium, and end with bites of left-sided valve tissue. Small pledgets of pericardium may be used to buttress sutures on left and right AV valve tissue. Several additional sutures complete closure of gap between LSL and LIL.

generally of pericardium; often a single strip is used on the left-sided aspect. The strip is made a little shorter than the anteroposterior width of the anulus to somewhat narrow the anulus and contribute to AV valve competency. The level of this suture line (in a cephalad-caudad direction) must ensure that height of the AV valve anulus is such that left AV valve regurgitation is avoided (patch too high) and LV outflow obstruction is not produced (patch too low). At this point, the LV is loaded by saline injection to test valve competency and VSD closure. The left AV valve cleft is closed.
with fine interrupted sutures at its opposing edges to the previously placed marking suture. At this point if necessary, anuloplasty sutures (horizontal mattress) are placed at the two lateral commissures. Repair of the remaining atrial defect proceeds as for the two-patch technique (Fig. 34-23, D), outside the rim of the coronary sinus and including the foramen ovale defect. The completed single pericardial patch has a lopsided, dumbbell-shaped configuration (Fig. 34-23, E).

Repair of Complete Atrioventricular Septal Defect with Modified Single-Patch Technique

In 1997, Wilcox and colleagues reported direct suturing of the AV valves to the ventricular septum in complete AV septal defects with a small ventricular component. Others extended the application of this technique to all forms of complete AV septal defects, with no division of valve leaflets or chordae, and reduced operative time.

Key features of the procedure are illustrated in Fig. 34-24. Interrupted pledgeted 5-0 braided sutures are placed on the right side of the interventricular septal crest (as in the ventricular septal suture line of the standard ventricular patch technique) and passed through the bridging LSL and LIL. These sutures are then passed through the edge of the autologous pericardial patch used to close the atrial defect and through a thin strip of polyester whose length is slightly shorter than the corresponding ventricular septum, with the intent of producing a central anuloplasty of the LSL and LIL. These sutures are tied, and the remainder of the operation proceeds as in the single- or two-patch techniques.

Nunn and colleagues reported uniform application for all patients with complete AV septal defects, 30-day mortality of less than 2%, no reoperations for residual VSDs, and no reoperations for LV outflow tract obstruction out to a median follow-up of 7.3 years. This procedure has now been widely applied in the setting of shallow ventricular defects. General acceptance of its wider application to all defects awaits analyses from other institutions.

Repair of Partial Atrioventricular Septal Defect with Little or No Left Atrioventricular Valve Regurgitation

Repair is similar to that described for complete AV septal defects, but no interventricular polyester patch is required. After CPB is established, intraatrial exposure is arranged, cold cardioplegic solution infused, and morphology studied. Attachments of the LSL and LIL to the crest of the ventricular septum are probed to be certain there are no small interventricular communications.

The “cleft” in the AV valve is then identified and its medial and septal extremities noted (Fig. 34-25, A-C). In the past, if there were no left AV valve regurgitation, nothing was done to the valve at the cleft (commissure). More recently, most surgeons obliterate this gap (close the cleft) using several interrupted simple sutures or pericardial pledgeted mattress sutures. The margins here are characterized by slightly thickened and rolled edges, and it is at these margins that sutures are based.

An anuloplasty stitch may also be placed at the LSL-LLL commissure. The intraatrial pericardial patch is sewn into place in the same way used for repairing complete AV septal defect (Fig. 34-25, D; see also Fig. 34-21). Small, pledgeted mattress sutures of 5-0 or 6-0 polyester are passed from the right ventricular side through the base of the RIL and the
bridging part of the LIL and through the pericardial patch. More cephalad, the patch is sewn to fibrous valvar tissue attached to the crest of the ventricular septum in this reinforced manner, analogous to its suturing to the top of the polyester patch (see Fig. 34-21).

Repair of Atrioventricular Septal Defect with Small Interchordal Interventricular Communications (Intermediate Form)

When two AV valve orifices are present but small interventricular communications exist between thick, short chordae attaching the LSL to the crest of the ventricular septum, repair is simple. The interventricular communication is simply closed by taking the anterior portion of the pericardial patch just to the right side of the septal crest, catching the base of the LSL with each stitch.

When the interventricular communications are beneath the LIL, the same maneuver may be followed. However, because of the bundle of His, care must be taken to keep the suture line well away from the crest of the septum and to attach the patch in the same manner in which the interventricular patch is attached in repair of complete AV septal defects.

Repair of Atrioventricular Septal Defect with Common Atrium

When a common atrium is present, either with or without an interventricular communication, special effort is made to ensure that there is no left superior vena cava or, if one is present, that there is not a completely unroofed coronary sinus, which would change the repair (see Technique of Operation in Chapter 33).

Repair is accomplished by sewing an appropriately larger pericardial patch to the atrial wall on the left atrial side of the orifice of the inferior vena cava, to the right of the right pulmonary veins, and beneath the superior vena cava (where there is usually a small septal remnant).

Repair of Complete or Partial Atrioventricular Septal Defect with Moderate or Severe Left Atrioventricular Valve Regurgitation

For repair of an AV septal defect with moderate or severe left AV valve regurgitation, results seem to vary from one institution to another, even when the same techniques have apparently been used.

In the repair of complete AV septal defects, the primary determinant of left AV valve competence, particularly when preoperative AV valve regurgitation is moderate or less, is accurate sizing of the ventricular patch (or patch component) to produce an anuloplasty effect (width somewhat less than the combined width of the LSL and LIL) and avoiding elevation by the patch of the LSL and LIL above their pre-repair level (see Fig. 34-22). If the size and placement of the patch have been imperfect, this should be corrected.

If the patch and its placement are considered optimal, the basic options depend on observations about location and mechanism of regurgitation by filling the LV with saline:

- If the major leakage is between the LSL and LIL, the “clef” is partially or completely closed with interrupted 5-0 polypropylene or braided sutures, which may be reinforced with small bovine pericardial pledgets if the leaflet tissue is fragile.
If the leakage is central or at the commissure between the LLL and LSL or between the LLL and LIL, anuloplasty sutures (with or without pledgets) are placed to reduce anular circumference. In cases of marked central leakage and an enlarged orifice, a more extensive anuloplasty of the LLL and its commissures using a polytetrafluoroethylene band has been reported.\textsuperscript{K5}

If leakage is through accessory clefts, they may be partially closed. When the repair is completed and leakage is trivial or absent by saline injection, the remaining orifice is sized with Hegar dilators; a measured diameter yielding a $z$ value of $-2$ or greater is generally adequate to avoid valve stenosis.

In the presence of persistent moderate to severe residual regurgitation (particularly in the reoperative setting) despite the maneuvers described above, two other more radical techniques may be applied:
When there is severe central regurgitation, particularly in the presence of leaflet prolapse, the LLL and the reconstructed anterior leaflet may be approximated with a pledgeted mattress suture, creating a double orifice valve. To avoid physiologic stenosis, care must be taken that the orifice of the reconstructed “mitral” valve is somewhat larger than normal (probably a z value of +1 or larger) before placing the approximation suture.

An additional procedure in the presence of leaflet deficiency that has reported short- and mid-term success is patch augmentation of the neoanterior leaflet.

If moderate or severe left AV valve regurgitation remains, repair should be immediately reassessed. If, in the surgeon’s judgment, improvement by further repair is possible, the patient is returned to CPB. If no further repair is likely, valve

**Figure 34-25, cont’d**  
C, Cleft is closed with interrupted sutures; if necessary, anuloplasty sutures are added. D, Defect is closed with a pericardial patch, placed in a fashion similar to that used in the two-patch technique for repair of complete AV septal defect. It is inserted using fine continuous polypropylene suture. Suture line begins at the confluence of left- and right-sided AV valves over ventricular septum and passes rightward and caudally over right inferior leaflet to surround the coronary sinus (CS), leaving coronary sinus draining to left atrium. E, An alternative to avoid the conduction system is the McGoon technique. Patch is sutured to base of left-sided valve tissue, and in area near conduction system, superficial bites are taken. Key: *LIL*, left inferior leaflet; *LSL*, left superior leaflet; *RIL*, right inferior leaflet; *RSL*, right superior leaflet.

**Figure 34-26**  
Creating a double orifice valve for persistent severe left ventricular valve regurgitation. Lateral leaflet and reconstructed anterior leaflet have been approximated. (From Mitchell and colleagues.)
areas are larger than usual and handicap exposure. Then they may be incised back to the anulus, once it is certain that this is commissural tissue! Tissue on the LV side is incorporated into the repair along with the LSL or LIL. That on the right side should be reattached to the patch with a few sutures at the end of the repair.

Replacement of Left Atrioventricular Valve

When severe left AV valve regurgitation cannot be repaired, or when it persists or develops postoperatively, left AV valve replacement may be necessary. Because the left AV valve nearly always encroaches on the LV outflow tract (see Figs. 34-5, A and 34-10), valve replacement may accentuate or produce subaortic stenosis. The prosthesis must therefore be kept away from the subaortic area. This may be accomplished by attaching a rectangular piece of polyester to the anulus of the left AV valve in the subaortic area (Fig. 34-28). (Poirier and colleagues describe the outcome of eight patients in which similar augmentation was used at reoperation to increase deficient bridging leaflet coaptation without valve replacement.) The prosthesis is then sutured to this artificial mitral-aortic anulus and to the natural anulus for the rest of its circumference. To minimize the chance of damage to the AV node and bundle of His, particular care is taken anteriorly and inferiorly to sew only to the fringe of left AV

Right Atrioventricular Valve

In hearts with or without interventricular communications, the right AV valve usually does not require attention. Two-patch repair leaves this valve without a complete “septal leaflet,” but in this and other situations, regurgitation does not result. The RSL and RIL (and the RLL) are well supported by chordae, and this, combined with their closure against the polyester patch or bare ventricular septum, generally results in adequate valve function. However, the right AV valve should be analyzed separately with saline injection and Hegar sizing (valve diameter should provide a z value of −2 or greater). If important leakage is identified, it should be surgically addressed. Often, attachment of the RIL to the VSD patch will correct the leakage.

Left Superior Leaflet–Right Superior Leaflet and Left Inferior Leaflet–Right Inferior Leaflet Commisures

Generally, repair of LSL-RSL and LIL-RIL commissures can be made without disturbing the commissural leaflet tissue in these areas. Occasionally, however, these commissural leaflet replacement is performed. If the patient is small, no further intervention is feasible, and the infant is managed as well as possible postoperatively.

Figure 34-27 Leaflet augmentation technique using glutaraldehyde-treated autologous pericardium for severely dysplastic left atrioventricular valves. A, Radial incision adjacent to anulus is made in superior and inferior bridging leaflets from commissure to commissure. B, Abnormal secondary chords to ventricular side of leaflet are divided. C, Patch of autologous glutaraldehyde-treated pericardium is sutured in place, augmenting anterior leaflet. Tension-free closure of cleft is now possible. Key: LIL, Left inferior leaflet; LLL, left lateral leaflet; LSL, left superior leaflet.
and anterior deviation of the infundibular septum is always present and must be considered in the repair. Preoperative cineangiographic studies are often necessary to delineate the surgically important details of right ventricular outflow obstruction and morphology of the pulmonary arteries.

Operation is begun as for repair of any complete AV septal defect. Before heparinization, however, if a right ventricular outflow patch is required, an appropriately sized patch is prepared as described in Section I of Chapter 38 (see “Decision and Technique for Transanular Patching” under Technique of Operation). The VSD patch is trimmed with a wide superior aspect, which is important in preventing left ventricular outflow obstruction.

Usually the anteriorly deviated parietal extension of the infundibular septum (band) can be seen through the AV valve, and it is cut and mobilized (see “Repair of Uncomplicated Tetralogy of Fallot with Pulmonary Stenosis via Right Atrium” under Technique of Operation in Section I of Chapter 38). Other muscular infundibular obstructions can be visualized and resected. The pulmonary valve can be visualized and fused commissures opened. The right ventricular outflow tract is sized with Hegar dilators. At this point the surgeon may decide on a combined right atrial–right ventricular (RA-RV) approach. If so, a small vertical incision is made in the right ventricular outflow tract, and parietal and septal extensions are mobilized and partially resected. This incision is later closed with a small patch.

Repair of Complete Atrioventricular Septal Defect with Tetralogy of Fallot

In complete AV septal defect associated with tetralogy of Fallot, the large VSD is also juxtaaortic. The LSL bridges moderately (grade 3) or markedly (grades 4 or 5) and is not attached to the crest of the ventricular septum. Any of the types of right ventricular outflow tract obstruction associated with tetralogy of Fallot may be present (see “Convenient Morphologic Categories of Right Ventricular Outflow Obstruction” under Morphology in Section I of Chapter 38), and anterior deviation of the infundibular septum is always present and must be considered in the repair. Preoperative cineangiographic studies are often necessary to delineate the surgically important details of right ventricular outflow obstruction and morphology of the pulmonary arteries.

Operation is begun as for repair of any complete AV septal defect. Before heparinization, however, if a right ventricular outflow patch is required, an appropriately sized patch is prepared as described in Section I of Chapter 38 (see “Decision and Technique for Transanular Patching” under Technique of Operation). The VSD patch is trimmed with a wide superior aspect, which is important in preventing left ventricular outflow obstruction.

Usually the anteriorly deviated parietal extension of the infundibular septum (band) can be seen through the AV valve, and it is cut and mobilized (see “Repair of Uncomplicated Tetralogy of Fallot with Pulmonary Stenosis via Right Atrium” under Technique of Operation in Section I of Chapter 38). Other muscular infundibular obstructions can be visualized and resected. The pulmonary valve can be visualized and fused commissures opened. The right ventricular outflow tract is sized with Hegar dilators. At this point the surgeon may decide on a combined right atrial–right ventricular (RA-RV) approach. If so, a small vertical incision is made in the right ventricular outflow tract, and parietal and septal extensions are mobilized and partially resected. This incision is later closed with a small patch.
The interventricular communication is closed by suturing into place a polyester or pericardial patch from this right atrial approach, sequencing the repair exactly as described for other complete AV septal defects. This can be accomplished with a single- or two-patch technique. With either, the shape of the ventricular component of the patch must be modified to account for the anterior-superior extension of the interventricular communication. Familiarity with the atrial approach for repair of isolated VSD (see Technique of Operation in Section I of Chapter 35) and for repair of the VSD in simple tetralogy of Fallot (see “Repair of Uncomplicated Tetralogy of Fallot with Pulmonary Stenosis via Right Atrium” under Technique of Operation in Section I of Chapter 38), as well as familiarity with repair of uncomplicated complete AV septal defects, are important preparations for this procedure. Stay sutures are placed as usual for transatrial repair. Repair is begun at the AV valve anulus superiorly, where the atrial septal remnant meets the anulus.

Care must be taken that repair does not begin too far rightward, in which case the right side of the surgically partitioned AV valve orifice will be too small. Because of the dextroposed aorta, attachment of the VSD patch to tissue over the aortic root (and beneath the commissural tissue and RSL) is particularly important. The patch is generally beneath (on the left ventricular side of) chordae attached to the right extremity of the bridging LSL and beneath this leaflet itself. Because this leaflet will be attached to the VSD patch, some of these chordae may be cut to facilitate exposure. In the single-patch technique, the entire bridging leaflet is incised. The suture line is then carried around the interventricular communication and along the base of the RIL as described earlier for the usual complete AV septal defect. When the aorta overrides the interventricular septum to a considerable degree (and when DORV is present), the juxtaaortic portion of the repair may be completed through a small infundibular incision. Remainder of the AV septal defect is repaired as described earlier.

The right ventricular outflow tract is again sized with Hegar dilators. If it is adequate, nothing further is done. Otherwise, it is enlarged by an infundibular patch, or, if necessary, a transanular patch (see “General Plan and Details of Repair Common to All Approaches” under Technique of Operation in Section I of Chapter 38). Moderate or severe pulmonary regurgitation should be avoided because associated right ventricular dilatation may result in severe right AV valve regurgitation from deficiency of right-sided AV valve tissue. Therefore, the threshold for inserting a valve (monocusp or allograft) in the right ventricular outflow tract is lower than usual.

Repair of Complete Atrioventricular Septal Defect with Double Outlet Right Ventricle

When the interventricular communication is large and subaortic, configuration and insertion of the interventricular patch are similar to that just described for tetralogy of Fallot. Pulmonary stenosis, when coexisting, is also treated similarly.

When the interventricular communication is not subaortic and cannot be converted into one by septal excision (see “Intraventricular Tunnel Repair of Double Outlet Right Ventricle with Noncommitted Ventricular Septal Defect” under Technique of Operation in Chapter 53), a Fontan repair (see Technique of Operation in Section IV of Chapter 41) is necessary if pulmonary stenosis coexists.

Repair with Transposition of the Great Arteries

When size of the LV allows it, usual repair of the AV septal defect is carried out and an arterial switch operation is performed (see “Arterial Switch Operation” under Technique of Operation in Chapter 52).

SPECIAL FEATURES OF POSTOPERATIVE CARE

Usual care as described in Chapter 5 is accorded patients after repair of AV septal defects, but certain features require emphasis. Because of the complexity of repair and despite the generally good results now obtained, vigilance must be exercised to detect any important imperfections in the repair. Thus, TEE or transthoracic echocardiography (if the infant is small) is of great help in the operating room and a few hours after the patient’s return to the intensive care unit to verify complete closure of the interatrial and interventricular communications and absence of important AV valve regurgitation. Left atrial pressure more than 6 mmHg higher than right atrial pressure raises the possibility of either severe left AV valve regurgitation or stenosis, although it can result simply from small size and low compliance of the LV (see Chapter 5). Height of the r wave is not helpful because, as in all circumstances, this correlates more with height of mean left atrial pressure than with degree of regurgitation. Usual prophylaxis is taken against pulmonary hypertensive crises. Generally this includes introducing a pulmonary artery catheter intraoperatively. Because average age at repair has decreased, this complication is seen less frequently now (see “General Care of Neonates and Infants,” Section IV of Chapter 5).

If the patient’s condition is not optimal and important residual left AV valve regurgitation is suspected—particularly if deterioration continues over several hours—repeat echocardiographic study in the intensive care unit is advisable. If results of this study are inconclusive, left ventriculographic studies (or some other reliable method of quantifying left AV valve regurgitation) should be considered. Indirect indications, both in the operating room and early postoperatively (including absence of a murmur), are unreliable. If severe regurgitation is demonstrated, reoperation is indicated. Likewise, if the patient’s condition is unsatisfactory and a large residual left-to-right shunt is present, reoperation is indicated.

When the patient does not convalesce normally, echocardiographic and possibly left ventriculographic studies before hospital discharge are indicated. Because left AV valve repair failure predisposes the patient to death within the first year after operation, consideration should be given to early reoperation if severe regurgitation is found.

RESULTS

Survival

Early (Hospital) Death

Hospital mortality after repair of partial AV septal defects has been low for a long time, dating back to the early experience reported from the Mayo Clinic. In the current era, hospital mortality generally is 1% or less. 

\footnote{M13}
Hospital mortality after repair of uncomplicated complete AV septal defects was 30% to 50% during the early years of cardiac surgery, but has declined steadily in recent years. This has been the result of greatly improved understanding of the morphology of this complex malformation, better surgical techniques, and general improvements in cardiac surgery in infants. These improvements are evident in most major pediatric cardiac surgical programs. Improvement in hospital mortality has been particularly evident in infants.

Major congenital heart disease centers report mortality of under 3% for patients with complete AV septal defects with balanced ventricles undergoing repair in the first 3 to 6 months of life. As is often the case, results from individual centers of excellence are superior to results from unselected institutional studies. The Pediatric Cardiac Care Consortium reported results of 10 years of activity in 25 institutions within the United States. Overall operative mortality was 14% and did not differ between Down and non-Down patients. There were a total of 768 cases, averaging three cases per year per institution. This report should be contrasted with individual institutional reports demonstrating low mortality representing caseloads of 20 to 50 yearly.

Even when complete AV septal defect coexists with other major cardiac anomalies such as tetralogy of Fallot, hospital mortality remains generally low. However, other less common major associated anomalies with both partial and complete AV septal defects impose a considerable increase in hospital mortality.

**Time-Related Survival**

Late outcomes are generally good, with reported 15-year survival of 80% to 90%.

### Incremental Risk Factors for Premature Death

#### Earlier Date of Operation

An earlier date of operation as a risk factor in a surgical experience that covers a large number of years, as that at UAB (Table 34-11), demonstrates that many risks of repair have been neutralized across the experience. Others report similar experiences. The effect of date of operation on outcome is just as evident in long-term events as it is in hospital mortality. This is dramatically evident in predicted 10-year survival after repair of partial and complete AV septal defects in patients operated on in 1967 versus 1977 and 1985 (Fig. 34-29).

#### Higher New York Heart Association Functional Class

As in most cardiac surgery, severe preoperative disability (higher New York Heart Association [NYHA] functional class) is a risk factor for premature death in both the early and constant hazard phases (see Table 34-11).

#### Important Pre-Repair Atrioventricular Valve Regurgitation

Important pre-repair regurgitation of either the left AV valve in partial AV septal defects or the common AV valve in complete AV septal defects increases risk of premature death, but only in the constant hazard phase (see Table 34-11). This suggests that post-repair moderate regurgitation, the prevalence of which is almost surely increased by severe preoperative regurgitation in patients with partial AV septal defects but probably less so in patients with complete AV septal defects, is reasonably well tolerated early postoperatively but becomes more serious several months later. However, severe left AV valve regurgitation is poorly tolerated in infants post-repair and is a risk factor for early mortality (see Table 34-11).

#### Interventricular Communication

An interventricular communication (complete AV septal defect) has been an important risk factor, but only in the early declining hazard phase. The effect of this aspect of morphology indicates that outcomes after repair of complete AV septal defects currently approximate those of partial AV septal defects, which have been excellent for many years (see Fig. 34-29). Residual interventricular communication after repair of complete AV septal defect may be an infrequent cause for reoperation and a risk factor for premature death. Early postoperative residual VSD should be suspected in the presence of “pulmonary hypertensive crisis” and low cardiac output.

<table>
<thead>
<tr>
<th>Table 34-11 Incremental Risk Factors (Hazard Function Domain) for Premature Death After Repair of Atrioventricular Septal Defects</th>
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<td><strong>Risk Factor</strong></td>
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<td>Greater severity of preoperative AV valve regurgitation</td>
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<td><strong>Morphologic Variables</strong></td>
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<tr>
<td>Accessory valve orifice</td>
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<td>Severe postoperative left AV valve regurgitation</td>
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<tr>
<td>Absence of sinus rhythm</td>
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<td>Higher left atrial, right atrial, or pulmonary artery pressure</td>
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<td><strong>Reoperation Variables</strong></td>
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<td>For pacemaker</td>
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<td>For VSD</td>
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<td>For left AV valve regurgitation</td>
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Data from Kirklin and colleagues and Hanley and colleagues. Key: AV, Atrioventricular; LV, left ventricular; NYHA, New York Heart Association; VSD, ventricular septal defect.
Unbalanced Atrioventricular Septal Defects

From Kirklin and colleagues.

Late death from mitral regurgitation. The left AV valve may also be easier to repair, lessening the likelihood of survival than patients without Down syndrome. The left AV valve function considerably. Also, decreased prevalence of LV inflow and outflow obstruction affects risk of premature death early or late after repair, except for complete AV septal defects with or without major associated cardiac anomalies, according to year in which operation was performed. Solid lines are survival estimates, and dashed lines are 70% confidence limits. (See original publication for details, risk factors, coefficients, and $P$ values of multivariable equation.) (From Kirklin and colleagues.)

Accessory Valve Orifice

An accessory valve orifice is an incremental risk factor for premature death (see Table 34-11), almost surely because of its potentially adverse effect on function of the surgically created left AV valve (see description under Morphology earlier in this chapter). Despite the realization that the accessory orifice should not be “tampered with,” this risk factor has not been neutralized.

Major Associated Cardiac Anomalies

Included among important risk factors are major associated cardiac anomalies (see Table 34-11), but some of them, particularly tetralogy of Fallot, have been largely neutralized. Young Age

Young age has been an incremental risk factor for death, usually hospital death, in all experiences that go back 30 years or so. However, it has been virtually eliminated as a risk factor, primarily because of overall improvement in knowledge and repair techniques, but also because of advances in intraoperative and early postoperative care of infants. However, despite low hospital mortality, lower weight among infants is associated with more frequent postoperative complications and longer hospital stay.

Down Syndrome

Risk-adjusted analysis does not show that Down syndrome affects risk of premature death early or late after repair, except when complete AV septal defect is associated with tetralogy of Fallot. However, in view of the considerably decreased prevalence of LV inflow and outflow obstruction in patients with AV septal defects and Down syndrome, these patients may in fact have a better early and intermediate-term survival than patients without Down syndrome. The left AV valve may also be easier to repair, lessening the likelihood of late death from mitral regurgitation.

Need for Reoperation

The need for reoperation to insert a pacemaker, close a residual interventricular communication, or deal with important left AV valve regurgitation has been associated with added risk of death.

Other Risk Factors

Other incremental risk factors for premature death after repair have been reported. A single papillary muscle (see description under Morphology earlier in this chapter) becomes a serious problem after repair because of its tendency to result in LV inflow obstruction. It may therefore be a contraindication to typical two-ventricle repair. Severe ventricular hypoplasia is a risk factor for hospital death after a two-ventricle repair. Severe LV hypoplasia is more common in patients with complete AV septal defects than is severe right ventricular hypoplasia (see "Unbalanced Atrioventricular Septal Defects" under Special Situations and Controversies). Most hearts with severe LV hypoplasia are properly classified and treated as part of hypoplastic left heart syndrome (see Chapter 49).

Heart Block and Other Arrhythmias

Since Lev described the architecture of the conduction system in AV septal defects in 1958, prevalence of surgically induced permanent complete heart block has been approximately 1%. Avoiding heart block is generally facilitated by incorporating the coronary sinus on the left atrial side of the atrial patch. An equally low occurrence of heart block can also be accomplished by maintaining the coronary sinus on the right atrial side as long as appropriate attention is given to the anatomy of the conduction system (see also discussion under Special Situations and Controversies). Heart block is more frequent after repair of AV septal defect associated with tetralogy of Fallot and after AV valve replacement.

First-degree AV block, present in about 30% of patients preoperatively, has been found in about 50% of patients after repair. Right bundle branch block is common after repair of complete AV septal defects but uncommon after repair of partial AV septal defects.

In an earlier UAB experience, when left AV valve replacement was required, heart block occurred in 4 of 20 patients (20%; CL 10%-33%). This is because sutures placed in the left AV valve anulus at about the 2-o’clock position overlie the AV node. A fringe of AV valve tissue must be left in this area so that valve replacement sutures can be placed there and more anteriorly in the interatrial pericardial patch, rather than along the ventricular septal crest. Placing the prosthesis in supraanular position is also helpful. With these precautions, complete heart block is minimized.

Functional Status

Most long-term survivors are in excellent health. In one center, 88% of surviving patients were in NYHA functional class I, and 11% were in class II.

Atrioventricular Valve Function

Doppler color flow interrogation combined with two-dimensional echocardiography have increased the knowledge about postrepair left AV valve function considerably. Also,
About 10% to 20% of infants and older patients have moderate or worse postoperative left AV valve regurgitation late postoperatively in about half of patients,

Partial Atrioventricular Septal Defects

After repair of partial AV septal defects, about 10% of patients have late severe left AV valve regurgitation, and such patients are more likely to have had severe regurgitation prior to the repair. Generally these patients have a deficiency of the LIL of the AV valve; to date, valve replacement has been the only certain method of achieving left AV valve competence in such patients. Lesser degrees of regurgitation are present late postoperatively in about half of patients; 30% to 40% have essentially no left AV valve regurgitation late postoperatively. Recent studies suggest that moderate or worse postoperative left AV valve regurgitation is more common in children repaired after about 4 years of age, possibly related to longer exposure to LV volume overload and anular dilation induced by the regurgitation.

In patients undergoing repair of complete AV septal defects, there appears to be little relationship between preoperative severity of AV valve regurgitation and that present late postoperatively in some studies, but in others, an association is suggested. Use of single- vs. two-patch technique of repair does not increase the likelihood of early or late post-repair left AV valve regurgitation.

More severe abnormalities of left AV valve morphology, including deficient LLL, papillary muscle abnormalities of the LLL, incomplete commissures, double orifice valve, and severe disparities in length of the LSL and LIL contributing to the “cleft,” have been associated with a greater likelihood of postoperative left AV valve regurgitation. Absence of “cleft” closure has been identified as a risk factor for late reoperation for valve regurgitation.

About 10% to 20% of infants and older patients have important regurgitation late postoperatively, with the remainder having little or none. Despite general improvements in surgical techniques, late reoperation for left AV valve regurgitation has remained a challenge. When reoperation is necessary, left AV valve repair is possible in about half the patients; the rest require valve replacement. Stulak and colleagues at the Mayo Clinic found no difference in subsequent survival or freedom from additional operations according to whether valve repair or replacement was performed.

Repair of uncomplicated partial and complete AV septal defects uncommonly results in stenosis of the left AV valve. More often, this complication results when an accessory valve orifice or single papillary muscle coexists with the AV septal defect.

Important regurgitation or stenosis of the right AV valve is rare after repair of AV septal defects.

Left Ventricular Outflow Tract Obstruction

Uncommonly, LV outflow tract obstruction develops after repair of AV septal defects. As predicted on anatomic grounds by Ebels and colleagues, the AV septal defect has usually been the partial form. Prevalence of clinically significant late outflow obstruction is probably about 5% after repair of partial AV septal defect, which is up to three times more frequent than with the complete form.

When LV outflow obstruction develops, it may be associated with worsening left AV valve regurgitation; its relief usually permits regression of the regurgitation.

Prevalence of subaortic LV outflow tract obstruction late after repair of complete AV septal defect is not precisely known, but not negligible. Obstruction may have the appearance characteristic of discrete subaortic stenosis, with an “acquired fibromuscular ridge” (see “Resection of Localized Subvalvar Aortic Stenosis” in Section II of Chapter 47), or it may appear to result from the long, narrow LV outflow tract itself. In either case, simple resection rarely suffices. Extensive transaortic myectomy or the modified Konno operation, without aortic valve replacement, is indicated (see “Modified Konno Operation” in Section II of Chapter 47). Other techniques have been described that specifically address the scooped-out deficiency in the ventricular septum by detaching the LSL attachments to the crest of the ventricular septum and augmenting the anterosuperior aspect of the VSD patch or the LSL with a pericardial patch, followed by reattachment of the LSL. This moves the left AV valve farther into the left atrium during systole.

Residual Pulmonary Hypertension

When important pulmonary hypertension is present preoperatively, it can be expected to regress postoperatively if pulmonary blood flow is large and the patient receives a timely operation, usually when younger than age 6 months.

INDICATIONS FOR OPERATION

Presence of an AV septal defect indicates need for operation, because an important hemodynamic derangement is nearly always present, and spontaneous closure does not occur.

Partial Atrioventricular Septal Defects

In partial AV septal defects, pulmonary hypertension is usually absent, and the optimal age for operation is 1 to 2 years, assuming a competent left AV valve. If AV valve regurgitation...
is present, earlier operation is indicated to prevent further damage to valve tissue. Also, when heart failure or severe growth failure is evident earlier in life, operation is indicated at that time.

Complete Atrioventricular Septal Defects

Operation is indicated early in the first year of life. When the infant’s general condition is good, repair can be delayed until about age 3 to 6 months. When refractory heart failure or severe growth failure is evident at an earlier age, repair at that time is indicated. Often in patients who are older than 1 year, and occasionally in those in the last part of the first year of life, pulmonary vascular disease may already be too severe to permit repair. Criteria of inoperability are the same as described for patients with VSD (see Indications for Operation in Section I of Chapter 35). Lung biopsy is not recommended as an aid in grading severity of pulmonary vascular disease because of its associated morbidity and mortality and because of the scatter between histopathologic findings and pulmonary vascular resistance.

Coexisting Cardiac Anomalies

Although certain major associated cardiac anomalies increase risk of repair of AV septal defects, their presence rarely alters the indication for operation. Thus, although a coexisting large patent ductus arteriosus has in the past increased risk of repair of complete AV septal defects, it increases the urgency of early repair rather than contraindicating it. When tetralogy of Fallot coexists, indication and timing of repair are similar to that for tetralogy of Fallot in general (see Indications for Operation in Section I of Chapter 38), although some favor elective operation for tetralogy of Fallot with complete AV septal defects at age 9 to 12 months. When complete AV septal defect with juxtaaortic VSD is combined with DORV without pulmonary stenosis, life history and indications for operation are the same as for isolated complete AV septal defect; in the past, risk of repair has been high, but in the current era, early risk has been much less and intermediate-term results good.²²,³³

SPECIAL SITUATIONS AND CONTROVERSIES

Pulmonary Trunk Banding

Pulmonary trunk banding has been used episodically as initial management for small infants with complete AV septal defects, and some excellent results have been reported.⁵⁹ This approach has been used only sparingly in recent years. However, Silverman and colleagues, as well as Williams and colleagues, demonstrated in the early era that some very sick, small infants can be well managed initially by banding and deferral of repair for 6 to 18 months.⁵⁵,⁵⁸ In the absence of other contraindications to repair (unbalanced ventricles, comorbid conditions), banding is not indicated, because age, left AV valve regurgitation, and many other risk factors have been neutralized, and overall results of complete repair are excellent. In the rare instances in which preliminary pulmonary banding is elected, a device that is adjustable by remote control has provided encouraging results.⁵¹,⁵⁴,⁵⁵

Septal Patches

There have been several reports of near-fatal hemolysis from the regurgitant jet of a left AV valve striking a synthetic interatrial patch after repair of AV septal defect.⁴⁴,⁵²,⁵⁶ Therefore, for maximal safety, the interatrial patch material should be pericardium.

Avoiding Heart Block

For years, McGoon and colleagues successfully used a method that involved keeping the suture line on the left and superior sides of the conduction tissue, rather than on the right side and inferiorly.⁴⁷ Starr’s group has used the same general method with good results.⁴³ The patch is sutured to the LSL-LIL complex on the left ventricular side of its attachment to the crest of the ventricular septum. Inferiorly, the suture line then goes to the edge of the ostium primum defect, posterior and central to the AV node and bundle of His, and posteriorly along the atrial septal edge. This method keeps the suture line to the left of, and away from, the AV node and bundle of His (see Fig. 34-25, E).

Unbalanced Atrioventricular Septal Defects

In about 10% of patients with complete AV septal defects, the common AV valve is unequally balanced over the right ventricle or LV. The majority of cases are right dominant with associated LV hypoplasia.⁴⁴,⁵⁶ The surgical options include biventricular repair or single-ventricle strategies. When one ventricle is severely hypoplastic, a repair resulting in a two-ventricle system frequently fails. Theoretically, a Fontan-type repair should be applicable to patients with this type of major associated cardiac anomaly. In the small number of patients treated in this manner, however, hospital mortality has been high.⁴⁸,⁵⁸ This may be related to very early development of pulmonary vascular disease in patients with complete AV septal defects.

Echocardiographic analyses have been proposed that define the degree of “balance” of the AV valve over each ventricle. Using the subcostal view, the area of the common orifice can be divided into right and left AV valve orifices by a line drawn from the caval septum to the crest of the muscular septum.⁴¹,⁵⁴ Cohen and colleagues used this method to calculate an AV valve index using the ratio of the left AV valve area divided by the right AV valve area in patients with a larger right AV valve (left/right valve area). In general, patients with a balanced complete AV septal defect have an area ratio greater than 0.67, and a value less than 0.67 indicates right ventricular dominance. Approximately one third of patients with right ventricular dominance have Down syndrome.⁴¹ Patients with Down syndrome frequently have traits that increase the risk of single-ventricle palliations, such as lung hypoplasia, increased pulmonary vascular resistance, hypotonia with hyperventilation, and upper airway obstruction with nocturnal hypercarbia.⁴¹ Additional left-sided anomalies are also common in patients with right-dominant complete AV septal defects. Precise guidelines have not been established for the degree of RV dominance that is consistent with a successful two-ventricle repair. Available analyses are also confounded by the important additional risk imposed by additional major anomalies.⁴¹
In data from Cohen and colleagues on patients undergoing two-ventricle repairs with left AV valve/right AV valve ratio between 0.27 and 0.65, the specific ratio failed to predict survivors. Similarly, a study by Van Son and colleagues examined outcomes with two-ventricle repair among five patients with a diameter ratio (left/right valve diameter) of 0.23 to 0.39. All survived hospitalization, but one died late from left AV valve dysfunction.

Others have examined calculated LV volumes in decision making. Van Son and colleagues suggested that the actual LV volume may be underestimated in right ventricle–dominant AV septal defects secondary to leftward septal bowing, and they introduced the concept of “potential LV volume” to predict the volume of the LV post-repair that could be accomplished with only a change in shape. Patients with a potential volume of 15 mL · m⁻² have survived repair. Individual reports have shown dramatic increases in LV size of twofold to threefold after repair. A small interventricular communication may be a favorable prognostic factor.

Another method of assessing dominance is the ratio of the left AV valve area to the total AV valve area. A ratio of 0.4 or less indicates right ventricular dominance, and a ratio of 0.6 or more indicates LV dominance. In a multicenter study from the Congenital Heart Surgeons Society, a ratio less than 0.2 (severe right ventricular dominance) uniformly predicted a single-ventricle strategy. A valve ratio of 0.4 to 0.6 indicated a “balanced” defect, and a two-ventricle repair was performed. A ratio of 0.2 to 0.4 represented the “gray zone” of moderately severe right ventricular dominance, in which either single- or two-ventricle strategies were applied, with a disproportionately high number of deaths in that range.

If biventricular repair is undertaken, placing a left atrial catheter for postoperative monitoring is advisable. A persistently elevated left atrial pressure and signs of low cardiac output, persistent pulmonary edema, or failure to wean from ventilator indicate need for reoperation and conversion to single-ventricle palliation. Unfortunately, outcomes after single-ventricle palliation in this setting are generally worse than for most other single-ventricle cohorts. Owens and colleagues noted a midterm survival of only 50% among 32 patients with severe right-dominant unbalanced AV septal defects, worse than that of a contemporary cohort of hypoplastic left heart syndrome patients. Thirty percent of the unbalanced AV septal defect patients required replacement or repair of their systemic AV valve.

**Left-dominant unbalanced complete AV septal defect** may be defined by a right AV valve area/left AV valve area less than 0.5 or a left AV valve area/total valve area greater than 0.6. Down syndrome has been reported in 80% of this subset. When the valve ratio is less than 0.5, risk of biventricular repair may carry an increased risk. De Oliveira and colleagues reported improved outcomes with a restrictive atrial fenestration intended to lower right atrial pressure and increase cardiac output with some degree of desaturation.

The general surgical strategies in this patient group are similar to those for pulmonary atresia with intact ventricular septum (see Chapter 40). When right ventricular hypoplasia is severe and success of biventricular repair is in question, a “one-and-a-half ventricle repair,” as suggested by Alvarado and colleagues and others, may be appropriate. In this repair, the usual procedure to correct the AV septal defect is accompanied by a bidirectional cavopulmonary anastomosis. Pulmonary blood flow is augmented, and the right ventricle is unloaded. A potential but unusual problem is pulmonary artery–to–right atrial circular flow if superior vena cava–to–right atrium continuity is maintained.

**Late Reoperation**

The only residual condition that remains an important cause of late reoperation is left AV valve regurgitation. Najm and colleagues reported that 9.4% of 363 patients operated on for complete AV septal defect underwent subsequent repair or replacement of the left AV valve; 3 of 34 (8.8%; CI 3.9%–17%) patients died. Intraoperative echocardiography reduces the occurrence of residual important left AV valve regurgitation. The report of Reddy and colleagues is illustrative: 72 infants (median age 3 to 9 months) underwent repair of complete AV septal defect, and cleft closure or anu-loplasty was done in 70. Based on TEE, 10 were returned to CPB for revision of the left AV valve. Among all 72 patients, there was 1 early death. There were 5 late reoperations with a median follow-up of 24 months; 2 were for AV valve regurgitation and 3 for subaortic obstruction. Although there may have been mild deterioration of AV valve function in patients with mild to moderate regurgitation early postoperatively, there was a 90% probability of not having severe late AV valve regurgitation at a mean follow-up of 45 months (range 3 to 169 months).

**REFERENCES**


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Section 1  Primary Ventricular Septal Defect

**DEFINITION**

Ventricular septal defect (VSD) is a hole or multiple holes in the interventricular septum. This chapter discusses VSDs that occur as the primary lesion, recognizing that hearts with primary VSDs may have minor coexisting morphologic abnormalities. VSD may be part of another major cardiovascular anomaly, such as tetralogy of Fallot (see Chapter 38), complete atroventricular (AV) septal defect (see Chapter 34), anatomically corrected malposition of the great arteries (see Chapter 57), truncus arteriosus (see Chapter 43), tricuspid atresia (see Chapter 41), sinus of Valsalva aneurysm (see Chapter 36), and interrupted aortic arch (see Chapter 48). VSDs also may be acquired, as discussed in Chapters 9 and 17.

**HISTORICAL NOTE**

In 1954, Lillehei, Varco, and colleagues at the University of Minnesota in Minneapolis began to repair VSDs using normothermic, low-flow, controlled cross-circulation based on the so-called azygos flow principle, with an adult human as the oxygenator (see Historical Note in Section II of Chapter 2). This was the beginning of the era of cardiac surgery using cardiopulmonary bypass (CPB), a term coined by Cooley a few years later. Five of the first eight patients were in their first year of life, and only two (40%; CL 14%-71%) of the five died, a tribute to surgical skill, lack of cardiac ischemia (the aorta was not clamped), and quality of their human oxygenator. The dramatic weight gain of the surgical team and interrupted aortic arch (see Chapter 48). VSDs also may be acquired, as discussed in Chapters 9 and 17.

Kirklin and DuShane developed a surgical technique that avoided producing heart block during VSD repair.

Lillehei showed the feasibility of an atrial approach to VSD in 1957. The technique of hypothermic circulatory arrest, with rewarming by a pump-oxygenator, was applied successfully to infants with VSD by Okamoto. Kirklin and DuShane (1961) and Sloan’s group (1967) reported the feasibility of primary repair of VSD in infants.

Barratt-Boyes and colleagues (1969-1971) found that routine primary repair of VSD in sick, small infants was superior to pulmonary artery banding.

**MORPHOLOGY**

Although this chapter considers VSD that occurs as the primary lesion, the method of morphologic description is applied in other chapters to VSDs that are part of other major cardiac malformations. The morphologic classification described here represents an attempt to simplify VSD classification by encompassing all variations of the lesion while conforming to other systems of classification (Table 35-1). This classification conforms generally with the consensus of the Congenital Heart Surgery Nomenclature and Database Project and includes many of the concepts of Anderson and Wilcox.

**Size**

VSDs are highly variable in size, and their division into size groups is arbitrary but useful. The echocardiographic criteria for VSD size are discussed in “Two-Dimensional Echocardiography” under Clinical Features and Diagnostic Criteria.

![Table 35-1 Morphologic Classification of Ventricular Septal Defect](image-url)
Large VSDs are approximately the size of the aortic orifice or larger. They offer little resistance to flow, and thus their VSD resistance index\(^1\) is less than 20 units \(\cdot\) m\(^2\) in situations in which the calculation of the index is valid.\(^{1,13,53}\) Right ventricular (RV) systolic pressure approximates left ventricular (LV) pressure, and the pulmonary to systemic blood flow ratio \((Q_P/Q_S)\) is increased to a degree dependent on the level of pulmonary vascular resistance \((R_p)\).

Moderate-sized VSDs, although still restrictive, are of sufficient size to raise RV systolic pressure to approximately half LV pressure and \(Q_P/Q_S\) to 2.0 or greater.

Small VSDs are of insufficient size to raise RV systolic pressure, and \(Q_P/Q_S\) is not increased above 1.75. Small VSDs have a VSD resistance index greater than 20 units \(\cdot\) m\(^2\).\(^{1,13}\) Multiple small defects behave in aggregate as a large defect.

Location in Septum and Relationship to Conduction System

VSDs can occur in all portions of the ventricular septum\(^2\) (Fig. 35-1). VSDs with entirely muscular borders (muscular VSDs) may occupy several areas of the ventricular septum; other VSDs have one or several nonmuscular borders consisting of spaces or structures against which they are juxtaposed (Table 35-2). These nonmuscular borders may be a semilunar valve, an AV valve, or the crux cordis (intersection of the posterior aspect of the interventricular septum and AV junction). Some VSDs in the periphery of the ventricular septum are bordered by the ventricular free wall, but such VSDs are conventionally considered to be muscular. VSDs in the category of subarterial may be (1) juxta-aortic, (2) juxta-arterial (bordered by both pulmonary and aortic valves), or (4) juxtaapical (bordered by the valve of a common arterial trunk). Subarterial VSDs are typically associated with some degree of overriding of the related arterial trunk, and the margin of the VSD is actually a space over which is a semilunar valve(s).\(^{3,9}\)

Many VSDs are associated with malalignment of portions of the ventricular septum or atrial septum relative to the interventricular septum, in which case an AV valve usually overrides the VSD. Malalignment VSD terminology results from two-dimensional (2D) echocardiographic examination of the heart regarding alignment of the trabecular and the outlet (conal) septum. In some cardiac anomalies, the aorta seems displaced relative to the VSD. The malalignment is referred to as anterior when the outlet septum appears anterior to the trabecular septum, with the VSD interposed. Tetralogy of Fallot–type defects are considered anterior malalignment types, with the aorta “overriding” the VSD (see Fig. 35-18, C). Malalignment is posterior when the outlet septum appears posterior to the trabecular septum in anomalies such as interrupted aortic arch and severe coarctation of the aorta. There may also be a rotational malalignment in anomalies characterized under the broad category of Taussig-Bing heart.

Anatomic location of the VSD determines its relation to the conduction system.

VSDs may also be characterized according to their commitment to the great arteries (Lev and colleagues\(^{4,10}\)): subaortic, subpulmonary, doubly committed, and noncommitted.

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**Table 35-2 Expanded Morphologic Classification of Ventricular Septal Defect**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Extension</th>
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<tbody>
<tr>
<td>Perimembranous</td>
<td>Inlet</td>
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<td></td>
<td>Anterior</td>
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<td></td>
<td>Outlet</td>
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<td>Muscular</td>
<td>Outlet (conal)</td>
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<td>Apical</td>
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<td>Doubly committed subarterial</td>
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<tr>
<td>Inlet septal</td>
<td>Atrioventricular septal type</td>
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<tr>
<td>Malalignment</td>
<td>Anterior (tetralogy of Fallot)</td>
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<td></td>
<td>Posterior (interrupted arch or</td>
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<td></td>
<td>coarctation)</td>
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<tr>
<td></td>
<td>Rotational (Taussig-Bing)</td>
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\(^1\) VSD resistance index = \(\frac{\Delta P_LV - \Delta P_RV}{\Delta Q + \Delta Q_s} \times BSA\)

where \(BSA\) is body surface area, \(\Delta P_LV\) is left ventricular systolic pressure, \(\Delta P_RV\) is right ventricular systolic pressure, \(\Delta Q\) is pulmonary blood flow, and \(\Delta Q_s\) is systemic blood flow.

\(^2\)The location is described in words that are relevant to the RV aspect of the VSD (see “Right Ventricle” under Cardiac Chambers and Major Vessels in Chapter 1), because most reparative procedures are performed from that aspect.
This type of characterization—which is relational, not morphologic—preferably is restricted to hearts with double outlet ventricles, because its use in other situations has resulted in considerable confusion.

All these features of the location of VSDs should be included in descriptions of these defects.

**Perimembranous Ventricular Septal Defect**

Approximately 80% of patients operated on for primary VSD have a perimembranous VSD. These defects could be called *junctional VSDs* because they are in the junctional area between the trabecular (sinus) and outlet (conal) portions of the ventricular septum (Fig. 35-2) and usually appear to be between the posterior and anterior divisions of the trabecula septomarginalis (septal band). Thus, these VSDs are between the outlet (conus) and inlet (ventricular) portions of the right ventricle, but characteristically they are in the outlet portion of the left ventricle.

Perimembranous VSDs are often associated with anomalies of the outlet septum and other adjacent structures, although when small, they may be truly isolated anomalies. Some perimembranous VSDs are *juxtaticuspid* (abutting the tricuspid valve), *juxtamitral*, and *juxta-aortic*. These perimembranous VSDs are also *conoventricular* (conotruncal) (Fig. 35-3). Such defects abut the commissural area between the noncoronary and right coronary cusps of the aortic valve. Others are only juxtaticuspid (conotruncal), and in hearts with these as well as in hearts with perimembranous VSDs, the bundle of His passes along the posteroinferior border of the defect. Some perimembranous VSDs abut none of these valvar structures and are separated from the tricuspid anulus posteriorly by a band of muscle that is part of the posterior division of the trabecula septomarginalis joining with the ventriculoinfundibular fold. The bundle of His is not in this muscular band but is in its usual position more posteriorly. Technically, although this type of defect is located in a perimembranous position, it is better classified as *muscular inlet-type VSD* because all borders are muscle.

VSDs have also been described in the past as *typically high, infracristal, membranous, or perimembranous*, without the original specific description.

As already indicated, the AV node and penetrating portion of the bundle of His are in their normal position in hearts with perimembranous VSDs. As the bundle penetrates the fibrous right trigone of the central fibrous body at the base of the noncoronary cusp of the aortic valve, it lies along the posteroinferior border of perimembranous and inlet-type VSDs. As the bundle continues along the inferior border of the VSD (at times slightly to the left or right of the free edge), the left bundle branch fascicles emerge from the branching portion. Only the right bundle branch remains when the bundle reaches the level of the muscle of Lancisi.

Abnormalities of the ventricular portion of the membranous septum are often associated with perimembranous VSDs. The membranous septum may be absent or nearly so, and then the right trigone (beneath the nadir of the noncoronary aortic valve cusp and base of the septal and anterior leaflets of the tricuspid valve are exposed and form the posteroinferior rim of the VSD (see Fig. 35-3). The bundle of His, as it penetrates the fibrous right trigone at the base of the noncoronary cusp, is intimately related to the posteroinferior angle of such a defect. This is associated with a deficiency in the posterior limb of the trabecula septomarginalis. Rarely the ventricular portion of the membranous septum may be well developed, thickened, and perforated by one or many holes, forming an *aneurysm of the membranous septum* that bulges toward the right in systole. This so-called aneurysm is simulated on angiography by the much more common tethered anterior leaflet and the involved and usually fused chordae. Accessory fibrous tissue not part
Thus, it is useful to Fig. 35-5 - Fig. 35-9 (arrows) are present. B, Same defect viewed from left ventricle. VSD lies below noncoronary cusp of aortic valve and is not juxta-aortic. Arrow indicates cleft in anterior mitral leaflet. Key: ALMV, Anterior leaflet of mitral valve; AV, aortic valve; LV, left ventricle; PV, pulmonary valve; RA, right atrium; SLTV, septal leaflet of tricuspid valve.

of the tricuspid valve mechanism may lie along the posterior or superior margin of the defect. This phenomenon is most marked in the flap valve VSD.

Not surprisingly, in hearts with perimembranous VSDs, still other adjacent structures may be abnormal. The medial papillary muscle characteristically joins the anteroinferior angle of the defect and receives chordae from adjacent portions of the tricuspid anterior and septal leaflets. These chordae may be increased in number and abnormally positioned around the edges of a perimembranous VSD, attached to the posterior edge, superior edge (Fig. 35-5), or most often anterior edge. A thick leash of chordae joining the center of the anterior edge of a large defect may produce an appearance on angiography or even at operation of a double defect. Chordae from the anterior leaflet may attach to all three margins, and the anterior leaflet then limits the shunt from left to right through the defect, as well as hinder its repair.

Close association of some perimembranous VSDs with the commissure between anterior and septal tricuspid leaflets sometimes results in adherence of leaflet tissue to edges of the defect and shunting directly from LV into right atrium (Fig. 35-6). This so-called LV–right atrial defect, which constitutes fewer than 5% of perimembranous VSDs in this region, rarely involves the AV septum. Adherence of tricuspid leaflet and chordal tissue is also an important mechanism of spontaneous closure of these VSDs.

**Ventricular Septal Defect in Right Ventricular Outlet (Doubly Committed Subarterial Ventricular Septal Defect)**

Some 5% to 10% of patients treated operatively have a single VSD, usually of moderate or large size, within the outlet portion of the RV. VSDs in this location are also in the outlet portion of the LV and, in contrast to perimembranous VSDs, are more beneath the right aortic cusp than the commissure between it and the noncoronary cusp. In the past, these have also been termed conal, infundibular, supracristal, and intracristal defects. The complex morphology of the ventricular septum in the outlet portion of the RV and many controversies concerning the term “outlet septum” support use of a simple descriptive terminology for this group of VSDs.

VSDs in this general location are bordered in part by a space over which lie the pulmonary and aortic valves (Fig. 35-7). As such, these VSDs are subarterial. VSDs of this type are more common in Asians than in white or black races. Subarterial VSDs may be circular, diamond shaped, or oval with the long axis lying transversely (Fig. 35-8). When viewed from the LV aspect, these defects are in the outflow portion of the ventricular septum (see Fig. 35-7, B), beneath the right coronary cusp (or commissure between it and the left cusp). The aortic and pulmonary valve cusps are separated by only a thin rim of fibrous tissue. The right aortic cusp and (less often) noncoronary cusp may prolapse into the upper margin of the defect, with or without aortic regurgitation (see Section II later in this chapter).

The posteroinferior margin of RV outlet VSDs is usually well separated from the tricuspid valve anulus by a band of muscle and is consequently well above the bundle of His. Occasionally, however, a particularly large confluent VSD may be both subarterial and perimembranous (Fig. 35-9). The conduction system is related to such a VSD as it is to other perimembranous defects. This particular type of VSD is sometimes associated with severe overriding of the aorta, and the cardiac anomaly is then termed double outlet right ventricle (DORV) with doubly committed VSD. The same type of VSD may also be seen in double outlet left ventricle (DOLV), in which the pulmonary artery severely overrides the VSD.

Morphology of these subarterial VSDs has been well elucidated by 2D echocardiography and color Doppler examinations. Despite the potential confusion of using Lev’s relational terminology in a morphologic sense, in the echocardiographic literature, subarterial defects are usually referred to as doubly committed VSDs. Thus, it is useful to
Figure 35-5 Perimembranous ventricular septal defect (VSD) associated with anomalous leaflet tissue. **A**, VSD viewed from right ventricle. Note chordal attachment (arrow) of anterior tricuspid leaflet to anterosuperior margin of defect. Normal position of infundibular (outlet) septum between two limbs of trabecula septomarginalis (septal band) is well seen. **B**, Same defect viewed from right atrium. VSD is partly obscured by tricuspid leaflet tissue, but its extent is indicated by dashed line. **C**, Same defect viewed from left ventricle. VSD is immediately beneath aortic valve (juxta-aortic), and its extent is indicated by dashed line. Abnormal tricuspid valve attachments are obvious and on an angiocardiogram are indistinguishable from an aneurysm of the membranous ventricular septum. Key: ALMV, Anterior leaflet of mitral valve; AV, aortic valve; InfS, infundibular (outlet) septum; PV, pulmonary valve, RA, right atrium; RV, right ventricle; TS, trabecula septomarginalis (septal band); TV, tricuspid valve.

combine morphologic and echocardiographic descriptions to characterize these VSDs occurring in the RV outlet as **doubly committed subarterial VSDs**. Echocardiography has demonstrated that aortic and pulmonary valves are frequently at the same level in the presence of subarterial (or doubly committed) VSDs, rather than the pulmonary valve being elevated above (cephalad to) or offset relative to the aortic valve, seemingly by the RV infundibulum. This description often provides a diagnostic tool useful in both echocardiography and angiography, along with the finding that the outlet septum appears to be absent and the subpulmonary infundibulum deficient. Echocardiography has also demonstrated the frequently associated prolapse of an aortic cusp and aortic regurgitation present in up to half of patients with this type of VSD. Aortic cusp prolapse may nearly close the VSD during diastole. At times the fibrous raphe between the arterial valves is displaced relative to the ventricular septum, resulting in overriding of one arterial valve and narrowing of the other.

Some VSDs in the RV outlet are only **juxta-aortic** and abut the nadir of the right coronary cusp. The cusp typically prolapses through this type of VSD, and aortic regurgitation frequently develops. Rarely, VSDs in the RV outlet are only juxtapulmonary and lie far to the left. Some defects in the outlet portion of the septum have **muscular** borders and lie in the substance of the infundibulum (muscular VSD, outlet type), with a muscle bridge of infundibular septum superior to the defect. The superior muscular bridge may be malaligned and displaced leftward into the aortic outflow tract (posterior malalignment type of VSD), producing muscular subaortic stenosis that lies above the VSD. This anomaly occasionally occurs in association with interrupted aortic arch and with coarctation, although perimembranous VSDs are more common in both settings.

Inlet Septal Ventricular Septal Defect

Five percent or less of surgical patients have *inlet septal VSD* (or *AV septal type* or *AV canal type of VSD*). This defect involves the RV *inlet septum* beneath the tricuspid septal leaflet and LV *outlet septum*. Its posterior margin is formed by the exposed AV valve anulus (juxtapacustricuspid), and its
Figure 35-6 Type of perimembranous ventricular septal defect (VSD) that ejects directly into right atrium, a so-called left ventricular–right atrial defect. A, VSD viewed from right atrium. Posterior part of tricuspid anulus is marked by dashed line. Tricuspid septal leaflet is anomalously adherent to underlying ventricular septum and edges of VSD, which is juxtraticuspid. Intact atrioventricular septum lies on atrial side of tricuspid anulus (beneath letters VSD). Bundle of His is along posterior angle of defect. B, Same defect viewed from left ventricle. VSD is juxta-aortic and beneath commissure between right and noncoronary aortic cusps. Key: ALMV, Anterior leaflet of mitral valve; ALTV, anterior leaflet of tricuspid valve; LV, left ventricle; NC, noncoronary aortic cusp; RA, right atrium; RV, right ventricle; SLTV, septal leaflet of tricuspid valve.

Figure 35-7 Doubly committed subarterial ventricular septal defect (VSD) in outlet portion of ventricular septum. A, VSD viewed from right ventricle. Its inferior margin is formed of thick septal tissue and its superior margin by confluent right pulmonary and right aortic cusps, which are separated by a thin ridge of fibrous tissue. B, Same defect viewed from left ventricle. VSD is beneath right coronary cusp of aortic valve and more anterior than a conoventricular VSD. Key: ALMV, Anterior leaflet of mitral valve; InfS, infundibular (outlet) septum; L, left pulmonary cusp; NC, noncoronary aortic cusp; R, right pulmonary cusp; TSM, trabecula septomarginalis (septal band).
Figure 35-8  Doubly committed subarterial ventricular septal defect (VSD) viewed from right ventricle. VSD lies immediately beneath pulmonary valve (and, although it is unseen, aortic valve). Inferior to defect are infundibular septum and trabecula septomarginalis (septal band). Tricuspid valve, papillary muscle of conus, and bundle of His are far from defect. Key: InfS, infundibular septum; PMC, papillary muscle of Lancisi; PV, pulmonary valve; TSM, trabecula septomarginalis (septal band); TV, tricuspid valve.

Figure 35-9  Large confluent ventricular septal defect (VSD) that is both subarterial and perimembranous, extending downward to reach tricuspid anulus. This type of VSD is also seen in double outlet right ventricle with doubly committed VSD and in double outlet left ventricle. A, VSD viewed from right ventricle. At superior margin of VSD, pulmonary and aortic cusps are in fibrous continuity. Arrow points toward aortic valve. B, Same defect viewed from left ventricle. Note additional small trabecular muscular defect. Key: Ao, Aorta; IS, infundibular septum; PA, pulmonary artery; PV, pulmonary and aortic cusps.

The anterior margin is muscular and crescentic (Fig. 35-10). Superiorly, inlet septal defects usually extend to the membranous septum. The AV septum is intact, in contrast to the situation in hearts with AV canal septal defects (see Morphology in Chapter 34). The anterior (septal) mitral leaflet occasionally may be cleft, either partially or completely, with associated mitral regurgitation. Rarely, VSDs in the inlet portion of the septum extend completely to the crux cordis and thus are also juxtacrural in position. The tricuspid valve is overriding and usually straddling.

In inlet septal VSDs, the AV node lies more laterally and anteriorly along the tricuspid anulus than normal and at the point at which the tricuspid anulus meets the underlying ventricular septum, because of straddling of the tricuspid valve. The bundle of His lies along the posteriorinferior rim of the inlet septal VSD, slightly on the LV side, as in juxtratricuspid VSDs.

A muscular VSD can occur in the inlet portion of the ventricular septum beneath the tricuspid septal leaflet (Fig. 35-11). The posterior margin of such a defect is separated from the tricuspid ring by muscle. A muscular VSD must be distinguished from the inlet septal type of VSD because the conducting tissue runs superior and anterior to a muscular defect.

Muscular Ventricular Septal Defect
VSDs in other locations are generally muscular VSDs. Such defects are frequently multiple and may be associated with perimembranous or subarterial VSDs. Single or multiple muscular defects in the trabecular septum are more common
Figure 35-10  Inlet septal ventricular septal defect (VSD) beneath septal leaflet of tricuspid valve. Posterior margin of defect is formed by tricuspid anulus. VSD is juxtratricuspid. A, VSD viewed from right ventricle. Note crescentic anterior margin of defect. (A previously placed polyester patch has been removed.) B, Same defect viewed from left ventricle. Superiorly, defect reaches almost to aortic valve; posteriorly, it extends to mitral valve. Key: AV, Aortic valve; MV, mitral valve; PV, pulmonary valve; RA, right atrium; SLTV, septal leaflet of tricuspid valve; TV, tricuspid valve.

Figure 35-11  Single, moderate-sized, muscular inlet septal ventricular septal defect (VSD) lying beneath tricuspid septal leaflet. A, VSD viewed from right ventricle. Note septal muscle between VSD and tricuspid valve. Bundle of His lies superior to VSD. This defect can easily be closed from a right atrial approach. B, Same defect viewed from left ventricle. VSD is in posterior part of nontrabeculated portion of left side of ventricular septum. Key: ALMV, Anterior leaflet of mitral valve; AV, aortic valve; LV, left ventricle; PV, pulmonary valve; TV, tricuspid valve.
Muscular defects can occur anywhere in the ventricular septum (see Fig. 35-1). Those in the middle portion of the trabecular septum are the most common (Fig. 35-12) and may be overlaid by the trabecula septomarginalis; thus, even when single on the LV side, these defects have at least two openings on the RV side. Anterior muscular defects are usually multiple and most often in the apical and outlet portions of the septum. They may extend all along the anterior part of the septum from apex to outlet septum. Typically there are more openings on the RV than LV side.

A particularly important group of patients are those with Swiss cheese defects (Fig. 35-13), many defects of variable size, not only along the anterior portion of the septum but throughout the midportion as well. These defects often pass obliquely through the septum to appear on both sides of the trabecula septomarginalis or in the anterior part of the septum. They may be associated with large or small perimembranous or subarterial defects. Major associated cardiac anomalies are common, especially severe coarctation of the aorta.

The bundle of His is not closely related to the borders of any muscular VSD.

**Confluent Ventricular Septal Defect**

Some unusually large, single confluent VSDs involve more than one area of the septum. Rarely a confluent VSD may involve most of the septum (Fig. 35-14), but hearts with such defects should not be classified as having a single ventricle.

**Ventricular Septal Defect with Straddling or Overriding Tricuspid Valve**

In rare instances, tricuspid valve chordae may straddle the ventricular septum in association with a large inlet septal defect resembling an inlet septal-type VSD but extending to the crux cordis. The tricuspid valve usually overrides both ventricles. When overriding is severe, the tricuspid anulus is usually very large, and many chordae from it are attached to the LV side of the septum (a combination of straddling and overriding). The atrial septum is malaligned relative to the ventricular septum. The RV is often hypoplastic. The tricuspid valve may be regurgitant.

**Associated Lesions**

Nearly half of patients undergoing surgical treatment for a primary VSD have an associated cardiac anomaly. A moderate-sized or large patent ductus arteriosus (PDA) is
Figure 35-13  “Swiss cheese” type of multiple ventricular septal defect (VSD) associated with a large perimembranous VSD. A, VSDs viewed from right ventricle. Perimembranous defect shows anomalous chordal attachment from tricuspid valve to posterosuperior margin of defect (arrow). Probes demonstrate five separate openings of small defects, one above and four below trabecula septomarginalis (septal band). B, Same defects viewed from left ventricle. Perimembranous defect is seen. Probes demonstrate three separate openings of Swiss cheese defects, but many more lie in grossly trabeculated lower portion of septum. Key: ALMV, Anterior leaflet of mitral valve; AV, aortic valve; InfS, infundibular septum; PV, pulmonary valve; TV, tricuspid valve.

Figure 35-14  Large confluent ventricular septal defect (VSD) is perimembranous and occupies upper half of muscular septum beneath infundibular septum (anterior extension). It is associated with Swiss cheese VSDs. A, VSD viewed from right ventricle. Surgeon’s initial impression would be that patient had a single ventricle. B, Same defect viewed from left ventricle. Malformation is clearly not a single ventricle. Key: ALMV, Anterior leaflet of mitral valve; AV, aortic valve; PV, pulmonary valve; TV, tricuspid valve.
Figure 35-15  Inlet septal type of ventricular septal defect (VSD) with posterior extension and straddling tricuspid valve.  

A, VSD viewed from right atrium.  Crest of ventricular septum forming lower boundary of defect (black arrow) crosses almost beneath center of large tricuspid orifice, indicating severe malalignment of atrial and ventricular septa.  

B, Same defect viewed from left ventricle.  Chordal attachments of tricuspid valve cross VSD to attach to septal surface of left ventricle.  This heart also exhibits transposition of the great arteries, with pulmonary trunk above left ventricle.  

Key:  

LV, Left ventricle;  
MV, mitral valve;  
PV, pulmonary valve;  
RA, right atrium;  
RV, right ventricle;  
TV, tricuspid valve orifice.

present in about 6% of patients of all ages, but about 25% of infants in heart failure.  VSD occurs in combination with moderate or severe coarctation of the aorta in about 5% of patients.  This combination is also much more common among infants with large VSD coming to operation younger than age 3 months.

Congenital aortic stenosis occurs in about 2% of patients requiring operation for VSD.  Subvalvar stenosis is more common than valvar and may also occur in association with infundibular pulmonary stenosis.  Subvalvar stenosis can be due to (1) a discrete fibromuscular bar lying inferior (caudal or upstream) to the VSD; (2) a discrete fibromuscular bar located distal (downstream) to the VSD, often consisting of displacement of infundibular septal muscle into the LV outflow tract (posterior malalignment), and often associated with aortic coarctation and interrupted arch; (3) pulmonary artery banding; and (4) excrescences of AV valvar tissue.

Congenital mitral valve disease occurs in about 2% of patients.  One of the pulmonary arteries may be absent or severely stenotic.  Severe peripheral pulmonary artery stenoses occur rarely.

Although atrial septal defects in general are not considered major associated anomalies, they may coexist with a large VSD in small infants and may be important lesions.

Severe positional cardiac anomalies (e.g., isolated dextrocardia, situs inversus totalis) are uncommon in patients with VSD.

Pulmonary Vascular Disease

The classic description of the pathology of hypertensive pulmonary vascular disease is that of Heath and Edwards (Box 35-1).

$\text{Rp}$ in patients with large VSD (and those with large PDA) is positively correlated with histologic severity of the hypertensive pulmonary vascular disease, classified by Heath and colleagues (Fig. 35-16).  A close positive correlation also exists between lowest $\text{Rp}$ at rest or with isoproterenol infusion and Heath-Edwards grade of vascular disease.  Heath-Edwards grades above 3 were not found in patients with $\text{Rp}$ index less than 7 units · m$^2$, whereas those with $\text{Rp}$ greater than 8.5 units · m$^2$ showed changes characteristic of grade 4 or greater.  Similarly, Fried and colleagues found a rather close negative correlation ($P = .001$) between magnitude of left-to-right shunt and Heath-Edwards grade in infants and children coming to VSD repair.  Variability in these matters is not unexpected because Heath-Edwards classification is based on the most severe lesion seen, regardless of its frequency.  As noted by Wagenvoort and colleagues and
Yamaki and Tezuka, grading should include assessment of the number of vessels affected. In addition, calculation of Rp is open to errors.

Hislop and colleagues provide a different view of hypertensive pulmonary vascular disease in infants with large VSD. Other investigators had noted earlier that intimal proliferation (and thus Heath-Edwards changes of grade 2 or greater) rarely develops in patients with large VSD until 1 or 2 years of age, despite infants occasionally having severely elevated Rp. Hislop and colleagues found that infants dying at 3 to 6 months of age with large VSD and high (>8 units · m²) Rp with intermittent right-to-left shunting have marked medial hypertrophy affecting both large and small pulmonary arteries, including those less than 200 µm in diameter. The usual number of intraacinar vessels was present. By contrast, these investigators found that infants 3 to 10 months of age with large VSDs dying with a history of large Qp and heart failure and normal or slightly elevated Rp have medial hypertrophy affecting mainly arteries larger than 200 µm. The intraacinar vessels were fewer than usual, so-called lessened arterial density. These histologic features have been shown by Rabinovitch and colleagues to correlate with pulmonary hemodynamic findings after repair of VSDs.

Histologic reversibility of pulmonary vascular disease after closure of VSD has not been documented. Favorable results in infants may be from an increase in arterial density as growth proceeds. Presumably, pulmonary vascular disease of Heath-Edwards grade 3 or greater severity is not reversible.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Clinical Findings

In infants, signs and symptoms of heart failure include tachypnea and liver enlargement, often associated with poor feeding and growth failure, and physical findings of a precordial pansystolic or more abbreviated systolic murmur and a hyperactive heart. These findings suggest the diagnosis of a large VSD. An apical diastolic murmur suggests large flow across the mitral valve during diastole, the result of a large Qp. Cardiomegaly and evidence of large Qp are seen on the chest radiograph (Fig. 35-17). The electrocardiogram (ECG) usually shows biventricular hypertrophy. In older patients with large VSD, the history is often nonspecific, but
examination also shows evidence of LV and RV enlargement and a systolic murmur usually best heard in the third and fourth left interspaces. In patients with doubly committed subarterial VSDs, the systolic murmur is maximal in the second and third interspaces, and in defects shunting mainly into the right atrium, in the fourth and fifth interspaces.

A high Rp from severe pulmonary vascular disease changes the hemodynamic state and clinical findings in patients with large VSDs. A large left-to-right shunt is no longer present because output resistances of the two pathways for LV emptying are similar, and the shunt is bidirectional and of about equal magnitude in both directions. The heart is not enlarged or hyperactive. A systolic murmur (produced by the large flow across the VSD) is soft or absent, and no apical diastolic murmur is heard. The pulmonary component of the second sound at the base is loud and sometimes palpable. Chest radiography reflects these features (see Fig. 35-17). ECG shows severe RV hypertrophy rather than combined ventricular hypertrophy, and evidence of LV volume overload. When pulmonary vascular disease is even more advanced, cyanosis develops (Eisenmenger complex) because the shunt across the VSD becomes right to left as RV output resistance through the pulmonary vascular bed becomes higher than that through the VSD and aorta.

Patients with small VSDs have small shunts and often no abnormal signs or symptoms other than a pansystolic murmur. Chest radiography and ECG both may be normal. When the defect is moderate in size, the LV is mildly or moderately enlarged (shown by physical examination, chest radiography, and ECG), and the volume of the RV is increased.

When there is associated pulmonary or aortic stenosis, diagnostic features are changed. Thus, with important pulmonary stenosis, Qp is reduced, and the shunt may even be right to left. RV hypertrophy is increased. With important aortic stenosis, the load on the LV is increased, and if the obstruction is cephalad to the VSD, left-to-right shunt is also greater, resulting in more than the expected degree of LV hypertrophy on ECG. Coarctation of the aorta may also produce these features in older children.

Two-Dimensional Echocardiography

Two-dimensional echocardiography imaging of the VSD with color Doppler flow evaluation of shunt flow by proximal isovelocity surface area (PISA) has changed traditional views about preoperative studies. Thus, cardiac catheterization and cineangiography are not necessary before closure of primary VSDs when (1) the clinical syndrome in neonates and infants indicates a large Qp/Qs; (2) noninvasive imaging clearly defines the morphology, including that of the aortic arch and ductus arteriosus; and (3) the surgeon is experienced in surgical identification and repair of congenital heart disease.

For identifying a large single perimembranous VSD, combined 2D echocardiography and Doppler flow interrogation is highly reliable in combination with clinical criteria (Fig. 35-18). Echocardiography adds to anatomic clarification, particularly in the case of doubly committed subarterial VSDs. Particularly for small VSDs and multiple muscular defects, 2D Doppler color flow echocardiographic imaging increases the sensitivity of echocardiography (Fig. 35-18, A and B). However, and particularly in the presence of a single large VSD, multiple muscular defects can go undetected even with refined techniques of echocardiography. Because perimembranous VSDs are infrequently (<3%) accompanied by additional muscular VSDs, this does not contraindicate proceeding to repair in infants without cardiac catheterization. Malalignment VSD is diagnosed by 2D echocardiography by the appearance of the alignment of the RV and pulmonary semilunar valves. Malalignment may be anterior as in tetralogy of Fallot (Fig. 35-18, C), posterior as in interrupted aortic arch, or rotational as in Taussig-Bing heart.

Size of a VSD is generally categorized echocardiographically as small, moderate, or large for purposes of decisions regarding surgery (see Morphology and Indications for Operation later in this chapter). A large defect has a diameter of 75% or greater of the aortic anulus and low-velocity flow by Doppler, measuring no more than 1 m · s⁻¹. A moderate defect has a diameter of 33% to 75% of the aortic anulus and flow velocity of 1 to 4 m · s⁻¹, indicating moderate flow restriction. (By the modified Bernoulli equation, gradient across the defect is calculated by multiplying velocity squared times 4.) A small defect has a diameter less than 33% of the aortic anulus and a flow velocity of 4 m · s⁻¹ or greater. When considering Rp, it is important to note that as resistance (or obstructions in the RV outflow tract) increases, flow velocity across the VSD decreases.

Other Noninvasive Diagnostic Methods

Other noninvasive imaging modalities may come into use. At present, only magnetic resonance imaging (MRI) has shown promise to provide accurate information about the morphology of all types of VSDs. Dynamic three-dimensional echocardiographic reconstructions may refine ability to image and portray VSDs spatially.

Cardiac Catheterization

When surgical intervention is under consideration in older children, cardiac catheterization and angiography are generally indicated to assess Rp and precisely identify location, size, and number of VSDs and any associated anomalies. Furthermore, preoperative sizing of VSDs is often important in arriving at management decisions. Sizing can be especially difficult when the VSD is associated with another lesion such as coarctation or pulmonary stenosis. The most reliable way to size the defect is to measure its diameter either by 2D color flow Doppler echocardiography or cineangiography. With cineangiography, the VSD must be accurately profiled and the measurement either corrected to allow for magnification or compared with aortic root diameter. In applying this method to perimembranous VSDs, the defect is smaller in a cranially tilted left anterior oblique (LAO) projection than in the conventional LAO position.

Cardiac catheterization should include both right-sided and left-sided heart studies, the latter mainly to obtain LV angiograms. Basic data obtained at cardiac catheterization should include oxygen consumption (VO₂); systolic, diastolic, and mean pulmonary arterial, pulmonary artery wedge, and systemic arterial pressures; oxygen content and saturation in right atrial, pulmonary arterial, aortic, or peripheral arterial blood and, when possible, left atrial blood. Pulmonary (Qp) and systemic (Qs) blood flows and Qp/Qs...
are calculated\(^3\) with Rp (Table 35-3). When left atrial (or pulmonary arterial wedge) pressure is not available, only total pulmonary resistance (TPR)\(^4\) can be calculated. Rp in absolute units \(\times\) body surface area is of more value in predicting operability than is the ratio of resistances in pulmonary and systemic circuits.\(^5\) When Rp is elevated, further information concerning operability should be obtained by assessing response to exercise and to isoproterenol (see Indications for Operation later in this chapter).

### Angiography

Angiographic assessment of VSD is best performed using biplane techniques in appropriate projections.\(^6\)\(^7\) Whereas cardiologists and radiologists carry primary responsibility for these studies, appreciation of their findings and limitations is essential to the surgeon, who must also understand when the study is incomplete.\(^8\)

Fig. 35-19 summarizes the surgically important features of angiograms of VSD by diagram. Fig. 35-20 presents representative angiograms of the various types of VSDs.

### NATURAL HISTORY

#### Spontaneous Closure

VSDs tend to close spontaneously.\(^9\) This is relevant to decisions about operation and explains, for the most part, the infrequency with which large VSDs are encountered in adults.\(^10\) Spontaneous closure can be complete by 1 year of

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\(\frac{Q_P}{Q_S} = \frac{V_o_1}{(C_a_0_1 - C_p_0_1)}\) in L·min\(^{-1}\)

where \(P_r\) is pulmonary vein and \(P_a\) is pulmonary artery. \(Q_P\) may be expressed as index \(L\cdot\text{min}^{-1}\cdot\text{m}^{-2}\) by dividing by body surface area (BSA) expressed in square meters.

\(Q_s = \frac{V_o_2}{(C_a_0_2 - C_v_0_2)}\) in L·min\(^{-1}\)

where \(a\) is aorta or arterial and \(v\) is mixed venous.

\(\frac{Q_P}{Q_S} = \frac{(C_a_0_1 - C_p_0_1)}{(C_a_0_2 - C_p_0_2)}\)

Note that total oxygen consumption is not needed for this calculation.

\(R_p = \frac{[P_p - P_a]}{Q_p}\cdot\text{BSA}\); Rp is expressed in units \(\text{m}^{-2}\).

\(\text{TPR} = \frac{[P_p / Q_p]}{\text{BSA}}\); TPR is expressed in units \(\text{m}^{-2}\).

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
\textbf{Resistance} & \textbf{\(\leq\ \text{units} \cdot \text{m}^2\)} & \textbf{\(<\)} & \textbf{Description} \\
\hline
4 & & Normal & \\
5 & & Mildly elevated & \\
8 & & Moderately elevated & \\
8 & & Severely elevated & \\
\hline
\end{tabular}
\caption{Pulmonary Vascular Resistance}
\end{table}
Chapter 35 Ventricular Septal Defect

A. Interrelationships of left ventricle (LV) and aortic root (thick line) with right ventricle (RV) and pulmonary trunk (thin line) in 40-degree right anterior oblique (RAO), 50-degree left anterior oblique (LAO), and 40-degree cranially tilted (CR. LAO) projections. RAO view profiles infundibular (conal) and high anterior portions of RV outlet septum below and in front of right coronary sinus and profiles atrioventricular (AV) septum beneath noncoronary sinus of aortic root. Both LAO views profile apical trabecular portion of septum. LAO view also partly profiles RV outlet septum but superimposes it on LV outflow tract and aortic root. CR. LAO projection views RV outlet septum en face and superimposes it on LV. Because orientation shows a horizontally lying heart, LAO view depicts full length (cranial to caudal) of apical and anterior trabecular portion of ventricular septum and AV valve anuli (interrupted lines), whereas CR. LAO view depicts full length of sinus portion of trabecular septum from base to apex. B. Both cranially tilted (CR. LAO) and conventional LAO views are required for a complete assessment of sinus septum. Basal (inlet) (O, x) VSDs are separated from more apical (o) VSDs by CR. LAO projection, whereas high (x) VSDs are separated from low (O) VSDs by LAO view. C, Anatomic and hemodynamic features of VSDs shown by LV angiograms. LAO diagrams show a compromise between conventional and cranially tilted options. LV and aorta are shown by thick lines, RV and pulmonary trunk by thin lines, and AV valves and nonprofiled VSDs by interrupted lines. C1, Perimembranous VSD. LAO view profiles VSD just beneath parietal band (ventriculoinfundibular fold) at upper margin of inlet septum. Flow enters base of RV above tricuspid valve, filling base before reaching infundibulum. Tricuspid valve is well seen in diastole, and lower margin of defect can be accurately related to tricuspid anulus in LAO. RAO view does not profile defect unless it extends into outlet septum. Note intact AV septum beneath noncoronary sinus of aortic root. Shunt enters RV infundibulum, crossing but not interrupting intact superior margin of LV, indicating intact conal and high anterior septal regions. C2, Doubly committed subarterial VSD (labeled conal septal VSD). LAO view shows an intact septum from aortic valve to apex. RV sinus usually fills only faintly by diastolic mixing from infundibular region, and tricuspid valve may not be seen. Defect is superimposed on aortic root. RAO view profiles defect beneath contiguous parts of aortic and pulmonary valves. Systolic streaming through RV infundibulum to pulmonary trunk is well shown, with some mixing to more anterior part of RV in diastole, but high anterior septal region is intact.

Figure 35-19 Line drawings of angiographic projections for assessment of ventricular septal defect (VSD). A, Interrelationships of left ventricle (LV) and aortic root (thick line) with right ventricle (RV) and pulmonary trunk (thin line) in 40-degree right anterior oblique (RAO), 50-degree left anterior oblique (LAO), and 40-degree cranially tilted (CR. LAO) projections. RAO view profiles infundibular (conal) and high anterior portions of RV outlet septum below and in front of right coronary sinus and profiles atrioventricular (AV) septum beneath noncoronary sinus of aortic root. Both LAO views profile apical trabecular portion of septum. LAO view also partly profiles RV outlet septum but superimposes it on LV outflow tract and aortic root. CR. LAO projection views RV outlet septum en face and superimposes it on LV. Because orientation shows a horizontally lying heart, LAO view depicts full length (cranial to caudal) of apical and anterior trabecular portion of ventricular septum and AV valve anuli (interrupted lines), whereas CR. LAO view depicts full length of sinus portion of trabecular septum from base to apex. B, Both cranially tilted (CR. LAO) and conventional LAO views are required for a complete assessment of sinus septum. Basal (inlet) (O, x) VSDs are separated from more apical (o) VSDs by CR. LAO projection, whereas high (x) VSDs are separated from low (O) VSDs by LAO view. C, Anatomic and hemodynamic features of VSDs shown by LV angiograms. LAO diagrams show a compromise between conventional and cranially tilted options. LV and aorta are shown by thick lines, RV and pulmonary trunk by thin lines, and AV valves and nonprofiled VSDs by interrupted lines. C1, Perimembranous VSD. LAO view profiles VSD just beneath parietal band (ventriculoinfundibular fold) at upper margin of inlet septum. Flow enters base of RV above tricuspid valve, filling base before reaching infundibulum. Tricuspid valve is well seen in diastole, and lower margin of defect can be accurately related to tricuspid anulus in LAO. RAO view does not profile defect unless it extends into outlet septum. Note intact AV septum beneath noncoronary sinus of aortic root. Shunt enters RV infundibulum, crossing but not interrupting intact superior margin of LV, indicating intact conal and high anterior septal regions. C2, Doubly committed subarterial VSD (labeled conal septal VSD). LAO view shows an intact septum from aortic valve to apex. RV sinus usually fills only faintly by diastolic mixing from infundibular region, and tricuspid valve may not be seen. Defect is superimposed on aortic root. RAO view profiles defect beneath contiguous parts of aortic and pulmonary valves. Systolic streaming through RV infundibulum to pulmonary trunk is well shown, with some mixing to more anterior part of RV in diastole, but high anterior septal region is intact.

Continued
Basal muscular VSD

LAO

RAO

Mid-muscular VSD

LAO

RAO

High anterior and apical muscular VSDs

LAO

RAO

C3

C4

C5

Figure 35-19, cont’d  C3, Inlet septal VSD (labeled basal muscular VSD). VSD is adjacent to tricuspid valve (AV septal type) or separated from it by a rim of muscle (muscular VSD). These two types of VSDs are not readily distinguished radiologically. In LAO view, defect is profiled between AV valves, replacing full height of basal septum (conventional LAO view), perhaps extending into adjacent middle portion of ventricular septum but not into apical region (cranially tilted LAO view). Contrast medium streams directly into base of RV sinus in systole, providing a good depiction of tricuspid orifice in diastole. Separate AV valves are present, in contrast to the finding in a complete AV septal defect (see Chapter 34). In RAO view, VSD is not profiled. Intact AV septum distinguishes this defect from a true AV septal defect. Note intact conal and high anterior septal regions. C4, Muscular, trabecular VSD (labeled mid-muscular VSD). LAO views show an intact inlet septum and no extension into apical region, although a small additional defect is seen in diastole, closing in systole. Some of the contrast medium streams directly into RV outflow during systole. Height of defect from floor of ventricle (bottom of AV valve) is appreciated in LAO view, and separation from basal and apical regions in cranially tilted LAO view. RAO features are as in parts C1 and C3. C5, Multiple muscular anterior and apical VSDs. Muscular VSDs in these regions frequently coexist and, if numerous, form a continuous series throughout trabeculated septum from high in RV infundibulum to apical sinus septum. For clarity, only highest and lowest are shown here. In LAO view, intact basal and middle septal regions are profiled. Apical defects are profiled, but high anterior defects are superimposed on LV outflow region. Contrast medium tends to stream to RV outflow tract without filling basal parts. In RAO view, high anterior defects are profiled, interrupting superior margin of LV anterior to intact outlet septum. More defects are open in diastole than in systole. Key: CR.LAO, Cranial left anterior oblique; L, left coronary; LAO, left anterior oblique; LV, left ventricle; N, noncoronary; R, right coronary; RAO, right anterior oblique; RV, right ventricle. (From Brandt.31)
A1, 40-degree cranially tilted 60-degree left anterior oblique (LAO) projection, systolic frame, early in perimembranous angiographic sequence. VSD (arrow) lies in basal part of ventricular septum adjacent to aortic root. No additional defects are seen in middle and apical portions of septum (catheter to LV through atrial septum and mitral valve). A2, 30-degree right anterior oblique (RAO) projection, systolic frame, slightly later than A1 in sequence. Patient was positioned to achieve cranial tilting of simultaneously exposed LAO view shown in A1. Note intact atrioventricular septum beneath noncoronary aortic sinus and intact outlet septum (C). Contrast medium from shunt through nonprofiled VSD fills right ventricular (RV) outflow tract, crossing (arrow) but not interrupting high anterior margin of LV. A3, 50-degree LAO projection, systolic frame early in sequence (second injection). Perimembranous VSD is profiled as in A1 beneath aortic root. Large arrow indicates flow into base of RV above tricuspid valve (identified in diastole but not illustrated). Downward extent of VSD (small arrow) is accurately shown, and there are no additional defects lower in septum. Perimembranous defects are frequently small, of dimensions profiled in cranially tilted LAO projection in A1, compared with LAO.

Figure 35-20 Angiograms of patients with ventricular septal defect (VSD). A, Left ventricular (LV) angiograms of a perimembranous VSD. A1, 40-degree cranially tilted 60-degree left anterior oblique (LAO) projection, systolic frame, early in perimembranous angiographic sequence. VSD (arrow) lies in basal part of ventricular septum adjacent to aortic root. No additional defects are seen in middle and apical portions of septum (catheter to LV through atrial septum and mitral valve). A2, 30-degree right anterior oblique (RAO) projection, systolic frame, slightly later than A1 in sequence. Patient was positioned to achieve cranial tilting of simultaneously exposed LAO view shown in A1. Note intact atrioventricular septum beneath noncoronary aortic sinus and intact outlet septum (C). Contrast medium from shunt through nonprofiled VSD fills right ventricular (RV) outflow tract, crossing (arrow) but not interrupting high anterior margin of LV. A3, 50-degree LAO projection, systolic frame early in sequence (second injection). Perimembranous VSD is profiled as in A1 beneath aortic root. Large arrow indicates flow into base of RV above tricuspid valve (identified in diastole but not illustrated). Downward extent of VSD (small arrow) is accurately shown, and there are no additional defects lower in septum. Perimembranous defects are frequently small, of dimensions profiled in cranially tilted LAO projection in A1, compared with LAO.

Continued
Figure 35-20, cont'd  B, LV angiograms of doubly committed subarterial VSD. B1, 60-degree LAO projection, systolic frame early in sequence. Pulmonary arteries are filled by shunt through RV outlet defect superimposed on LV outflow tract. Only slight contrast medium is seen in RV sinus, and whole of sinus septum is shown to be intact. B2, 30-degree RAO projection, diastolic or very early systolic frame early in sequence. Doubly committed subarterial VSD is profiled immediately beneath contiguous parts of aortic and pulmonary valves, still closed. Arrows show streaming from VSD toward pulmonary valve, with some filling of remainder of RV infundibulum, but high anterior LV margin is intact. C, LV angiocardiograms of muscular VSDs. C1, Muscular anterior VSD. 30-degree RAO projection, diastolic or very early systolic frame early in sequence. Shunt through large, high-anterior muscular VSD fills anterior part of RV infundibulum. Arrows show the main stream toward pulmonary valve, which is still closed. There is a little mixing in RV sinus, but outlet septum is intact. C2, Multiple muscular VSDs (Swiss cheese septum); 40-degree cranially tilted 60-degree LAO projection, systolic cine frame. Large muscular trabecular VSD (large arrow), accompanied by numerous small muscular apical defects (small arrows), is profiled, but basal part of ventricular septum beneath aortic root is intact. In diastole (not shown), more numerous apical defects were apparent. C3, 30-degree RAO projection, diastolic frame in same patient as in C2. Numerous muscular anterior VSDs (arrows) interrupt LV margin. Note intact outlet septal margin of LV near aortic valve. Earlier in sequence, intact atrioventricular septum was identified, but base of filled RV overlaps base of LV in this frame. Note that position of large muscular VSD is incompletely evaluated (trabecular); an LAO view would be necessary. Note surgically banded pulmonary trunk. Key: A, Aortic valve; Ao, Aorta; C, septum; D, subarterial ventricular septal defect; P, pulmonary valve; PT, pulmonary trunk; R, right ventricle; V, atrioventricular septum.
close than juxtaglutaric or subarterial muscular VSDs.  
Perimembranous VSD with LV-to–right atrial shunt (Gerbode defect) in infancy is also associated with less chance of spontaneous closure.

Inferences about the tendency toward spontaneous closure seem to be in disagreement with the results of some studies. Hoffman and Rudolph’s data (one of the sources for Fig. 35-21) indicate that 80% of infants aged 6 weeks with large VSDs will experience spontaneous closure or reduction in size of the VSD. Rowe found that none of 11 infants (mean age 46 days) with a VSD 80% or greater in diameter than that of the aorta showed subsequent reduction in size during the period of observation. These apparent discrepancies may be explained by lack of information about location or size of VSDs.

Pulmonary Vascular Disease

A large VSD exposes the patient to risk of developing increased Rp from hypertensive pulmonary vascular disease, which tends to worsen with age. Thus, the proportion of patients with large VSDs who have severely elevated Rp is directly related to age (Fig. 35-22). The statement that some infants younger than 2 years of age with large VSDs have severely elevated Rp is doubted by some, but its occurrence is well documented.

Some infants and children with severely elevated Rp have not undergone the usual fall in Rp a few weeks to a few months after birth. Others have undergone this decrease, but later in the first 2 years of life, they have developed a rapid increase in Rp.  
Some infants with large VSDs and most of those with moderate-sized VSDs have normal or mildly elevated Rp and retain this through the first decade of life. Then, if their VSD is still large, more severe pulmonary vascular changes may or may not develop as they age. In infants with small VSDs, pulmonary vascular disease does not develop.

Infective Endocarditis

Infective endocarditis is rare in patients with VSD, occurring at a rate of about 0.15% to 0.3% per year. Its prevalence is greater in males and individuals older than 20 years of age. Infective endocarditis is more common in small and moderate VSDs than in large VSDs. Often a pulmonary process is the presenting feature, presumably developing from emboli secondary to right-sided bacterial vegetations or bacteria carried to the lungs by left-to-right–directed flow through the VSD. Prognosis with modern antibiotic treatment regimens is good.

Premature Death

Past experience and reports in the literature indicate that without surgical treatment, about 9% of infants with large VSDs die from them in the first year of life. Death may also result from recurrent pulmonary infections, often viral in origin, secondary to pulmonary edema from high pulmonary venous pressure. Death is most likely to occur in those infants with large VSDs who have associated conditions of major anatomic or functional importance, such as PDA, coarctation of the aorta, or large atrial septal defect.

After the age of 1 year, few if any patients die of their VSD until the second decade of life. By then, many patients whose VSDs have remained large have pulmonary vascular disease and ultimately die with complications of Eisenmenger complex (Fig. 35-23). These include hemoptysis, polycythemia, cerebral abscess or infarction, and right-sided heart failure.

Patients with small VSDs die very rarely as a result of bacterial endocarditis. However, in common with patients with larger VSDs, some of these patients may develop disturbed systolic function and increased compliance in both ventricles.

Figure 35-21 Probability of eventual spontaneous closure of a large ventricular septal defect (VSD) according to age at which patient is observed. Dotted lines enclose 70% confidence limits. Specific ratios, with 70% confidence limits, reported by Hoffman and Rudolph and Keith and colleagues are shown centered on mean or assumed ages of patients in their reports. P for age <.0001. See original sources for equations and statistics. (From Blackstone and colleagues.)

Figure 35-22 Estimated (not calculated) probability of developing severe pulmonary vascular disease (pulmonary vascular resistance 8 units · m-2 or greater) in patients with large ventricular septal defects, according to age. (From Keith and colleagues.)

Chapter 35 Ventricular Septal Defect
as well as some of the more important pulmonary stenoses, probably develop in this way. Stenosis may become severe enough to produce shunt reversal and cyanosis, and the condition then can properly be termed tetralogy of Fallot (see Chapter 38). Those who undergo the transformation probably are born with a mild degree of anterior displacement of the infundibular septum and its extensions.

**TECHNIQUE OF OPERATION**

VSDs are repaired either through the right atrium, RV, or in special circumstances, LV or pulmonary trunk. Currently, RV and LV approaches are rarely used. Repair is done on conventional CPB at 20°C to 28°C, with direct caval cannulation and brief periods of low flow perfusion or (rarely) total circulatory arrest (see Sections III and IV of Chapter 2). For infants weighing less than about 3 kg, a single venous cannula may be used, and the repair is performed during hypothermic circulatory arrest (see Section IV of Chapter 2). Cold cardioplegia is used in all cases.

After the usual anesthetic and surgical preparations (see Chapter 4), a median sternotomy is made. Presence of anomalies of pulmonary or systemic venous return is determined. It should be known from preoperative study whether the ductus arteriosus is open or closed. An open ductus during open cardiotomy, particularly during hypothermic circulatory arrest, allows air to enter the aorta and later migrate to the brain; during CPB an open ductus increases intracardiac return and overdistends the pulmonary circulation. A patent ductus is ligated from the anterior approach, usually during cooling. In neonates and infants undergoing hypothermic circulatory arrest, the ductus is ligated as a routine procedure.

**Repair of Perimembranous Ventricular Septal Defect**

After CPB (with or without circulatory arrest) has been established, the aorta is occluded, cold cardioplegic solution injected, and the right atrium opened obliquely. A suction device is placed across the naturally present or surgically created foramen ovale (Fig. 35-24). Before repair is started, the defect is carefully examined to establish that all margins can be seen and reached. In rare circumstances in which this is not possible because of chordal arrangement, an incision is made to disconnect a portion of the tricuspid valve from the annulus, and the VSD is exposed through the resulting aperture. Particular attention is directed toward determining whether the VSD is juxtratricuspid, in which case it abuts the tricuspid valve in the region of the commissure between septal and anterior leaflets. If the VSD has a bar of muscle of varying width between it and the tricuspid valve, it is not juxtratricuspid. Relationship of the bundle of His to the posterior and inferior margins of the defect must be clearly understood (see Morphology earlier in this section) to accomplish a safe repair (Fig. 35-24, A).

In older infants and children, the VSD is repaired with a polyester patch sewn in place with continuous polypropylene sutures (Fig. 35-24, B), a technique confirmed to be entirely adequate in such patients. In neonates and small infants, the technique may not be adequate because of the delicate nature and friability of the structures. In these patients, the patch may be sewn into place using a combination of continuous and interrupted pledgeted mattress sutures or, alternatively,
Employing exclusively interrupted mattress sutures reinforced with small pledgets.

A ventricular approach may be used when the VSD cannot be well visualized from the right atrium. An RV approach is performed through a transverse incision. The patch is sewn into place with continuous or interrupted sutures (Fig. 35-25). Technique of repair and sequence for suturing shown in Fig. 35-25 are slightly different from those shown for the atrial approach. Suturing begins at the transition point between the septal leaflet of the tricuspid valve and the...
ventricular septum, 5 to 7 mm below the edge of the septal defect. This critical point is given attention by all experienced surgeons.  

Usual de-airing procedures are performed, and the remainder of the operation is completed as usual.

Repair of Doubly Committed Subarterial Ventricular Septal Defect

Transverse incision in the RV infundibulum is the classic approach for repair of doubly committed subarterial VSDs  
(Fig. 35-26). These defects should always be closed with a patch to reduce the possibility of distorting the semilunar valves. A continuous stitch technique is employed. When pledged sutures are used, they are placed from just above the pulmonary valve leaflets, and pledgets come to lie in the pulmonary valve sinuses. Care is taken not to damage the left main coronary artery. An approach through the pulmonary trunk is also convenient for repairing doubly committed subarterial VSDs.

Repair of Inlet Septal Ventricular Septal Defect

Inlet septal (AV septal type) VSD is most easily repaired through the right atrium (see Technique of Operation in Chapter 34). Such defects are always repaired with a patch. The defect lies beneath the septal leaflet of the tricuspid valve, and care is taken to avoid damage to the leaflet or its chordae and to tailor the patch such that it is not too bulky beneath the leaflet. One method of avoiding damage to the leaflet and improving exposure is to temporarily detach the base of the septal leaflet and a portion of the anterior leaflet of the tricuspid valve and retract the leaflet anteriorly.

Repair of Muscular Ventricular Septal Defect

A right-sided approach is used for repair of muscular VSDs. Left ventriculotomy provides excellent exposure, and although it has been reported not to be disadvantageous in infants, it can produce ventricular aneurysm and important LV dysfunction early and late postoperatively. Therefore, use of left ventriculotomy is not recommended. Defects in the lower part of the muscular septum may be obscured by trabeculations and thus difficult to visualize, resulting in incomplete closure. Wollenek and colleagues found that an apical left ventriculotomy was a useful approach in 23 patients, and in follow-up over 3 to 18 years (mean 11 years), echocardiography showed no residual VSD, normal LV shortening, no regional wall motion abnormality, and small LV aneurysm in only two patients.

Single or multiple muscular defects in the inlet and trabecular septum (see Figs. 35-1 and 35-12) are approached through the right atrium. When a single defect is slitlike or oval, direct suture (often in part at least with pledged mattress sutures) is satisfactory, but when it is large and circular, a patch is used. A cluster of defects can be closed with a single patch or individually.

Division of RV trabeculations can aid exposure of the defects, which may be difficult to close because of multiple
sites of jet penetration. A heavy traction stitch passed through the defect and back through the left side of the defect may improve exposure. A single patch of autologous pericardium supported by pledget-reinforced sutures covering an extensive portion of the trabecular septum is useful when there are multiple defects. Kitagawa and colleagues described resection of trabeculations to expose the defect and attaching an oversized patch to the left side of the ventricular septum by sutures passed through the septum from the left side. They also described placing pledget-supported sutures through the rim of an anterior muscular defect, passing the sutures to the outside and tying down on the epicardial surface.

When a muscular VSD coexists with a perimembranous VSD, a single patch may be used to avoid damaging the bundle of His.

VSDs with a single LV opening but two or more openings into the RV on both sides of the trabecula septomarginalis

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5The pledget is a “firm” polyester mini-pledget, 3/16 inch × 3/16 inch × 3/16 inch.
Figure 35-25, cont’d  C, Septal leaflet of tricuspid valve is retracted to expose junction of tricuspid anulus with ventricular septum. A pledget-reinforced mattress stitch of 4-0 polypropylene suture is placed to create a transition from septal leaflet to ventricular septum. One arm of suture is placed entirely on septal leaflet, and other arm is placed into ventricular septum at hinge point of septal leaflet on ventricular septum. Stitch is at least 5 to 7 mm below rim of VSD. Suture is passed through a knitted double-velour polyester patch fashioned to be somewhat larger than VSD. Alternative patch material could be pericardium or polytetrafluoroethylene. D, Several pledget-reinforced mattress stitches are placed around perimeter of VSD. Stitches are placed entirely in septal leaflet tissue between transition stitch and junction of septal and anterior leaflets of tricuspid valve. Stitches are placed 5 to 7 mm below rim of defect between transition stitch and papillary muscle of Lancisi, which demarcates anterior extent of specialized conduction system. Rest of stitches may be placed in rim of septal defect. All stitches are placed through ventricular septum and septal leaflet of tricuspid valve before approximating patch to ventricular septum. E, Patch is attached securely to ventricular septum by tying all sutures. Key: Ao, Aorta; PT, pulmonary trunk; RA, right atrium.
are also approached through the right atrium. The defect is converted into a single LV orifice by detaching the lower end of the trabecula septomarginalis and moderator band from the septum and retracting them (see Fig. 35-12). The VSD is closed with a patch. The trabecula septomarginalis then falls back into place.

Multiple defects in the anterior portion of the septum may be closed through a high transverse ventriculotomy. At times, VSDs may be considered too numerous to close individually; these VSDs are simply compressed and often totally closed by interrupted mattress sutures between a felt strip on the anterior ventricular wall (away from the left anterior descending coronary artery) and pledges inside the RV and inferior to the VSDs. This repair may be done from the right atrium or through a right ventriculotomy.

Apical muscular VSDs can be exposed through the right atrium and tricuspid valve or through a low vertical right ventriculotomy. This can be extended around the apex for a short distance onto the posterior wall.

The rare Swiss cheese septum, with features resembling ventricular noncompaction (spongy ventricular septum) and defects involving all components of the ventricular septum,
may not be correctable through the right side. Its repair requires an LV approach, and a patch over the entire muscular septum may be necessary. An associated perimembranous defect should be repaired through the right atrium because its repair from the LV side increases risk of heart block. Incisions into both ventricles are avoided whenever possible. Great care is used in making and closing the left ventriculotomy incision so as not to damage coronary artery branches. A continuous mattress suture over fine polytetrafluoroethylene (PTFE) felt strips plus an over-and-over stitch give a secure closure. Mace and colleagues used a right atrial approach and inserted a single large patch to cover the right side of the trabecular septum, adding several intermediate fixation stitches to prevent septal bulging. Regardless of the approach employed, these patients often have poor LV function after repair and may ultimately require transplantation for heart failure. This group of patients may be better served by pulmonary trunk banding with the hope that some of these defects may close as a result of ventricular hypertrophy.

Although it is important to avoid residual shunts, multiple incisions and a prolonged search for a few small additional muscular VSDs are generally not advisable. Preoperative echocardiography should accurately delineate the size as well as position of all the defects.

Closure of Associated Patent Ductus Arteriosus

Dissection of the ductus arteriosus is done after establishing CPB; this reduces the risk of hemorrhage should an error in dissection occur because of exposure, which can be difficult. After establishing CPB with the perfusate temperature at about 34°C, with caval tapes still unsnugged (so the heart will not distend) and right atrial pressure at zero, the ductus is dissected. The heart must continue to beat; otherwise a large shunt will rapidly overdistend the right side of the heart and lungs as it steals from the systemic and cerebral circulation. If the heart does fibrillate, CPB flow is immediately reduced while the dissection is rapidly completed. With downward traction on the pulmonary trunk (see Technique of Operation in Chapter 37), the ductus can usually be seen through its pericardial reflection and surrounding adventitial tissue. The left pulmonary artery and undersurface of the aorta—both proximal and distal to the ductus—are clearly identified to prevent these structures from being damaged or ligated after being mistaken for the ductus. The delicate pericardial reflection and adventitial tissue on both sides of the ductus are sharply dissected from it. The adventitia of the ductus itself and of the adjacent pulmonary artery and aorta must not be entered. The recurrent laryngeal nerve is not seen. Only when the dissection is complete, the left pulmonary artery visualized, and the ductus identified with absolute certainty is a right-angled clamp passed behind it to grasp the 2-0 silk ligature. One ligature, tied on the ductus side of the pulmonary trunk banding with the hope of reducing while the dissection is rapidly completed. With subsequent adhesions, the pericardial incision should be limited to the area needed to expose the great vessels. The pulmonary trunk is separated from the aorta by dissecting close to the aorta. A right-angled clamp is passed around and behind the aorta to grasp one end of the band and pull it through. The other end of the band is retrieved by a clamp passed through the transverse sinus. Small angiocatheters are placed in the aorta and left pulmonary artery for pressure monitoring. Transesophageal echocardiography (TEE) may be useful during the procedure to estimate gradient across the band.

With the band now safely around the proximal portion of the pulmonary trunk, the marked points on the band are joined temporarily with a hemoclip to produce the desired circumference. With proper band tightening in patients with a two-ventricle circulation, systolic and mean blood pressures will be less than 1, and the band is too tight. The distal pulmonary artery systolic pressure should be less than 50% of systemic systolic blood pressure. In cases of complete mixing, arterial oxygen saturation will vary with band tightening and should be set at 80% to 85% by pulse oximetry with FiO₂ of 50%. This implies a Qp/Qs of about 1 (see "Pulmonary Trunk Banding in Section II of Chapter 41"). If bradycardia or cyanosis develops, the band must be slightly loosened by placing a hemoclip more distally and removing the initial clip. If the narrowing is insufficient, as judged by the criteria mentioned earlier, it is tightened by adding a hemoclip more proximally.

When the ideal diameter is obtained, the band is joined by sutures. It is essential that stitches be placed between the band and the pulmonary trunk adventitia to prevent migration of the band. The pericardium is loosely closed to facilitate dissection at subsequent operation.

Pulmonary Trunk Debanding

When a pulmonary trunk band has been properly applied for 6 months or less, simple band removal may be all that is necessary. When the band must remain in place longer, reconstruction of the pulmonary trunk is usually required.
The band can almost always be cut and removed without damaging the underlying artery. The tip of the left atrial appendage actually is more likely to be damaged, because it is always adherent to the banded area. Dissection is usually delayed until CPB has been established, when if necessary, CPB flow can be reduced to facilitate exposure and dissection.

The VSD is usually closed after repair of the pulmonary trunk. The pulmonary trunk is usually reconstructed. The most satisfactory technique is local excision of the short, narrowed, scarred segment of artery and reanastomosis of the divided pulmonary trunk using a continuous polypropylene suture.28 This technique can usually be employed even when the band lies close to the pulmonary valve, by extending the incision vertically into the most anterior sinus between the valve commissures to enlarge the diameter of the proximal end. A similar technique can be used to enlarge an orifice stenosis involving only one branch of the pulmonary trunk. When the pulmonary valve cusps have become excessively thick, their edges may require excision. If an adequate diameter is unobtainable by the technique of excision and end-to-end anastomosis, an oval-shaped patch is inserted. To adequately enlarge the stenotic area, the patch (autologous pericardium, bovine pericardium, pulmonary allograft, or thin PTFE) should extend from within the sinus of Valsalva of the pulmonary trunk proximally and across the anastomosis to the distal trunk. Extensive reconstruction (see “Repair of Tetralogy of Fallot with Bifurcation Stenosis of Pulmonary Trunk” in Section I of Chapter 38) is required when the band constricts the origin of the pulmonary arteries.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

General measures and management of complications described in Chapter 5 are used for postoperative care of patients undergoing repair of primary VSD.

Hemodynamic state typically is good early postoperatively after closure of VSD. In the unusual situation of poor hemodynamic performance, the possibility of residual left-to-right shunting must be considered, particularly if left atrial pressure is considerably higher than right atrial pressure.6 Also, the finding of a considerably higher oxygen content or saturation in blood from the pulmonary artery than that from the right atrium establishes existence of a shunt.28 Two-dimensional Doppler color flow echocardiography can be used to settle the matter.1,18 Although some shunting may occur for 12 to 24 hours after VSD closure with a porous patch, the usual cause of poor hemodynamic state from a left-to-right shunt is patch dehiscence. Thus, if the hemodynamic state is poor or a large left-to-right shunt is present, prompt reoperation is probably indicated. Intraoperative echocardiography at the original operation, if done, will usually have indicated residual shunting, as confirmed by postoperative echocardiography, which may be done transesophageally for greatest resolution and quality of images.

It is prudent to place temporary pacing wires on the RV after VSD repair. Complete AV dissociation is often present for a short time intraoperatively. Even if this resolves promptly to normal sinus rhythm, it is advisable to leave pacing wires in place and have an external pacemaker available while the patient is hospitalized, because AV dissociation may occur temporarily.

**RESULTS**

**Early (Hospital) Death**

Hospital mortality is low for repair of single large VSDs, most of which are now repaired in early infancy. In the current era in experienced centers, hospital mortality for isolated VSD closure is 1% or less.30 Risk is higher when VSDs are multiple and when major associated cardiac anomalies coexist.

**Mode of Early Death**

The most common mode of death after repair of a primary VSD is acute cardiac failure.36 This may be related to failure of intraoperative myocardial protection in the face of myocardial dysfunction, often present in sick small patients coming to operation. Occasionally, paroxysms of pulmonary arterial hypertension (see “Pulmonary Hypertensive Crises” under Pulmonary Subsystem in Section I of Chapter 5) precipitate acute cardiac failure.321 Persisting severe pulmonary dysfunction, often from viral pneumonitis present before operation, characterizes death of a few infants after repair of VSD.

**Incremental Risk Factors for Hospital Death**

Studies of experiences extending back a number of years permit identification of incremental risk factors. With death after repair now less common, risk factors are now more difficult to identify.

Risk of repair has decreased, and thus early date of operation is an incremental risk factor.320,322,328 Improvement from an original risk of hospital death of 20% began in the experience at the Mayo Clinic during the early 1960s. This type of improvement has been demonstrated in other centers.1,18,37

In previous eras, **young age** increased the risk of operation.87,14 However, in the current era at experienced centers, this risk factor has been neutralized.15,35 Young age may still be an incremental risk factor when major associated anomalies coexist.

**Multiple VSDs** increased risk of operation in the past,1,17,12 but risk has declined considerably in the current era. However, multiple VSDs complicated by additional cardiac anomalies impose a higher risk of hospital death than uncomplicated ones.87 This again may not be an immutable risk and may be improved by better myocardial management, avoidance of ventricular incisions, and device closure.37
Changes in weight after repair of ventricular septal defect in 96 patients aged 10 years or less, with ratio of pulmonary and systemic pressures greater than 0.45 and ratio of pulmonary and systemic resistances less than 0.75 preoperatively. (From Cartmill and colleagues.)

**Survival**

Premature late death occurs in less than 2.5% of patients when Rp is low preoperatively. Presumably, the few deaths in this setting are from arrhythmias, either ventricular fibrillation or sudden development of heart block late postoperatively. Patients with a high Rp preoperatively often die from progression of pulmonary vascular disease.

Repair of VSD during the first 1 or 2 years of life is curative for most patients, resulting in full functional activity and normal or near-normal life expectancy.

**Physical Development**

A prominent feature of the late postoperative course after repair of large VSDs in infants is improved physical development, and an impressive increase in weight may also be seen, as Lillehei and colleagues first showed in 1955. There is a less impressive increase in length and head circumference. This improved physical development is usually associated with complete relief of symptoms. Postoperative weight increase also occurs in children in whom a large VSD is repaired later in the first decade of life (Fig. 35-27).

These generalizations were refined by Weintraub and Menahem in a definitive study. They confirmed that repair of a large VSD in the first 6 months of life results in near-normal long-term growth in most patients, so that by age 5 years, weight, length, and head circumference are normal. Low-birth-weight infants were an exception, and catch-up occurred only in their weight.

**Conduction Disturbances**

Conduction disturbances are frequent after repair of VSDs.

**Right Bundle Branch Block**

Right bundle branch block (RBBB) is present late postoperatively in many patients in whom VSDs are repaired via right ventriculotomy. In one series of infants, prevalence was 80% (CL 72%-86%). Based on their studies, Gelband and colleagues concluded that the cause is the ventriculotomy. However, Weidman and colleagues at Mayo Clinic reported that 44% (CL 35%-54%) of 36 patients undergoing repair of perimembranous VSDs through a right atriotomy developed new RBBB. Rein and colleagues reported RBBB in 34% (CL 26%-43%) of infants undergoing repair via right atriotomy. Thus, in some patients, RBBB must result from damage to the right bundle by sutures along the inferior border of perimembranous VSDs. In any event, RBBB is less prevalent when the right atrial approach is used for VSD repair. Although an adverse effect on late ventricular function has not been established, at least one study has associated RBBB with increased risk of late diastolic dysfunction.
techniques through the right atrium or RV. Others have found persisting abnormalities of LV size and function after repair of large VSDs at an older age, although all patients were asymptomatic. This information suggests that in general, patients with large VSDs should be operated on before they reach 2 years of age, preferably during the first year of life.

Experience with LV function after left ventriculotomy for repairing VSDs in infants has been sobering; in some patients, cardiac output has been low and left atrial pressure high despite absence of a shunt. False aneurysm has occurred after closure of VSD through a left ventriculotomy.

Residual Shunting
Postoperative left-to-right shunts large enough to require reoperation are uncommon when proper techniques are used. In experienced centers, reoperation for residual VSD should be 2% or less. Small but hemodynamically unimportant residual VSDs cannot be entirely ignored; theoretically, the possibility of infective endocarditis at such sites exists. Accurate estimation of their prevalence would require routine postoperative left ventriculography, however, and this has not been done. With near-routine intra- and postoperative assessment of cardiac function, such shunts are usually detected.
reparations by echocardiography, detection of even small residual defects late after operation is uncommon. Among early residual defects of less than 2 mm detected by echocardiography, greater than 80% are undetectable at 1 year.

Pulmonary Hyperinflation Syndrome

When pulmonary hyperinflation syndrome is present in infants before VSD repair, it usually resolves within 1 to 2 months after repair.

Surgically Produced Aortic or Tricuspid Regurgitation

As complications of repair of primary VSD, surgically produced aortic and tricuspid regurgitation are rare.

Rarity of surgically induced tricuspid regurgitation is surprising considering how often abnormal chordae are attached around the defect. Aortic valve regurgitation occurring after patch closure of doubly committed subarterial VSD may be a special problem. Tomita and colleagues reported that aortic valve regurgitation was detected by echocardiography in 6 of 23 patients (26%; CI:16%-39%) having neither aortic valve prolapse nor regurgitation before operation. Among early repairs by echocardiography, detection of even small residual defects late after operation is uncommon. Among early residual defects of less than 2 mm detected by echocardiography, greater than 80% are undetectable at 1 year.

Pulmonary Hypertension

When severe pulmonary hypertension persists after operation, it may worsen with passage of time and may cause premature late death. About 25% of patients with preoperative pulmonary hypertension and high Rp (at least 10 units · m⁻²) die with pulmonary hypertension within 5 years of operation (Fig. 35-29). However, some patients with pulmonary hypertension and elevated Rp late postoperatively have neither progression nor regression of their disease for as long as 20 years, although they have some limitation in exercise tolerance.

In general, the younger the child at time of repair, the better are the chances of surviving and having an essentially normal PPA 5 years and more later. The lower the Rp at repair, the better the chances of having normal pressure late postoperatively (Fig. 35-31). These two factors, age and preoperative Rp, interact in determining late postoperative PPA.

A more specific correlate of survival and good outcome in patients with important preoperative pulmonary hypertension is preoperative response to infusion of a pulmonary vascular dilator such as isoproterenol. Generally, outcome is good in patients of all ages when preoperative Rp is only mildly or moderately elevated (<8 units · m⁻²; see Table 35-3). Outcome is good in patients with severely elevated Rp only
when it drops below 7.0 units · m$^{-2}$ with preoperative infusion of isoproterenol. Sodium nitroprusside infusion or nitric oxide may also be used and has the advantage of not producing tachycardia.

**Surgical Cure**

Combining data on PPA late postoperatively with the proportion of patients dying early and late postoperatively, chances of “surgical cure” (defined as surviving the early postoperative period and being alive late postoperatively with essentially normal PPA) can be estimated for an individual patient (Fig. 35-32). If repair of a large VSD is performed in a patient at 6 months of age, there is at least a 95% chance of surgical cure, unless preoperative Rp is greater than about 8 units · m$^{-2}$ and does not fall to less than 7 units · m$^{-2}$ with infusion of isoproterenol (which is rare at that age). This is supported by studies by Rabinovitch and colleagues, in which it was also found that surgical cure is likely to result in any infant in whom the VSD is repaired before age 6 to 9 months, irrespective of degree of pulmonary vascular disease. In a 2-year-old patient, chances of cure are this good only if preoperative Rp is less than about 5 units · m$^{-2}$. In a patient operated on for repair of large VSD at age 4 years, chances are that good only if Rp is normal preoperatively (which is unusual). This unfavorable effect of older age has been confirmed by John and colleagues. This finding supports the practice of repair of large defects at least by age 12 months and can be used to predict results of operation in individual patients.

**INDICATIONS FOR OPERATION**

In earlier eras, great emphasis was placed on details of calculated Rp and $Q_p/Q_s$ in determining appropriate timing of surgical intervention or whether continued observation was advisable. In the current era in which hospital mortality after surgical closure of isolated VSD approaches 1% or less, and the majority of infants and children undergo transthoracic echocardiography (without cardiac catheterization) as the definitive diagnostic study, the decision-making process has evolved away from these hemodynamic measurements.

Decisions regarding operation vary somewhat among experienced institutions, but generally relate to size of the defect as assessed echocardiographically (see “Two-Dimensional Echocardiography” under Clinical Features and Diagnostic Criteria), morphologic characteristics related to likelihood of spontaneous closure (see Fig. 35-32), estimated Rp, and presence or absence of Down syndrome.

Infants with an isolated large VSD are rarely truly asymptomatic in the absence of elevated Rp, which results in lower $Q_p$. In addition to overt signs of heart failure or failure to thrive, the experienced pediatric cardiologist will note subtle signs of failure such as enlarged tachypnea or decrease in the slope of the growth curve even with adequate feeding. Left atrial enlargement detected echocardiographically supports the presence of LV volume overload secondary to increased $Q_p$. In the presence of a large defect and absence of such symptoms or signs, specific echocardiographic interrogation for signs of elevated Rp or associated obstructive lesions in the RV outflow tract is warranted. In infants with a large VSD and major symptoms of heart failure or failure to thrive, operation is advisable irrespective of age. In the presence of mild symptoms, elective repair of isolated large VSD is advisable during the first 6 months of life or at the time of diagnosis if older. Infants with Down syndrome and large VSD are likely at increased risk for developing pulmonary vascular disease; therefore, operation should be undertaken within the first few months of life.

Infants with a moderate or large perimembranous VSD associated with aneurysm of the membranous system or a VSD partially covered by accessory tricuspid valve tissue have increased likelihood of spontaneous closure, and operation can be deferred for 6 to 12 months in the absence of symptoms, with planned reevaluation for signs of decreasing size. A VSD of moderate size still carries an ongoing risk of pulmonary vascular disease, and surgical closure is recommended by 12 months of age (or at the time of diagnosis if older) unless there are signs of decreasing defect size. Appearance of decreasing flow velocity in the absence of decreasing size suggests increasing Rp, although such findings may appear transiently in the face of bronchiolitis or other self-limited reasons for increased Rp. If increasing Rp is identified, prompt surgical closure is advisable.

Exceptions to this general practice are made for rare infants with Swiss cheese septum, who present a special problem because of higher risk of surgery. In this setting during the first 3 months of life, pulmonary trunk banding may be indicated; when there are no complications from the band, repair of the Swiss cheese septum and debanding are postponed until age 2 to 4 years. This general plan is also followed when Swiss cheese septum coexists with coarctation of the aorta. Other exceptions to primary repair during the first 3 months of life include infants with straddling tricuspid valve.

In patients with evidence of important elevation of Rp by echocardiography, cardiac catheterization is advisable. When Rp is truly and precisely measured at preoperative cardiac catheterization and is only mildly or moderately elevated (<8 units · m$^{-2}$), operation can be undertaken with near certainty that the early and late outcome will be good (Fig. 35-33). Such patients usually have a large $Q_p/Q_s$. 

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**Figure 35-32** Probability of overall surgical cure (survival at least 5 years postoperatively with a mean pulmonary artery pressure of <25 mm Hg) according to age (months) at repair for all patients with single large ventricular septal defects (VSD). Dashed lines enclose 70% confidence limits. Analysis is based on data of DuShane and Kirklin. Natural history is also shown, with vertical axis the probability of long-term survival and ultimate spontaneous closure of the defect and horizontal axis the age at observation of a patient with a large VSD. (From Blackstone EH, Kirklin JW: Unpublished study, 1982.)
In older patients, operation is generally advisable with a $Q_p/Q_s$ above 1.5 in the absence of additional major operative risk factors. However, in patients with a large VSD, a $Q_p/Q_s$ of 1.5 to 1.8 at rest that becomes 1.0 or less during moderate exercise (from systemic peripheral vasodilatation, increased $Q_s$, and a fixed and high $R_p$ preventing increased $Q_p$) is an indication of probable inoperability. An important fall in $S_aO_2$ during exercise (from right-to-left shunting across the VSD for the reasons described) also suggests inoperability, but a more complete investigation with determination of response to nitric oxide is required for a final decision. Response of $R_p$ to inhalation of mixtures high in oxygen alone is not useful in determining operability in borderline situations.

Children with small VSDs can be safely observed unless other cardiac anomalies (e.g., aortic regurgitation from aortic cusp prolapse, subaortic stenosis, subpulmonary stenosis) are observed. Periodic reevaluation is advisable to verify that observed clinical and echocardiographic findings are compatible with safe continued observation.

Doubly committed subarterial and juxta-aortic VSDs constitute a special situation. Even though apparently small, they should not be left untreated if there is any aortic cusp deformity on 2D echocardiography or cineangiography; development of aortic regurgitation must be prevented (see Section II). These defects should be repaired promptly if an aortic diastolic murmur develops.

### SPECIAL SITUATIONS AND CONTROVERSIES

#### Ventricular Septal Defect and Patent Ductus Arteriosus

Combination of large VSD and moderate-sized or large PDA is particularly likely to cause severe symptoms and require operation early in infancy. During the first 6 to 8 weeks of life in patients with a very large ductus and only a moderate-sized or small VSD, the PDA alone may be repaired because the VSD may narrow or close spontaneously. If this does not occur, the VSD is closed at an appropriate time. When the VSD is large, both it and the PDA are closed simultaneously if operation is required in early life. Risk of operation should not be higher than that for isolated VSD.

#### Ventricular Septal Defect and Coarctation of Aorta

Combination of VSD and aortic coarctation frequently causes severe symptoms in infancy. Both coarctation and VSD are variable in severity. Clearly, the worst combination is a large VSD and severe coarctation, but even a small VSD in association with important coarctation may produce heart failure early in life.

Management options for this combination of defects include simultaneous repair of both lesions, sequential single-stage repair through separate incisions, initial repair of the coarctation alone, initial coarctation repair and pulmonary trunk banding, or initial VSD closure alone. With a large VSD and severe coarctation, repairing the VSD first has certain theoretic advantages but has been practiced.
rarely under such circumstances. Repair of the coarctation only as the initial operation has the advantage of reducing afterload on the LV and, theoretically at least, reducing shunt through the defect. It also avoids a second operation if the VSD closes spontaneously. Mortality with repair of aortic coarctation in this setting has been high in the past, but more recent experience has been good. The results have also been good with initial coarctation repair with pulmonary trunk banding.

Simultaneous repair of both the coarctation and a large VSD in early infancy in the current era in experienced institutions carries a low risk, with hospital mortality of about 5%. The operation is generally performed via a median sternotomy and combined regional perfusion and circulatory arrest. Alternatively, the operation can be performed as a single stage with repair of coarctation through a left thoracotomy followed by repair of a VSD via median sternotomy using standard CPB. Kanter and colleagues have reported excellent survival with this method. In the current era, the following practice can be recommended:

1. When the VSD is large, the coarctation is severe, and the infant presents with severe heart failure, a single-stage repair of coarctation and VSD is advisable, using one of the techniques described previously. When multiple VSDs or Swiss cheese septum is present, the pulmonary trunk is banded, and debanding and repair are delayed if possible until the patient is about age 3 years.
2. When the coarctation is severe and VSD small or moderate-sized, only the coarctation is repaired, and subsequent repair of the VSD is performed according to standard indications.
3. When the coarctation is moderately severe and VSD large, the VSD may be repaired initially and the coarctation repaired either at the same operation or as a second procedure within a few months. Techniques of CPB are standard, with perfusion of the lower body satisfactory in this situation.

**Pulmonary Trunk Banding**

Civin and Edwards noted good prognosis and freedom from pulmonary vascular disease in patients with single ventricle and moderate pulmonary stenosis. Based on that observation, Muller and Dammann performed pulmonary trunk banding in 1952. For many years thereafter, this procedure was used by many for infants who required operation for large VSD, thereby allowing deferral of the intracardiac repair until an older age.

For several reasons, banding is seldom indicated for primary isolated large VSDs. Hospital mortality of patients with pulmonary trunk banding has been substantial, and a second operation, which carries additional mortality, is always required. Early mortality is independent of type of VSD. It is difficult to adjust the tightness of the band perfectly, and reentry a few days later may be needed to modify the tightness. Furthermore, good palliation is not always achieved by banding, and there may be important intermediate mortality before second-stage repair. Complications result from banding in some patients, including development of infundibular and valvar pulmonary stenosis, subaortic stenosis, and migration of the band to the pulmonary trunk bifurcation (Fig. 35-35). Although hospital mortality from pulmonary trunk debanding and VSD repair is low, combined mortality of the banding procedure and subsequent debanding and VSD closure is at least as high as primary VSD repair. Furthermore, restenosis of the pulmonary trunk may follow debanding and VSD repair, necessitating a third operation.

Pulmonary trunk banding as an initial palliative procedure in very young or very small patients with refractory heart failure may still be appropriate in some centers. For a number of years, however, there have been only two standard indications for pulmonary trunk banding in infants with primary VSD: (1) severe heart failure from Swiss cheese septum and (2) associated severe coarctation of the aorta and severe heart failure during the first few months of life. The second is no longer an indication for banding.
Right Atrial versus Right Ventricular Approach for Perimembranous Ventricular Septal Defect

The RV approach may be used for repair of perimembranous VSDs and results in low hospital mortality even in patients with high Rp. The RV approach has the advantage that the nadir of the noncoronary cusp of the aortic valve, which is the area of the right trigone and bundle of His, can be accurately visualized, which may be helpful in choosing the suture technique that will minimize prevalence of heart block (see Fig. 35-25). The RV approach has the disadvantages of (1) leaving a scar in the RV, (2) being associated with a higher prevalence of complete RBBB than with an atrial approach, and (3) possibly resulting in more ventricular arrhythmias late postoperatively.

The right atrial approach may be used almost exclusively, a practice begun in about 1960 at the Mayo Clinic. An accurate repair can be obtained through a right atrial approach in nearly all cases. Associated infundibular pulmonary stenosis can be excised. An RV scar is avoided, and occurrence of RBBB is lower than with the transventricular approach. With the right atrial approach, however, techniques must be accurate to avoid damaging the tricuspid valve leaflets or chordae.

Closure of Ventricular Septal Defect Through Less Invasive Approaches

Smaller incisions (less invasive approaches) have been used for closure of VSDs. Although it is technically feasible to close a VSD successfully through a variety of these techniques, no advantages have been demonstrated other than the smaller incision.

Percutaneous Closure of Ventricular Septal Defects

In selected cases, especially in patients with complex cardiac anomalies (e.g., multiple muscular VSDs) and those with overlooked VSDs after surgical repair of a large defect, transcatheter closure of the VSD by a percutaneously placed double umbrella can be considered. This may be particularly advantageous in apical muscular defects. This method in general should be considered only when surgery is contraindicated or has unusually high risks and when suitable skill and equipment are available.

A current perception is that primary multiple muscular VSDs, particularly those near the apex, are more suitable closed by a percutaneous catheter technique than by operation. This remains unproven, however, particularly for multiple muscular VSDs that can be closed from the right atrium after taking down the trabecula septomarginalis. The technique is a promising one, but additional experience and information are required for definitive evaluation.

These devices may also be deployed intraoperatively.

Closure of Ventricular Septal Defect When Pulmonary Resistance Is High

Patients with VSD in which pulmonary hypertension is severe, with PPA at or above systemic blood pressure, have traditionally been thought to be inoperable because of the high risk of operation. Zhou and colleagues reported use of unidirectional valve patch closure of cardiac septal defects with severe pulmonary hypertension. There was a VSD in 22 of 24 patients in the series, all with marked elevation of PPA (80 ± 12 mm Hg) and increased Qp/Qs (1.1 ± 0.11). SaO₂ was reduced to 88% ± 4%. The patch consisted of polyester fabric with a 0.5- to 1.0-cm hole covered by a pericardial patch left open at one side to function as a one-way valve, placed on the systemic side of the defect. Two patients died after operation (8.3%). PPA fell to 56 ± 19 mm Hg and Qp/Qs to 0.7 ± 0.1, while SaO₂ rose to 96% ± 1%. Excellent improvement of functional state was noted. These results were corroborated by Ad and colleagues while claiming earlier right of discovery of this method (see Fig. 30-26 in Chapter 30).

Section II Ventricular Septal Defect and Aortic Regurgitation

DEFINITION

Ventricular septal defect and aortic regurgitation (VSD-AR) syndrome includes hearts in which AR is of congenital origin, although rarely present at birth, and caused by cusp prolapse or a bicuspid aortic valve. The VSD is doubly committed subarterial, perimembranous (with outlet extension or simply juxta-aortic), or rare, outlet muscular. These locations are in fact a continuum, with the subarterial VSD lying farthest to the patient’s left (and anteriorly), the perimembranous VSD with outlet extension lying more rightward (and slightly inferior) than the subarterial, and the perimembranous juxta-aortic VSD lying still more rightward (and inferiorly). VSD-AR syndrome is related to congenital sinus of Val-salva aneurysm (see Chapter 36) and tetralogy of Fallot with AR (see Chapter 38).

HISTORICAL NOTE

Initial description of VSD-AR syndrome due to aortic cusp prolapse is attributed to Lauby and Pezzl’s publication in 1921. First reports of operative correction were those of Garamella and Starr and their colleagues in 1960. On review of this experience in 1965, of the 30 patients in whom the aortic valve cusps were reconstructed and repaired, 10 (33%; CL 24%-44%) still had important AR. This and other reports in which results of cusp reconstruction were equally unsatisfactory led to adoption of aortic valve replacement using either an allograft or prosthetic valve. During this period, operations were delayed beyond childhood whenever possible to avoid valve replacement at a young age. Renewed interest in use of cusp reconstruction dates from publications of Spencer and Trusler and their colleagues in 1973, which followed the work of Frater. Tatsuno and colleagues in Japan have done much to elucidate the nature of the anomaly and document the good results obtained by VSD closure alone when AR is mild.
MORPHOLOGY AND MORPHOGENESIS

Perimembranous VSDs are most prevalent among predominantly white patients with VSD and AR. Among Asians with VSD and AR, VSDs are more prevalent in the RV outlet, particularly doubly committed subarterial VSDs. Rarely, the defect may be a muscular outlet (also called “intracristal”) defect in which the superior rim is formed by the remnant of a deficient subpulmonary infundibulum. The posteroinferior margin of the defect is formed by fusion of the posteroinferior rim of the trabecula septomarginalis with the ventriculoinfundibular fold. AR is most often caused by prolapse of the right cusp of the aortic valve (about two thirds of patients); the remaining third have prolapse of the noncoronary cusp or of both noncoronary and right coronary cusps, with about equal prevalence. The common feature of all these defects associated with AR is that the affected cusp or cusps lack the normal muscular support provided by attachment of the sinus of Valsalva to the muscular ventricular septum. Infrequently, no cusp is prolapsing, but the aortic valve is bicuspid and regurgitant.

Variable degrees of RV outflow obstruction are present in many patients. The infundibular septum may be underdeveloped and displaced anteriorly and leftward (malaligned as in tetralogy of Fallot), a feature responsible for mild infundibular stenosis that may be present. Occasionally, RV trabeculae near the junction of the infundibular septum and free wall may contribute to infundibular stenosis, as may hypertrophy of the moderator band at a lower level. Typical low-lying infundibular pulmonary stenosis (double-chambered RV) accounts for the gradient in some patients.

The aortic root and valve exhibit a variety of anomalies. Cusps may prolapse not only into but at times through the VSD. Prolusion through the VSD increases during diastole and effectively plugs the defect, limiting the shunt even when the defect is large. Extensive cusp prolapse through a large VSD can also produce some obstruction to RV outflow. In advanced cases, the center of the prolapsed free margin of the cusp is thickened and retracted, a feature that makes resuspension of the leaflet less effective. Some patients have additional damage produced by endocarditis.

The sinus of Valsalva adjacent to the prolapsed leaflet is enlarged, often considerably. This enlarged sinus is associated with asymmetric splaying and dilatation of the aortic “anulus,” a feature aggravated by severe AR and volume changes in the LV. It is virtually impossible to distinguish the junction between the prolapsed cusp and dilated sinus at cineangiography and at times at operation. The wall of the enlarged sinus may be thinned and aneurysmal adjacent to the cusp hinge line and rarely may protrude into the RV immediately above the prolapsed cusp. Such a finding indicates the close similarity between this condition and that of ruptured congenital sinus of Valsalva aneurysm with VSD.

Mechanism of Aortic Regurgitation

The mechanism for cusp prolapse remains speculative; multiple theories have been proposed. Prolapse may result in part from lack of support of the aortic sinus of Valsalva and “anulus” by the infundibular septum, although because most large perimembranous defects are closely adjacent to the aortic “anulus” and very few have associated regurgitation, this cannot be the entire explanation. A structural defect in the base of the sinus itself may also play a role, particularly when the VSD is small. Loss of continuity of the aortic media from the aortic “anulus” and the ventricular septum has also been proposed. Hemodynamic influences during both systole and diastole aggravate the tendencies toward AR. Such influences are more marked once AR develops, resulting in progressive prolapse and distortion.

The most widely accepted predominant mechanism of cusp prolapse is the Venturi effect, which describes changes in velocity and pressure that occur when fluid passes through conduits of varying diameter. As conduit caliber decreases, fluid velocity increases and pressure decreases. If there is restriction to flow through a VSD and an aortic valve cusp is adjacent to the defect, it is vulnerable to being drawn into the high-velocity, low-pressure jet as blood shunts left to right through the restrictive VSD (Fig. 35-36). This tends to displace the unsupported “anulus” outward and downward into the RV. Later in systole, the aortic cusp prolapses into the VSD and is acted upon by direct pressure from the cavity of the LV, displacing both “anulus” and cusp into the RV. During diastole, the high pressure in the aortic root distends the dilated sinus, with further displacement of the aortic “anulus” toward the RV. As the sinus dilates, the distending force becomes greater from increase in wall tension.

Observations supporting the Venturi effect as the predominant cause of aortic cusp prolapse and subsequent AR include:

- The Venturi effect requires a restrictive VSD. Previous studies in the era of near-routine cardiac catheterization indicate that with occasional exceptions, most
such defects are restrictive, and PTA is usually near normal. In a study from Taiwan, Chiu and colleagues found that among patients who developed aortic valve prolapse, mean $Qp/Qs$ for perimembranous VSDs was 1.7; for subarterial defects, 1.6; and for muscular outlet VSDs, 1.45. 

- There appears to be a minimum shunt size required to induce sufficient cusp distortion for development of prolapse. The lower limit of $Qp/Qs$ among patients with VSD and aortic valve prolapse or AR appears to be about 1.4. 

- AR in association with VSD is an acquired lesion. AR or prolapse with VSD is not present at birth and is rarely diagnosed in infancy.

- The nadir of the affected leaflet would be expected to lie within the stream of the shunt. This is consistent with observations that overriding of the involved cusp is commonly noted, and override of the aortic cusp in perimembranous VSDs has been identified as a risk factor for developing cusp prolapse and subsequent AR. 

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Potential for development of AR can be assessed by noting the possible presence of aortic cusp prolapse at echocardiography or cineangiography. Studies in such patients should include 2D echocardiography with Doppler flow velocity evaluation. Anatomic relationships of the aortic valve and VSD should be easily demonstrated. AR is estimated qualitatively. Aortic root dimensions are measured accurately. Usually, echocardiography provides sufficient information on which to base clinical decisions.

In some patients, it is desirable to have cardiac catheterization, which should include (1) right-sided heart catheterization (for calculating shunt and measuring pressures in the pulmonary artery and RV), (2) right ventriculography (for studying possible infundibular pulmonary stenosis), (3) left ventriculography (for identifying location and size of VSD), and (4) aortography (for estimating magnitude of AR and morphology of aortic root). Finding a normal aortic root diameter without cusp prolapse suggests that AR is caused by a bicuspid valve and may not be amenable to repair. Anatomic size of the VSD cannot be demonstrated angiographically when, as often occurs, it is occluded throughout the cardiac cycle by the prolapsed aortic cusp.

In patients with mild AR (e.g., younger patients), signs of the VSD dominate the clinical picture, but as AR increases, the shunt decreases. Such patients characteristically have a to-and-fro murmur that may simulate the continuous murmur of PDA, but occasionally may be mistaken for that of isolated AR or combined AR and stenosis.

NATURAL HISTORY

Among all patients with VSD, the prevalence of aortic valve prolapse and AR is reported to be 4% to 9% and 2% to 6%, respectively. Prevalence is also related to type of VSD. The reported prevalence of aortic cusp prolapse in subarterial VSD exceeds 40%, with over half demonstrating progression of AR. Eroglu and colleagues reported a prevalence of aortic cusp prolapse of 12% and aortic regurgitation of 7% among patients with perimembranous VSD. Aortic cusp prolapse and AR are more frequently reported with VSD among Asian populations because of the greater prevalence of subarterial VSD in China and Japan.

Prevalence is related in part to age at which the population is studied. AR is rarely present at birth but develops during the first decade of life (after age 2 years), then gradually worsens, such that by the end of the second decade it is usually severe. This rate of progression is similar whether the VSD is subarterial or perimembranous. At repair, the AR is mild to moderate in about half of patients and severe in about half.

As regurgitation increases, VSD shunt flow often decreases from occlusion of the VSD by the prolapsed aortic cusp. If the defect remains open through adolescence, about 10% of patients develop aortic valve prolapse or AR.

Secondary effects of AR on the LV are at least as marked as those of rheumatic AR and may be more severe because of additional volume load from the VSD. Rp is seldom if ever elevated, presumably because functionally the VSD is usually not large. Risk of infective endocarditis is high.

Aneurysms of the sinuses of Valsalva also may develop as part of the natural history of patients with doubly committed subarterial VSD or perimembranous VSD with outlet extension. This is a slower process than development of AR, and Momma and colleagues did not observe sinus of Valsalva aneurysms before age 10 years in patients with perimembranous VSDs. Most often the aneurysm is observed during the third decade, when it may be present in 10% of patients whose VSDs of these types are still open.

TECHNIQUE OF OPERATION

In patients in whom AR is trivial or absent, only the VSD is repaired. When AR is moderate or severe and often when it is mild, the aortic valve is repaired. The aortic valve is usually replaced in adults, and this is done only when AR is moderate or severe.

TEE is performed after induction of anesthesia and before incision for a final analysis of the aortic valve and VSD. For myocardial protection, operation is performed on CPB with cold cardioplegia. A transverse aortotomy is made. Dimensions of the aortic root are measured at the ventriculoaortic junction (“anulus”) and sinutubular junction. These dimensions are compared with normal valves adjusted for size of the patient (see “Dimensions of Normal Cardiac and Great Artery Pathways” in Chapter 1). The aortic valve is examined to assess feasibility of repair rather than replacement. If the cusp edge is retracted and thickened or the valve bicuspid, repair is usually not possible.

One or more leaflets may be repaired by the Trusler method of plication. This procedure is carried out at the commissure adjacent to the prolapsed cusp (usually the right or noncoronary cusp). A 5-0 or 6-0 polypropylene suture is placed through the fibrous lacunae at the midpoint of each cusp. Cusps can then be assessed for elongation and attenuation. Cusp plication is performed at the elongated free edges of the aortic valve cusps. A 5-0 or 6-0 PTFE suture is woven between the right and noncoronary cusps to adjust the excessive length of the prolapsed cusp to the adjacent aortic wall. Repair may be reinforced by pledgets (pericardial or felt) or a small cap of polyester secured as a pledget over both affected cusps adjacent to the commissure. Hisatomi and colleagues proposed pledget stitch aortoplasty to make
An entirely different technique has been successfully used by Carpentier, Chauvaud, and colleagues. Its basic feature is triangular excision and reconstruction of the prolapsing cusp. Combined with this is an anuloplasty of the left ventriculoaortic junction. They also recommend that the VSD be repaired through the aortic root, using a glutaraldehyde-treated pericardial patch.

Yacoub and colleagues have proposed another alternative repair (Fig. 35-38) that addresses the basic morphologic defect more completely. All anatomic components of the aortic cusps protrude for even greater aortic cusp coaptation. The stitch at the center of the valve is removed after VSD repair.

Approach to the VSD is appropriate to the location of the defect and may be transaortic if the defect is accessible. Any infundibular stenosis is relieved by excising trabecular muscle bands between the infundibular septum and free wall of the RV and, when necessary, by mobilizing and excising parietal and septal extensions of the infundibular septum and portions of the moderator bands.

Figure 35-37 Repair of prolapsed aortic valve cusp by Trusler technique in patients with ventricular septal defect and aortic valve regurgitation. A, Transverse aortotomy is made at a level just downstream from commissural attachments of aortic valve. B, A stitch of 5-0 or 6-0 polypropylene is placed through midpoint of each cusp. Traction on this stitch allows identification of redundant or elongated free edges of a cusp, as shown here in the case of right coronary cusp near its commissure with noncoronary cusp. C, A 5-0 or 6-0 polytetrafluoroethylene suture is used to “reef up” redundant and attenuated portions of aortic valve. Double row of reefing stitches is used to bring ends of suture to outside of aorta at commissures. Pledget is added to strengthen repair.
defect are corrected by a simple transaortic repair. A transverse aortotomy is made (Fig. 35-38, A). Extent of dilatation of the right coronary sinus and exact definition of the thin area of sinus resulting from discontinuity between aortic valve “anulus” and media of aorta are accurately defined. A series of pledget-reinforced mattress sutures are placed through the crest of the ventricular septum slightly on the RV side to avoid injuring the conduction system. Sutures are passed through the “anulus” of the aortic valve and then used to plicate the thin portion of the sinus of Valsalva and continued until strong aortic tissue supported by aortic media is reached. Tying of sutures results in closing the VSD, elevating the right coronary anulus and cusp, and reducing the size of the right coronary sinus and RV outflow tract bulge (Fig. 35-38, B). Repair of the defect is possible in all cases regardless of VSD size, which is usually slitlike, because there are always redundant tissues in the septum and aortic sinus in the vertical plane. Plication of redundant tissues toward the media of the

Figure 35-38 Repair of aortic valve in syndrome of ventricular septal defect (VSD) and aortic valve regurgitation by Yacoub technique. A, Aortic valve and VSD are approached through a transverse aortotomy. Morphologic defect causing lack of coaptation of aortic cusps is considered to be discontinuity between aortic media and “anulus” of aortic valve, resulting in lack of support to “anulus” and sinus of Valsalva, with downward and outward displacement of “anulus” into right ventricle. VSD is closed by plication suture, which elevates crest of septum to aortic media and plicates unsupported sinus of Valsalva. A series of interrupted mattress stitches using 4-0 braided polyester suture with pericardial pledgets are placed from crest of ventricular septum slightly toward its right ventricular aspect. Stitches are passed through “anulus” of aortic valve and reeved through unsupported sinus of Valsalva to strong tissue of aortic media. B, Stitches are tied down (knots inside aortic sinus), elevating ventricular crest to aortic valve “anulus” to close VSD as well as displacing “anulus” and aortic valve cusp centrally to achieve greater aortic cusp coaptation, restoring valve competence. (Modified from Yacoub and colleagues.)
aortic sinus elevates the aortic valve cusp and anulus, displacing them centrally toward the aortic lumen. This results in increased aortic valve coaptation and restored aortic valve competence. This operation can be applied to patients with doubly committed subarterial VSDs with AR and thus may apply to the Asian population, in whom these types of defects are common.

If the valve requires replacement, the RV (or pulmonary trunk) should be opened before valve insertion, the VSD repaired, the RV closed, and then the aortic valve replaced. This sequence is advised because occasionally it may be necessary to place sutures from the prosthetic valve ring across the upper margin of the VSD patch where it extends between the base of the right and noncoronary cusps (in the region normally occupied by the membranous septum). Sutures in this area should be securely buttressed with pledgets. Although a freehand allograft has been used successfully for valve replacement under such circumstances, degree of distortion of the aortic sinuses often makes accurate placement difficult. Allograft aortic root replacement or aortic valve replacement with a pulmonary autograft (Ross procedure) is probably a better choice (see “Autograft Pulmonary Valve” under Technique of Operation in Chapter 12).

When there is also a true thin-walled aneurysm of the sinus of Valsalva at the base of the right aortic cusp and a VSD, repair is more difficult because the sinus must also be repaired. If the aortic valve requires excision and replacement, excision should include the base of the cusp and the thinned area of the sinus wall, which becomes continuous with the VSD and is incorporated into its closure. Again, under such circumstances, the prosthetic valve suture line will cross the polyester patch. Aortic root replacement may be a simpler solution. When the valve is suitable for plication, the base of the cusp is preserved and sutured back to the patch.

**RESULTS**

**Survival**

Only 1 of 76 patients operated on by the UAB and GLH groups died in hospital (1.3%; CL 0.2%-4.4%); at last follow-up, no late deaths had occurred, an experience similar to that of Okita and colleagues over an 18-year follow-up and Yacoub and colleagues over 24 years with a mean follow-up of 8.4 years. Thus, in the current era, risk of operation should approach 1%.

**Heart Block**

Heart block rarely occurs, even though operation is in the region of the conduction system. In Yacoub and colleagues’ series of 38 patients, there were no cases of conduction abnormality, and ECG remained normal.

**Relief of Aortic Regurgitation**

When AR is mild, VSD closure alone usually prevents progression of regurgitation. When AR is moderate before repair, about two thirds of patients have no or trivial AR after repair using the Trusler technique. Satisfactory late outcomes have also been reported with techniques described by Carpenterie and Yacoub. Infrequently, AR is severe preoperatively, and chances of a good result decrease in this setting.

Okita and colleagues have determined perimembranous VSD (rather than VSDs in the RV outlet) to be a risk factor for important residual AR, possibly because factors other than cusp prolapse are partly responsible for preoperative AR when the VSD is perimembranous. Bicuspid aortic valves are less satisfactorily repaired than tricuspid ones.

Older age at operation also contributes to presence of important AR after repair.

**Freedom from Aortic Valve Replacement**

Some patients will probably require aortic valve replacement in later life, although freedom from aortic valve reoperation using the Trusler technique was 89% at 8 years in the UAB group’s series; parametrically predicted freedom at 20 years was 81% (Fig. 35-39). Elgamal and colleagues confirmed these data, reporting 15-year freedom from reoperation of 81% ± 19% after Trusler repair of the aortic valve. Adequacy of repair at operation was the most important determinant of long-term results. Yacoub and colleagues reported 5 valve replacements among 38 patients 8 to 11 years after operation.

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**Table 35-4** Grade of Aortic Regurgitation (AR) Late after Repair of Ventricular Septal Defect and AR, According to Preoperative AR Grade

<table>
<thead>
<tr>
<th>Preoperative AR Grade</th>
<th>None</th>
<th>Mild</th>
<th>Mild to Moderate</th>
<th>Moderate</th>
<th>Moderate to Severe</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Mild</td>
<td>10</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>6</td>
<td>60</td>
</tr>
<tr>
<td>Mild to moderate</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>25</td>
</tr>
<tr>
<td>Moderate</td>
<td>12</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>Moderate to severe</td>
<td>9</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>Severe</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>36</td>
<td>9</td>
<td>25</td>
<td>10</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>

Data from Maehera and colleagues. Data from 36 patients operated on from 1967 to 1987. Three patients who had aortic valve replacement at the original operation after failure of Trusler repair and two other patients who had missing values for postoperative aortic regurgitation are not included. These two patients received late postoperative aortic valve replacement.

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and parametric estimation of freedom from aortic valve reoperation (one second repair, two valve replacements) after repair of ventricular septal defect and aortic regurgitation in 38 patients. (From Maehara and colleagues.)

INDICATIONS FOR OPERATION

When the murmur of AR first develops in a child with a VSD, the VSD should be promptly repaired while the AR is still mild. If cusp prolapse without AR is demonstrated by 2D echocardiography or on the aortogram in association with any perimembranous VSD, early repair is also indicated. Even if cusp prolapse has not occurred, doubly committed subarterial and moderate or large perimembranous VSDs with outlet extension should be closed before the patient is about 3 years of age to prevent cusp prolapse. Patients having doubly committed subarterial VSD should have prompt operation regardless of age if any aortic valve deformity or regurgitation is detected; anatomic and hemodynamic features of the VSD contribute greatly to development of aortic valve cusp deformity and subsequent AR. When AR is moderate or severe and cusp prolapse is noted on the 2D echocardiogram or aortogram, operation should be undertaken promptly. Operation certainly should be done before the patient reaches age 10, because reconstruction of the valve is usually possible when operation is done during the first decade of life; thus, valve replacement is prevented or at least postponed. This fact is confirmed by the UAB experience, in which the average age of patients requiring replacement was 20 years, compared with 12 years for the remainder of the group.

When 2D echocardiography shows bicuspid aortic valve, or when the aortogram shows minimal enlargement of the sinuses and no cusp prolapse in the presence of severe AR, a bicuspid valve is probably present and valve replacement may be required. Operation should therefore be postponed until symptoms develop or LV enlargement indicates need for operation.

When operation is delayed until adult life, aortic valve replacement is usually required.

SPECIAL SITUATIONS AND CONTROVERSIES

Some surgeons prefer to visualize and repair VSDs through an aortotomy. This practice can produce good results, but if the VSD is perimembranous rather than in the RV outflow tract, possibility of permanent damage to the bundle of His may be increased by this essentially LV approach to repair. Repair through the pulmonary trunk or RV is recommended for subarterial and anterior muscular defects, and through the right atrium or RV for perimembranous defects.

Section III Straddling and Overriding Tricuspid (or Mitral) Valve

A straddling and overriding tricuspid valve sometimes coexists with an otherwise isolated VSD, usually one that extends posteriorly to the crux. Straddling and overriding of an AV valve may also coexist with a VSD that is simply part of a congenital cardiac anomaly (e.g., transposition of the great arteries, congenitally corrected transposition of the great arteries, univentricular AV connection). The subject is considered in its entirety in this chapter, with reference to other chapters.

Straddling and overriding of an AV valve always occur in relation to a VSD close to the valve. When straddling or overriding of an AV valve is mild, surgical considerations are usually related primarily to associated anomalies. When straddling or overriding is severe, or when there is associated hypoplasia of the ventricle to which the AV valve is appropriately (see following text) connected, surgical considerations are usually based primarily on straddling and overriding and severity of any coexisting ventricular hypoplasia.

Hypoplasia of the ventricle guarded by the straddling or overriding valve (termed the appropriate ventricle) usually coexists. Generally, the more severe the overriding, the greater the ventricular hypoplasia. Occasionally, a straddling or overriding AV valve has leaflets that differ from normal in number and morphology. Overriding and straddling AV valves may occasionally produce subpulmonary or subaortic obstruction.

DEFINITION

An AV valve is considered to be straddling when part of the tension apparatus of the valve crosses the VSD and the crest of the interventricular septum to attach to the septum or a papillary muscle in the opposite (inappropriate) ventricle. The tension apparatus is thus attached within both ventricles, and blood passing through the valve is directed into both ventricles. An AV valve is considered to be overriding when the AV junction to which the AV valve leaflets attach is connected to both ventricles. AV valve straddling and overriding usually occur in combination, and occasionally both AV valves are involved with these anomalies in the same heart.

HISTORICAL NOTE

Lambert in 1951 and Van Praagh and colleagues in 1964 appeared to be aware of AV valve straddling and overriding, although they were not explicit about it. In 1966, Mehrizi and colleagues referred to overriding and straddling of the right AV valve onto the RV in hearts with double inlet left
ventricle (DILV) and the LV lying posteriorly and to the left.\textsuperscript{518} Subsequently, de la Cruz and Miller in 1968 and Lev and colleagues in 1969 referred to this occurrence in hearts with various types of “single ventricle” (generally double inlet ventricles).\textsuperscript{3,11}

Rastelli and colleagues reported “straddling right atrioventricular valves” in hearts with a large VSD, but the right AV valve in their cases appears to have been both overriding and straddling.\textsuperscript{83} These investigators identified malalignment of atrial and ventricular septa as the characteristic of hearts with overriding AV valves, along with cleft leaflets often present and juxta-crucial position of the VSD. Libeithson, one of whose coauthors was Lev, clearly distinguished between overriding and straddling AV valves in hearts with double inlet ventricles in 1971, although those terms were not used or defined.\textsuperscript{112} Again, in the context of double inlet ventricles, Tandon and colleagues discussed “straddling AV valves.”\textsuperscript{112} Thereafter, ease of diagnosis provided by 2D echocardiography rapidly led to broader recognition and improved understanding of these AV valve abnormalities.\textsuperscript{1,12,28}

Surgical management of straddling and overriding AV valves was first reported in 1979, independently by Pacifico and by Tabry and their colleagues.\textsuperscript{21,21,21} Surgical possibilities, rapidly expanding knowledge of morphology of congenital heart disease, and increased use of 2D echocardiography resulted in clear perception of the morphology and implications of these AV valve anomalies.

Clarifying terminology used in this section was evolved by Milo and Ho and their colleagues in studies of straddling and overriding AV valves.\textsuperscript{117,110} Milo and colleagues described disposition of the conduction system in hearts with overriding AV valves.\textsuperscript{110} and Anderson and colleagues formulated the basis for categorizing these hearts as well as those with univentricular AV connections (“single ventricle”).\textsuperscript{111}

**MORPHOLOGY**

**Morphologic Syndromes**

When atria are in usual (solitus) situs, ventricular topology is right-handed, and AV and ventriculoarterial (VA) connections are concordant (see “Terminology and Classification of Heart Disease” in Chapter 1), the right AV valve sometimes overrides or straddles. This anomaly is associated with a posteriorly placed (juxta-crucial) VSD in the inlet portion of the ventricular septum when viewed from the RV aspect. The interventricular septum does not attach to the crux cordis in this situation. The overriding tricuspid valve is associated with malalignment of the atrial and interventricular septa. The RV is usually somewhat hypoplastic.

When there is atrial situs solitus, ventricular right-handedness (D-loop), AV concordant connection, and discordant VA connection (complete transposition of the great arteries), the left AV valve may be overriding, in this case over a VSD in the anterior portion of the ventricular septum.

When there is atrial situs solitus, ventricular right-handedness, AV concordant connection, and DORV (one of the most common situations in which overriding and straddling of an AV valve occur\textsuperscript{58}), the right AV valve may be overriding and is usually straddling in hearts with a VSD that is juxta-aortic, and usually also perimembranous and juxta-crucial. When the VSD is juxta-pulmonary and somewhat anterior (Taussig-Bing heart), the left AV valve may be straddling and overriding a VSD that does not extend to the crux cordis.\textsuperscript{519}

When there is atrial situs solitus, left-handed ventricular topology (L-loop), AV discordant connection, and VA discordant connection (congenitally corrected transposition of the great arteries), the right AV valve (which generally in this setting has two leaflets) may override an anteriorly situated VSD. The intraventricular septum does reach the crux cordis. When overriding of the right AV valve in this setting is more than 50%, there is double inlet right ventricle (DIRV) with the RV lying to the left and more or less posterior, and an anterior, right-sided, and often hypoplastic and rudimentary (incomplete) LV. In hearts with congenitally corrected transposition of the great arteries, the left-sided AV valve may override a posteriorly placed VSD; in these hearts, the intraventricular septum does not reach the crux cordis. When overriding is more than 50%, the condition is DILV with left-sided and anteriorly placed hypoplastic and rudimentary (incomplete) RV, the most common type of double inlet ventricle. A special group of cases with AV discordant connection, usually with DORV, involves a VSD that is juxta-crucial and in which one or both AV valves are overriding and straddling. Ventricles in this setting are usually in an over-and-under position, and circulations appear to crisscross within the heart.

Similar patterns may occur with atrial situs inversus and with atrial situs ambiguous.

**Conduction System**

Knowledge of location of the AV node and bundle of His is required for satisfactory surgical treatment of cardiac malformations. When the AV valve is overriding or straddling a VSD that does not reach the crux cordis, the conduction system is usually unaffected by the overriding valve.\textsuperscript{112} Thus, the AV node is in its usual location in the AV septum when the ventricular topology is right-handed and the AV connection concordant. When the ventricular topology is left-handed and the AV connection discordant, the conduction system generally arises from an anomalous anterolateral node, and this is unaffected by the overriding valve.

When in hearts with AV concordant connection the AV valve (in this case the tricuspid valve) overrides a VSD that is juxta-crucial (such defects may be perimembranous as well), the AV node is situated anomalously.\textsuperscript{112} It lies at the point inferiorly at which the ventricular septum attatches to the anulus (or circumference) of the right AV valve.\textsuperscript{110}

When the VSD is juxta-crucial and the AV connection discordant, the left AV valve overrides and the AV node occupies an anterolateral position near the right AV valve anulus, as is usual in hearts with AV discordant connection.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Straddling and overriding of an AV valve are uncommon, occurring as an added anomaly in about 3% of patients with congenital heart disease. They seem to be more prevalent in hearts with AV discordant connection than in those with AV concordant connections (Table 35-5). Among hearts with AV discordant connections, straddling and overriding of an AV valve occur most often in hearts with DORV and in those with complete transposition of the great arteries.
Straddling and overriding AV valves are usually competent and have no features that permit their identification by history, physical examination, chest radiograph, or ECG. Echocardiography is the technique by which they are generally diagnosed, although overriding can often be diagnosed or inferred from the angiogram.

### TECHNIQUE OF OPERATION

When an AV valve is only overriding, repair of the associated VSD or other cardiac anomalies can usually be done in essentially the normal manner, except for some deviation of the patch to accommodate the overriding. Straddling presents a more severe surgical challenge, particularly when it is moderate or severe in degree and when the inappropriate ventricle into which the straddling cords enter is not the one the surgeon is working in which. For these reasons, the Fontan operation (see Section IV of Chapter 41) is often the most appropriate option when severe straddling or overriding is present.

#### Cardiac Morphology and Mortality after Operation in Patients with Overriding and Straddling Atrioventricular Valves

<table>
<thead>
<tr>
<th>Cardiac Morphology</th>
<th>n</th>
<th>Hospital Deaths</th>
<th>Total Deaths</th>
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<tbody>
<tr>
<td><strong>AV Concordant Connection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VSD (RAVV)</td>
<td>6</td>
<td>0</td>
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<tr>
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<td><strong>AV Discordant Connection</strong></td>
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<tr>
<td>PS</td>
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<td>2</td>
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<tr>
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<tr>
<td>DORV PS (RAVV)</td>
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<td>0</td>
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<td>5</td>
<td>10</td>
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*Data from 35 patients operated on at UAB from 1967 to 1985. Total deaths include hospital deaths and those in follow-up period.
*Several cords from mitral valve straddled to insert on right ventricular side of septum near ventricular septal defect.
*One patient also had right atrioventricular valve atresia.

Key: AV, Atrioventricular; CTGA, corrected transposition of the great arteries; DORV, double outlet right ventricle; LAVV, left atrioventricular valve; PS, pulmonary stenosis; RAVV, right atrioventricular valve; TF, tetralogy of Fallot; TGA, transposition of the great arteries; VSD, ventricular septal defect.

#### Section of Straddling Cords

Rarely, a single straddling cord can be sectioned to permit repair of a VSD or an intraventricular tunnel repair, without rendering the AV valve regurgitant. This technique can probably be used only when straddling is mild.

#### Slotting of Repair Patch

Rarely, straddling cords can fit into a slot or cut made in the patch used to close the VSD or make an intraventricular tunnel. The slot is then closed by sutures. This technique is applicable only to mild or possibly moderate straddling involving just a few cords, and it probably results in loss of free motion of the cords.

#### Reattachment of Sectioned Tensor Apparatus

When straddling is mild or moderate, and when the straddling tensor apparatus attaches to only one papillary muscle or area of the muscular interventricular septum in the inappropriate ventricle, and when that muscle has no other cord attachments, the muscle may be sectioned at its base. Then, along with its straddling cords, the muscle is brought back into the appropriate ventricle. The VSD is closed with a patch, or if indicated, an intraventricular tunnel repair is performed. Finally, the muscle to which the straddling cords connect is reattached to the patch or tunnel.

This technique is used infrequently and is applicable only when surgery is being performed from within the appropriate ventricle, approached either through its atrium or a ventriculotomy. Probability of dehiscence of a reattached papillary muscle or tendinous cord has not been determined.

#### Minor Septation

The patch used to close a VSD or create an intraventricular tunnel may be deviated around the papillary muscle and septal attachments of a straddling AV valve so that they lie within the appropriate ventricle after repair (Figs. 35-40 and 35-41). This approach is most easily performed when straddling is into the ventricle the surgeon is working in, through its atrium or a ventriculotomy. This is usually the ventricle ejecting into the pulmonary trunk: the right-sided RV in DORV with concordant AV connection, or the right-sided LV in hearts with discordant AV connection. In some cases, however, the technique of minor septation can be applied when straddling is into the ventricle ejecting into the aorta (see Fig. 35-40).

#### Replacement of Straddling Atrioventricular Valve

When the straddling AV valve is regurgitant (a relatively unusual situation), operation usually includes valve replacement. In some cases, this approach may be used simply because of complexity and severity of the straddling. The valve replacement device may face onto the patch used for repair of the VSD or creation of an intraventricular tunnel, because of the malalignment of the atrial and ventricular septa. This possibility emphasizes the value of a low-profile device in this setting, and even with such a device, some functional impairment may result.
Particular care and thoughtfulness are required when straddling or overriding occurs in the setting of ventricular L-loop, when valve replacement appears to be indicated. This situation, along with the sometimes associated complete heart block, may compromise long-term outlook sufficiently that a Fontan operation is preferable to a two-ventricle repair (see Chapter 41).

**Fontan Operation**

The Fontan operation is also the only method that can be used when moderate or severe hypoplasia of a ventricle is associated with straddling and overriding AV valves. Current information concerning early and intermediate-term results of this operation encourages its wider use when AV
Figure 35-41 Intraventricular tunnel repair incorporating a minor septation for straddling and overriding left atrioventricular (AV) tricuspid valve in a patient with congenitally corrected transposition of the great arteries and about 40% overriding of aorta onto right-sided left ventricle. A, Vertical left (right-sided) ventriculotomy is shown, but an approach through right atrium is preferred. Straddling and overriding left AV (tricuspid) valve is shown, as well as ventricular septal defect and aortic overriding. B, Repair patch creates an intraventricular tunnel conducting systemic arterial blood flow from left-sided right ventricle to aorta and keeping entire left AV valve apparatus on appropriate side of patch. (From Pacifico and colleagues.)

valve straddling or overriding is moderate or severe (see Chapter 41).

Cardiac Transplantation
Cardiac transplantation is reserved for patients with straddling and overriding AV valves in whom a severe secondary cardiomyopathy has developed (see Section II in Chapter 21).

RESULTS
Early and intermediate-term (5 to 15 years) survival after surgery in patients with straddling and overriding AV valves is determined primarily by the cardiac defect with which the AV valve anomaly is associated. However, survival is somewhat less satisfactory than that in general after repair of the primary cardiac defect. Exceptions are patients in whom the Fontan operation or cardiac transplantation is performed;
survival after these operations is unrelated to the cardiac anomaly for which the operation was done and is not lessened by presence of a straddling or overriding AV valve.

Heart block has occurred more frequently than usual after repair of hearts with concordant AV connection and overriding AV valves associated with a VSD extending to the crux cordis and in patients with discordant AV connection. Because position of the AV node and conduction system in such hearts is now known, heart block should now occur less frequently.

INDICATIONS FOR OPERATION

*Indications* for operation in patients with overriding and straddling AV valves lie with the coexisting anomalies rather than with the AV valve anomaly.

*Strategy* of operation is greatly influenced by the AV valve anomaly, and whenever possible that strategy should be decided in early life. If straddling is mild, the strategy can probably be that for the coexisting anomaly in general, and the AV valve anomaly can be managed by the technique of minor septation or an even lesser procedure.

When straddling is severe, these techniques seem likely to be associated with a relatively high early risk. Valve replacement in this setting carries more than the usual early and intermediate risks and improbables. A Fontan operation probably is associated with better early and late results than these procedures and is the only type of procedure that can be considered when the patient has important ventricular hypoplasia. Therefore, diagnosis of AV valve straddling or overriding should be made in early infancy. If the patient has cyanosis from reduced pulmonary blood flow, a PTFE interposition systemic-pulmonary arterial shunt or a bidirectional cavopulmonary anastomosis should be performed (see Chapters 38 and 41). If there is a large left-to-right shunt, pulmonary trunk banding should be performed in early life. In either case, the Fontan operation is then performed in patients aged 1 to 2 years, before ventricular hypertrophy becomes marked (see Chapter 41).

REFERENCES

**A**


**B**


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D
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P


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2. Ramaciotti C, Keren A, Silverman NH. Importance of (perimembranous) ventricular septal aneurysm in the natural history of
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36 Congenital Sinus of Valsalva Aneurysm and Aortico–Left Ventricular Tunnel

Section I: Unruptured and Ruptured Sinus of Valsalva Aneurysms

DEFINITION

Congenital sinus of Valsalva aneurysms are thin-walled saccular or tubular outpouchings usually located in the right sinus or adjacent half of the noncoronary sinus. They generally have an intracardiac course but may protrude into the pericardial space. They may rupture into the right (or rarely the left) heart chambers to form an aortocardioc fistula, or into the pericardial cavity. Associated congenital cardiac anomalies are common.

HISTORICAL NOTE

The syndrome of acute rupture of a congenital sinus of Valsalva aneurysm was apparently first described by Hope in 1839. A year later, Thurman published the first important paper on the subject. He discussed Hope’s case and added five of his own, none of which had ruptured. Eighty years later, Abbott reviewed the clinical features of acute rupture from eight previous cases and reported another case. At that time, and even as late as 1937, most ruptured and unruptured sinus of Valsalva aneurysms were considered syphilitic. Smith stated in 1914 that “the lesion, which is usually syphilitic, is not so rare as to be altogether devoid of clinical interest, but the diagnosis, perforating or otherwise, presents almost insurmountable difficulties.” Jones and Langley reviewed congenital and acquired aneurysms in 1949. They accepted 25 cases as being of congenital origin and elucidated most of the important features of the condition. In 1951, Venning may have been the first to diagnose acute rupture during life, although Oram and East claimed this distinction in 1955, as did Brown and colleagues. In Oram and East’s patients, cardiac catheterization confirmed the presence of a left-to-right shunt, although angiography was not performed. The earliest report of using aortography to diagnose an unruptured aneurysm was that of Falholt and Thomsen in 1953. The first successful surgical repairs of sinus of Valsalva aneurysms were performed in 1956 at the Mayo Clinic and the University of Minnesota, using cardiopulmonary bypass (CPB). Spencer, Blake, and Bahnson and Morris and colleagues also reported early successful cases. In 1957, both Morrow and colleagues and Bigelow and Barnes successfully closed a ruptured congenital sinus of Valsalva aneurysm using mild hypothermia with inflow stasis, but this...

Section II: Aortico–Left Ventricular Tunnel

DEFINITION

Congenital sinus of Valsalva and Aortico–Left Ventricular Tunnel
Precise location of this basic congenital abnormality, which may be accompanied by an adjacent separation of the ventricular septum from the aorta to form a VSD, tends to be different in Asians and non-Asians. In Asians, the basic abnormality is located leftward and toward the commissural area between the right and left coronary cusps, so compared with non-Asians, rupture occurs more often into the right ventricle than right atrium (94% vs. 77%, \( P[\chi^2] = .0001 \)). The coexisting VSD in Asian patients is usually leftward and juxta-arterial, whereas in non-Asians it is usually rightward and only juxta-aortic (see Chapter 35 for definitions). The leftward tendency in Asians is also manifested by fewer aneurysms of the more rightward noncoronary sinus than in non-Asians (11% vs. 32%, \( P < .0001 \)). Left sinus of Valsalva aneurysms are uncommon in both Asians (2%) and non-Asians (5%) (\( P[\chi^2] \) for difference = .11).\(^{55}\)

**Aquired** sinus of Valsalva aneurysms caused by syphilis,\(^{54}\) atherosclerosis,\(^{52}\) endocarditis,\(^{51}\) Behçet disease,\(^{54,51}\) or penetrating injuries\(^{55}\) are usually readily distinguishable from congenital forms. They are more diffuse, involving more of the sinus or multiple sinuses and often the ascending aorta, and therefore project into the pericardium outside the heart. A congenital aneurysm is frequently diagnosed by exclusion of other etiologies as well as by presence of associated congenital cardiac defects. Difficulties arise in establishing a diagnosis of mycotic aneurysms,\(^{11,52}\) because endocarditis complicates about 5% to 10% of congenital aneurysms.\(^{51}\) Similarly, difficulty exists in diagnosing the presence of medionecrosis (cystic medial degeneration), because it and Marfan syndrome are both present in some patients with congenital sinus of Valsalva aneurysms.\(^{53,52}\)

**Rupture**

In some patients, the aneurysm gradually develops a localized windsock, which ultimately ruptures into an adjacent low-pressure cardiac chamber (Fig. 36-3). The thin-walled, ruptured aneurysm characteristically has an intracardiac fistulous portion and a nipplelike projection into the cardiac chamber, with one or more points of rupture at its apex (Fig. 36-4). Rarely it projects outside the aortic root or heart. When the aneurysm coexists with a VSD, the windsock usually projects into the right ventricle through a thinned area of myocardium just downstream from the VSD; the aneurysm is separated from the VSD by the hinge line of the aortic valve cusp, at the septal portion of the left ventriculooaortic junction (Fig. 36-5; see also Fig. 36-2, C).

About one fourth of patients have no windsock or other suggestion of aneurysm formation, but rather have a direct fistulous communication between the aortic sinus and the heart.\(^{11,53}\) This defect has been recognized in a few patients at or soon after birth.\(^{54,53,52,53}\) Windsock deformity is typical in lesions originating from the right sinus and communicating with the right ventricle; a direct fistula is typical in those from the noncoronary sinus to the right atrium.\(^{57,53}\) and an extra-cardiac aneurysm is typical \(^{53,52,53,51,516}\) in the rare cases of left sinus origin.\(^{53}\)

Although the prevalence of aneurysms of the sinus of Valsalva in various locations is different among Asians and non-Asians, in both groups the **sinus of origin** is the main determinant of the direction of protrusion and rupture of the aneurysm, and thus of the chamber into which it ruptures (Fig. 36-6). Also in both populations, but with differing
Figure 36-2 Unruptured right sinus of Valsalva aneurysm. **A,** Viewed from the aorta, aneurysm has a well-defined origin, or neck, presenting as an almost circular ostium in the base of the sinus of Valsalva just above the hinge line of the aortic cusp. **B,** Viewed from right ventricle, aneurysm protrudes into right ventricular outflow tract just below pulmonary valve. **C,** Anatomic depiction of a specimen with coexisting juxta-aortic ventricular septal defect (VSD) in right ventricular outlet portion of ventricular septum. The narrow band of aortic wall and septum separating aneurysm from VSD is located behind the aneurysm. Key: **An,** Aneurysm of right aortic sinus of Valsalva; **L,** left aortic valve cusp; **P,** posterior (noncoronary) aortic valve cusp; **PT,** pulmonary trunk; **R,** right aortic valve cusp; **RCA,** right coronary artery; **RV,** right ventricle; **TV,** tricuspid valve; **VSD,** ventricular septal defect. (From Edwards and Burchell.)

Figure 36-3 Cineangiograms in right anterior oblique projection of a right sinus of Valsalva aneurysm ruptured into right ventricle in systole (**A**) and diastole (**B**). Noncoronary and left coronary sinuses and cusps are normal. Right coronary sinus is enlarged, and there is an aneurysm (windsock) protruding into right ventricular infundibulum. Arrows indicate contrast medium shunting through holes in aneurysm and filling right ventricular infundibulum in diastole and pulmonary trunk in systole (when the aneurysm almost prolapses through the pulmonary valve). There is no aortic regurgitation, but the ruptured aneurysm is associated with a large conoventricular juxta-aortic ventricular septal defect. Key: **A,** Aneurysm; **L,** left coronary sinus; **N,** noncoronary sinus; **PT,** pulmonary trunk; **R,** right coronary sinus; **RV,** right ventricular infundibulum.
prevalence, aneurysms of the right aortic sinus of Valsalva are most common.\textsuperscript{5,6,8,13,25,51,63} The aneurysm may arise from the leftward portion of this sinus, with the windsock projecting into the adjacent right ventricular outflow tract just below the pulmonary valve, termed type I by Sakakibara and Konno.\textsuperscript{51} It may also originate more centrally and project through the substance of the outlet portion of the right ventricular aspect of the ventricular septum (Fig. 36-7), or from the rightward portion of the sinus, entering the right ventricle beneath the parietal band (parietal extension of the nutrient aortic sinus).
Figure 36-8  Cineangiogram in right anterior oblique projection (diastole) of a large aneurysmal connection of noncoronary sinus (N) to right atrium (RA). Contrast flow (arrows) was observed to enter RA close to tricuspid anulus (dashed line) before passing through tricuspid valve to right ventricle (RV). Right (R) and left (L) coronary sinuses appear normal. There is no aortic regurgitation and no ventricular septal defect. At operation a 15-mm-long windsock aneurysm was projecting into the right atrium adjacent to anteroseptal commissure of tricuspid valve.

infundibular septum) in the region of the membranous septum. Rarely the aneurysm may project into the pulmonary trunk.510

Aneurysms from the noncoronary sinus usually originate from its anterior portion and project into the right atrium (Fig. 36-8), but in rare cases they project and rupture into the right ventricle. Rarely, rupture can occur simultaneously into the right ventricle and right atrium or into the muscular ventricular septum.511 Aneurysms arising from the posterior portion of the noncoronary sinus may rupture into the pericardium.59,72,108 Another rare occurrence is a right sinus or noncoronary sinus aneurysm that ruptures into the left ventricle.74,91,92,94 Rarity of rupture into the left ventricle may be related to the relatively thick wall and high pressure in that chamber. Aneurysms arising from the left coronary sinus may rupture into the left atrium, left ventricle, or rarely the pulmonary trunk or pericardium.113,116

Sinus of Valsalva aneurysms rupturing into areas adjacent to the tricuspid valve are also adjacent to the atrioventricular (AV) node and His bundle and may be a cause of heart block, bundle branch block, and ventricular fibrillation.5,519,71,92

Table 36-1 shows the overall distribution of the various sites of rupture, based on analysis by Chu and colleagues of 361 cases in the literature, including 57 from their own institution.58

### Associated Cardiac Anomalies

#### Ventricular Septal Defect

A VSD is the most common coexisting cardiac anomaly and may arise from the same congenital anomaly that produced the aneurysm. VSDs occur in 30% to 50% of patients,5,54,59,101,104,107,112,113,116 but prevalence is higher when the aneurysm arises from the right sinus.54,59 When the aneurysm arises from the left third of the right aortic sinus, the VSD is **juxta-arterial**, with its upper margin formed by the confluent aortic and pulmonary valves. When the aneurysm arises from the central third of the right sinus, the VSD may be **juxta-aortic** or may lie within the muscle of the outlet portion of the septum. When the aneurysm arises from the right third of the right sinus (or rarely, the anterior portion of the noncoronary sinus),2,52 the VSD is usually **conoventricular** and may be **perimembranous** as well (see Chapter 35 for definitions). Rarely, a conoventricular VSD occurs in association with an aneurysm arising from the central or leftward third of the right sinus. Sakakibara and Konno considered this a coincidental association between two independent malformations rather than a combined developmental anomaly.52

#### Aortic Valve Abnormalities and Aortic Regurgitation

Aortic valve abnormalities and AR are common in patients with sinus of Valsalva aneurysms.5,54,59,101 When a VSD is present, AR usually results from a prolapsed aortic cusp, similar to the finding in the syndrome of VSD and AR (see Section II of Chapter 35). When a VSD is not present, AR usually arises from other aortic valve abnormalities, including a bicuspid valve.

As in VSD and AR, when prolapse of the aortic cusp into a VSD is the cause, severity of AR progressively worsens.2 If the fibrous hinge line remains intact at the base of a prolapsed cusp, a sinus of Valsalva aneurysm projects toward the ventricle superior to the hinge line, and the cusp projects through the VSD inferior to it. When the hinge line does not retain its integrity, however, as in long-standing cases, both structures form a single sac.51,52,2,116 Taguchi and colleagues noted that prolonged AR produces a fixed fibrous deformity of the prolapsed cusp.71

The frequency of aortic cusp prolapse in sinus of Valsalva aneurysms was undoubtedly underestimated in earlier reports, particularly when no aortograms or echocardiograms were obtained and the aorta was not opened at operation. Aortic cusp prolapse is also less common if only ruptured sinus aneurysm is considered. Thus, in the series of Taguchi and colleagues, which included unruptured cases, AR (although usually mild) was present in 75% of patients,71 whereas in the

<table>
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<th>Site of Rupture</th>
<th>Asian (% of 195)</th>
<th>Non-Asian (% of 166)</th>
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</table>

Data from Chu and colleagues.55
series of Okada and colleagues from Japan, which included only ruptured cases, the prevalence was 17%.  

A complicating problem is the difficulty of determining what constitutes a true (unruptured) sinus aneurysm with combined VSD and AR. Aneurysmal enlargement of the aortic sinus is common in this setting, and the distinction from unruptured sinus aneurysm is difficult to delineate by aortography and even at operation or autopsy. However, 7 (15%) of 48 surgical patients with VSD and AR operated on at GLH from 1960 to 1982 had a distinct but unruptured sinus of Valsalva aneurysm.

**Pulmonary Stenosis**

Important pulmonary stenosis is uncommon in patients with congenital sinus of Valsalva aneurysms, but small gradients are common. The stenosis may be mild but is usually caused by either a projection of the windsock in front of the infundibular septum or a developmental anomaly of the right ventricular outflow tract similar to that present in tetralogy of Fallot and VSD-AR syndrome.

**Other Anomalies**

Infrequently, other congenital cardiac anomalies coexist with sinus of Valsalva aneurysms, including aortic coarctation, patent ductus arteriosus, atrial septal defect, subaortic stenosis, and tetralogy of Fallot.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Unruptured congenital sinus of Valsalva aneurysms are usually silent lesions; their diagnosis depends on echocardiograms or aortograms usually obtained to demonstrate associated symptomatic lesions such as VSD or AR. Diagnosis can be made incidentally during echocardiography or coronary angiography. Rarely, unruptured aneurysms produce tricuspid valve dysfunction or right ventricular outflow obstruction, bringing the patient to medical attention. These aneurysms may also produce severe myocardial ischemia by compressing the right or left main coronary artery.

Embolization from unruptured sinus of Valsalva aneurysms and complete heart block have also been reported. Embolization from unruptured sinus of Valsalva aneurysms and complete heart block have also been reported.

Presence of this anomaly should be considered in men, who represent 80% of patients with sinus of Valsalva aneurysms.

Acute symptoms occur in about 35% of patients with rupture of the aneurysm. In 45% of patients, surprisingly, rupture is associated only with gradual onset of effort dyspnea, and in 20%, no symptoms develop. Acute symptoms consist of sudden breathlessness and pain. The pain is usually precordial and may also be epigastric, probably because of acute hepatic congestion. Precordial pain may mimic myocardial infarction, although radiation of the pain beyond the substernal area is unusual. In a few patients, death occurs within days of rupture from right-sided heart failure, but most patients improve during the latent period, which may last for weeks, months, or years. This improvement may occur without specific medical therapy. The latent period is usually followed by recurrence of dyspnea and signs of right-sided heart failure. Characteristic features at this final stage are aortic and tricuspid regurgitation, an unusual combination.

The infrequency of severe symptoms at rupture may be due to the initially small size of the rupture in many patients. Studies by Sawyers and colleagues in dogs indicate that symptoms are severe when the fistula is greater than 5 mm in diameter. However, in humans, Taguchi and colleagues found little correlation between size of the fistulous opening at operation and a history of acute symptoms. Acute symptoms at rupture may occur less often with a VSD and more often with severe AR.

Acute symptomatic ruptures may be precipitated by heavy exertion, but they also occur after serious automobile accidents and at cardiac catheterization. Rarely, an episode of infective endocarditis may be the precipitating factor. Marfan syndrome may also predispose the aneurysm to rupture.

Rupture is heralded not only by pain and dyspnea but also by a characteristic murmur that is loud, harsh, superficial, and accompanied by a coarse thrill. The murmur is usually continuous with either systolic or diastolic accentuation, but it may be to and fro, similar to that present in the VSD-AR syndrome. In the past, this murmur has been mistaken for that of patent ductus arteriosus, but it is maximal at a lower site, usually the left second, third, or fourth intercostal space. With rupture into the sinus portion of the right ventricle or right atrium, the murmur tends to be maximal at a low level over the sternum or to the right of the lower sternum.

Rarely the murmur is systolic only, possibly because the communication is small. Alternatively, the murmur may be confined to diastole in those few cases when rupture occurs into the high-pressure left ventricle or when right ventricular pressure is at systemic level, as in the neonate.

When the murmur is continuous, its timing and accentuation are a function of several factors including degree of associated AR, degree of aortic systolic murmur, functional size of the VSD, and size of the fistula. Morehead and Greenwood assessed the various causes of murmurs that were believed to be continuous and associated with signs of rapid aortic runoff in their adult patients and found that ruptured sinus aneurysm (8 cases) was the second most common cause after patent ductus arteriosus (33 cases), followed by VSD and AR (3 cases), aortopulmonary window (3 cases), coronary arteriovenous fistula (1 case), and pulmonary arteriovenous fistula (1 case).

Other physical signs of ruptured aneurysm include widened aortic pulse pressure, suggesting mild to severe AR. An elevated jugular venous pressure with a prominent v wave, suggesting tricuspid regurgitation, may be caused by direct entrance of a fistula into the right atrium, but in most cases this sign is absent until onset of right-sided heart failure, when liver enlargement and pulsation also occur.

The chest radiograph does not show enlargement of the aortic root. Plethora may be present, although the left-to-right shunt through both the fistula and any associated VSD is usually small. The electrocardiogram shows either left ventricular or biventricular hypertrophy. Right bundle branch block may occur and may be more common in aneurysms with an intracardiac course close to the AV node and bundle of His. Complete heart block can also occur.

Although the diagnosis is virtually certain on clinical grounds in patients with acute symptoms and sudden appearance of a continuous murmur, two-dimensional Doppler color flow echocardiography is used for verification (Fig. 36-9). Cardiac catheterization and angiography are generally performed to study the site of origin and termination of the fistula and the presence of associated anomalies, particularly VSD, AR, and pulmonary stenosis (see Figs. 36-2, 36-4, 36-7, and 36-8). The true size of the VSD cannot be
Although death after intracardiac rupture of a sinus of Valsalva aneurysm is usually from heart failure, infective endocarditis complicates heart failure in about 10% of patients and may itself be a cause of death.

When a VSD coexists with the aneurysm, the aortic valve is usually at least mildly regurgitant. The natural history then becomes similar to that of VSD and AR (see Section II of Chapter 35). The AR becomes progressively more severe, as does prolapse of the right aortic cusp and aneurysmal sac. This process gradually reduces the size of the VSD until even an anatomically large defect becomes functionally small. Pulmonary arterial hypertension and increased pulmonary vascular resistance therefore are rare. By the time most patients with this combination of anomalies reach age 15 to 20 years, a fixed fibrous deformity of the prolapsed cusp has developed.

**TECHNIQUE OF OPERATION**

The many types and variations of ruptured and unruptured sinus of Valsalva aneurysms, as well as the rarity of some, make detailed description of repair of each impractical. Instead, this section details repair of three of the most common varieties; from these, the techniques of repair for most other aneurysms can be deduced. For example, an aneurysm of the right sinus of Valsalva, without VSD, that has ruptured into the right ventricle is repaired much the same as described for this type of aneurysm that has ruptured into the right atrium, but substituting “ventricle” for “atrium.” Some rare and difficult types may be most simply repaired through an aortic approach, closing the origin of the aneurysm from the sinus with a patch.

Unruptured sinus of Valsalva aneurysms are probably best repaired by excision or, occasionally, by exclusion of the aneurysm and reconstruction by the identical method used for a similar but ruptured aneurysm.

Ruptured Right Sinus of Valsalva Aneurysm, with Ventricular Septal Defect

Repair of a ruptured aneurysm at the midportion of the right sinus of Valsalva with coexisting juxta-aortic VSD is described first because the surgical principles are more easily appreciated in this setting. If the aneurysm is in the rightward portion of the right sinus, the VSD is probably conoventricular (perimembranous) and would be approached through the right atrium, often with detachment of the anterior and septal leaflets of the tricuspid valve. If the aneurysm is in the leftward portion of the right sinus of Valsalva, the associated VSD in the infundibular septum would be juxta-arterial, and the approach would be through the right ventricle or pulmonary trunk. In either case, operation is usually facilitated by a combined aortic and right ventricular, pulmonary trunk, or right atrial approach.

Initial preparations follow the usual routine (see Section III of Chapter 2). After median sternotomy, the pericardium is opened and complete external evaluation of the heart is made. The protruding nipple of the ruptured aneurysm may be palpated through the free wall of the right ventricle. It is important to note that no external evidence of the aneurysm itself is usually seen, and the aortic root appears to be normal on inspection. Intracardiac transesophageal echocardiography (TEE) is useful for defining the location of the aneurysm.
and the cardiac chamber into which it has ruptured (see Fig. 36-9), and for assessing completeness of the fistula and VSD repair and severity of AR before and after repair.

CPB is established after ascending aorta and direct caval cannulation, and body temperature is reduced. The aorta is clamped promptly, caval tapes are placed and secured, the right atrium is opened through a short oblique incision, and a sump suction catheter is placed across the foramen ovale. In most cases the aortic valve is at least mildly regurgitant. The aortic root is opened transversely (Fig. 36-10, A), and cold cardioplegic solution is infused directly into the left and right coronary ostia or retrogradely through the coronary sinus, which is cannulated directly through the opened right atrium (see Chapter 3).

Exposure is obtained by placing stay sutures on the edges of the aortotomy. The orifice of the aneurysm is visualized, and elevating the right aortic cusp reveals the underlying VSD. No attempt is made to determine the feasibility of

Figure 36-10  Repair of ruptured sinus of Valsalva aneurysm into right ventricle, with ventricular septal defect (VSD). A, Initial incision is a transverse aortotomy. The orifice of the aneurysm in the right sinus is visualized. The right ventricle is opened through a transverse incision. Care must be taken to ensure that the aortic incision does not extend into right coronary artery. B, Windsock of ruptured aneurysm is seen overlying VSD. The thinned-out portion of the windsock containing the perforation is excised, taking care not to damage the hinge line of the right aortic valve cusp.
C, Hinge line is now visible between orifice of the aneurysm and VSD. D, Repair is performed using one patch and inserting it through right ventriculotomy. The patch is first sutured to inferior rim of VSD, incorporating septal leaflet of tricuspid valve and avoiding conduction system, using a continuous polypropylene suture. E, Midportion of patch is sutured to hinge line of right aortic cusp using interrupted polypropylene mattress sutures. This step is accomplished before remainder of patch is sewn into place. F, Superior aspect of patch is sewn into place over orifice of the aneurysm in the aortic sinus, completing the repair.
repairing the VSD through the aortic root; it may be difficult through the aortotomy to distinguish between a conoventricular VSD adjacent to the His bundle and a juxta-aortic VSD in the right ventricular outflow tract that does not border the His bundle. Any redundancy or tendency of the right coronary cusp to prolapse is noted, but its repair is deferred.

The right ventricle is opened through a transverse or vertical incision, depending on distribution of the branches of the right coronary artery. Alternatively, an approach is made through the pulmonary trunk. The anatomy is visualized (Fig. 36-10, B). The thinned-out windsock, often containing one or more perforations, is resected, creating a large defect in the right sinus of Valsalva. This defect is downstream (cephalad) from the VSD and separated from it by the hinge line of the right aortic cusp (Fig. 36-10, C). Most of the excised windsock is devoid of aortic media (see Fig. 36-1). A polyester or pericardial patch is sewn into place to close the VSD and the defect in the sinus of Valsalva, and the area of the hinge line of the right aortic cusp, which has been isolated by the resection, is sutured to the patch at an appropriate level (Fig. 36-10, D-F).

After closing the ventriculotomy (or pulmonary trunk) with polypropylene suture placed as a continuous stitch, the interior of the aortic root is again exposed through the aortotomy. When AR coexists and the patient is young with pathology limited to prolapse, all or part of a Trusler repair of the aortic valve is then performed (see Chapter 35, Figs. 35-37 and 35-38). In older patients with AR or when the aortic valve defect is more extensive, valve replacement is necessary (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 12). Either before or after closing the aortic root, the controlled, initially hyperkalemic reperfusion is begun if indicated (see Chapter 3), the sump suction catheter is removed, and the foramen ovale and then the right atrium are closed. The remainder of the operation is completed in the usual manner (see Section III of Chapter 2). Alternatively, when it is certain that the VSD is not conoventricular, the entire repair can be performed through the aortic root. Attachment of the base of the right coronary cusp to the patch is more conveniently accomplished from this exposure than from the right ventricular approach.

Ruptured Sinus of Valsalva Aneurysm into Right Atrium, without Ventricular Septal Defect

When the sinus of Valsalva aneurysm, usually from the non-coronary sinus but occasionally from the right coronary sinus, ruptures into the right atrium, the approach may be through both aorta and right atrium. If AR and VSD can be securely excluded, the approach may be from the right atrium or aorta alone. Intraoperative TEE facilitates this assessment.

In either situation, CPB is established using direct caval cannulation, an aortic root cannula is inserted, and the aorta is clamped (see Section III of Chapter 2). After placing and securing caval tapes, the right atrium is opened obliquely and a sump suction catheter inserted across the foramen ovale. A clamp can be placed across the windsock, or it can be occluded with a finger. Infusion of cardioplegic solution into the aortic root is begun. If the aortic valve is not completely competent, the root infusion is stopped, a transverse aortotomy is made, and cardioplegic solution is infused directly into the coronary ostia (see “Perfusion of Individual Coronary Arteries” in Chapter 3). Alternatively, cardioplegic solution is administered retrogradely through the coronary sinus, which is cannulated directly (see “Technique of Retrograde Infusion” in Chapter 3).

A coexisting VSD is always sought because it may be overlooked during preoperative evaluation if it is plugged by a prolapsing aneurysm or valve cusp. The windsock is then excised, remembering the precise location of the hinge line of the valve cusp. When the windsock is narrow and the bordering edges of the sinus are of good quality, direct closure of the defect is safe. Usually, however, closure is made with a polyester or pericardial patch.

The remainder of the operation is completed in the usual manner (see Section III of Chapter 2).

Unruptured Sinus of Valsalva Aneurysm

Most unruptured sinus of Valsalva aneurysms can be repaired through the ascending aorta. CPB is established using a single cannula in the right atrium (see Section III of Chapter 2). A venting catheter is placed into the left atrium through the right superior pulmonary vein. A catheter is placed into the ascending aorta for delivery of cardioplegic solution; alternatively, a cannula can be placed into the coronary sinus for delivery of cardioplegic solution retrogradely. The ascending aorta is occluded and cardioplegic solution administered. The aorta is opened transversely and the site of origin of the aneurysm identified (Fig. 36-11, A-B). The orifice of the aneurysm is closed with a polyester or pericardial patch, avoiding injury to the aortic cusp and ostium of the coronary artery (Fig. 36-11, C). If the aneurysm is large with associated AR, valve replacement, aortic root replacement with a composite valve-graft or aortic allograft, or a valve-sparing procedure may be necessary.

SPECIAL FEATURES OF POSTOPERATIVE CARE

The usual care is given to patients after repair of sinus of Valsalva aneurysm (see Chapter 5).

RESULTS

Survival

Most patients survive the early period after operation. Hospital mortality has not exceeded 5% in the largest reported series. 

A long-term results are excellent, particularly when aortic valve replacement is not required. Abe and Komatsu reported 86% survival at 25 years in 31 surgical patients. All patients who died late after operation had undergone aortic valve replacement. In the report by van Son and colleagues of the entire Mayo Clinic experience, survival of 31 patients was 95% at 20 years. The single late death resulted from endocarditis 9 years after a subsequent aortic valve replacement.

Risk Factors for Premature Late Death

Severe AR accompanied by marked left ventricle enlargement is a risk factor for premature death in the late postoperative period. Aortic valve replacement appears to be a risk factor
Figure 36-11  Repair of unruptured sinus of Valsalva aneurysm. A, Aneurysm is approached through a transverse aortotomy. B, Orifice of aneurysm in right coronary sinus is identified, noting its proximity to the right coronary artery (RCA) and hinge point of the aortic cusp. C, Orifice is closed with a polyester or pericardial patch using a continuous 5-0 or 6-0 polypropylene suture.

for late death, as does dehiscence of an aortic valve prosthesis.

Functional Status
Most surviving patients are asymptomatic. Abe and Komatsu found that 22 (86%) of 26 surviving patients were in New York Heart Association (NYHA) functional class I, and the other four were in class II. Similar results were observed in the Mayo Clinic series; 25 of 28 known surviving patients were in NYHA class I (89%), and the other three were in class II. Persistent or worsening AR accounted for most of the functional disability after operation.

Complications
Direct closure of the ruptured aneurysm, with or without repair of a coexisting VSD, has resulted in a 20% to 30% prevalence of reoperation for recurrence of the fistula. Other groups have experienced a lower prevalence of reoperations. When the defect left by excision of the ruptured aneurysm is repaired with a patch, reoperation is rare. Heart block occurs in 2% to 3% of patients postoperatively, occasionally late postoperatively. This complication is not surprising given the proximity of the His bundle and its branches to the area of repair.

INDICATIONS FOR OPERATION
When congenital sinus of Valsalva aneurysm ruptures or is associated with VSD or with VSD and AR, prompt operation is advisable.

Unruptured sinus of Valsalva aneurysms that are (1) producing hemodynamic derangements and (2) enlarging should be repaired. Small and moderate-sized unruptured aneurysms probably should not be repaired surgically, at least with the present state of knowledge about the natural history of these lesions, although this issue is controversial.
SPECIAL SITUATIONS AND CONTROVERSIES

Transcatheter Closure of Ruptured Sinus of Valsalva Aneurysm

With improved cardiac imaging and advances in percutaneous interventional therapy, percutaneous closure of ruptured sinus of Valsalva aneurysms represents a therapeutic alternative. Percutaneous closure of a congenital ruptured sinus of Valsalva aneurysm was first described by Cullen and colleagues in 1994.57 Arora and colleagues employed percutaneous closure devices (Rashkind umbrella device, Amplatzer occluder) in eight patients with ruptured sinuses of Valsalva aneurysms.44 One patient required surgical repair because of hemolysis, and one died of progressive cardiac failure. The remaining six patients were asymptomatic from 2 to 96 months following repair. Chang and colleagues subsequently reported successful treatment of four patients using the Amplatzer duct occluder in three and a Gianturco coil in one.43 One patient had a small residual shunt.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Patients with an aortico–LV tunnel usually have severe AR into the LV. They present with heart failure and marked cardiomegaly as well as symptoms and signs of severe AR.1,2,52 Diagnosis can usually be made with two-dimensional echocardiography and Doppler color flow imaging (Fig. 36-12).82,83,84,85,86 Cardiac catheterization and angiography are usually performed to exclude uncommon associated cardiac anomalies.

NATURAL HISTORY

In view of the rarity of the condition, the natural history of patients with aortico–LV tunnel can be outlined only in general terms. Age at presentation and severity of symptoms are related to cross-sectional area of the tunnel and severity of AR. Some patients present as neonates with cardiomegaly and severe heart failure; others who have a smaller tunnel present in childhood without symptoms.107,109 Patients rarely present beyond the second decade of life. When symptoms are present, marked LV enlargement has already occurred, and the natural history thereafter is that of severe AR (see Chapter 12). When symptoms are present in infancy and surgical repair is not accomplished, death usually occurs within a few months.

TECHNIQUE OF OPERATION

Repair is performed using CPB, and a single venous cannula may be used in most cases. In neonates and small infants, hypothermic circulatory arrest may be advantageous. The aorta must be clamped soon after cooling the patient with CPB to prevent LV distention from rapid aortic runoff. Cardioplegic solution must be infused directly into the coronary ostia or retrogradely via the coronary sinus (see “Perfusion of Individual Coronary Arteries” and “Technique of Retrograde Infusion” in Chapter 3).

A transverse aortotomy is made just downstream from the external bulge in the region of the right sinus of Valsalva. The ostium of the right coronary artery is identified and protected. Care is taken to avoid damaging the aortic cusps while visualizing the opening of the tunnel into the LV cavity through the aortic valve. If possible, both ends of the tunnel should be closed. The ventricular end is closed by sutures, usually pledgeted, or with a polyester or pericardial patch.107,108,109 The aortic end of the tunnel is closed by suturing a pericardial patch into place; direct suture closure distorts the sinus and may aggravate the tendency to develop AR postoperatively.109 If necessary, the ostium of the right coronary artery is excised before placing the patch and is reimplanted.107

The aortotomy is closed, and the remainder of the operation is completed in the usual manner. Particular care is taken to avoid LV distention from residual AR, because the heart is recovering from the period of global myocardial ischemia.

Section II  Aortico–Left Ventricular Tunnel

DEFINITION

Aortico–left ventricular (LV) tunnel, or communication, is a short abnormal pathway that begins in an aneurysmal dilatation of the aortic root and upper portion of the right sinus of Valsalva (rarely the left), just to the left of the orifice of the right coronary artery. The defect then passes through the upper end of the ventricular septum to open into the LV cavity.

HISTORICAL NOTE

Aortico–LV tunnel, a rare congenital cardiac anomaly, was first described by Levy and colleagues in 1963.11

MORPHOLOGY

In its most characteristic form, the aortic orifice of the aortico–LV tunnel is anterior and just downstream from the commissural level of the aortic valve and separated from the right sinus of Valsalva by a prominent transverse supra-valsar ridge.58,59,60,11,12,13 The anomaly is visible externally, and the extracardiac bulge can often be seen on the chest radiograph. The tunnel passes directly downward, alongside the aortic valve and through the junction between the aorta and ventricular septum, to communicate with the LV. The tunnel may displace the outlet portion of the ventricular septum into the right ventricle and produce important subpulmonary stenosis.17 A VSD may coexist.82 Rarely the tunnel may communicate with the infundibulum of the right ventricle rather than the left.

In one patient the orifice of the right coronary artery was shown to arise from the extracardiac portion of the tunnel.55 This finding, coupled with demonstration of elastic fibers in the extracardiac portion of some tunnels, suggests that some may actually be examples of coronary artery fistulae. However, most observers believe this anomaly is related to a congenital weakness in the region of the right sinus of Valsalva. In several patients the ostium and proximal portion of the right coronary artery were absent.515

A transverse aortotomy is made just downstream from the external bulge in the region of the right sinus of Valsalva. The ostium of the right coronary artery is identified and protected. Care is taken to avoid damaging the aortic cusps while visualizing the opening of the tunnel into the LV cavity through the aortic valve. If possible, both ends of the tunnel should be closed. The ventricular end is closed by sutures, usually pledgeted, or with a polyester or pericardial patch.107,108,109 The aortic end of the tunnel is closed by suturing a pericardial patch into place; direct suture closure distorts the sinus and may aggravate the tendency to develop AR postoperatively.109 If necessary, the ostium of the right coronary artery is excised before placing the patch and is reimplanted.107

The aortotomy is closed, and the remainder of the operation is completed in the usual manner. Particular care is taken to avoid LV distention from residual AR, because the heart is recovering from the period of global myocardial ischemia.
SPECIAL FEATURES OF POSTOPERATIVE CARE

The usual care is given to patients after the repair (see Chapter 5).

RESULTS

Risk of hospital death has been 5% to 20%. Most patients have at least mild AR after the operation, and in about half of these the regurgitation becomes severe enough to require later aortic valve replacement. The reason for postoperative AR is poorly understood, although in some patients it appears to be due to anuloaortic ectasia. Patients who do not require aortic valve replacement have excellent functional status.

INDICATIONS FOR OPERATION

Diagnosis of aortico–LV tunnel is an indication for operation. Surgery should be performed as early in life as possible to minimize damage to the LV from chronic volume overload imposed by AR.

REFERENCES

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1340

PART VII Congenital Heart Disease

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### Patent Ductus Arteriosus

**Definition**

Patent ductus arteriosus (PDA) is abnormal persistence of a patent lumen in the fetal ductus arteriosus, which usually connects the upper descending thoracic aorta with the proximal portion of the left pulmonary artery (LPA). When the aortic arch is right-sided, the ductus usually connects to the proximal right pulmonary artery. The ductus may at times connect to the adjacent subclavian or brachiocephalic artery rather than to the upper descending thoracic aorta.

This chapter is primarily concerned with isolated PDA. PDA associated with other anomalies is discussed briefly here and in more detail in other chapters (Coarctation of the Aorta and Interrupted Aortic Arch, Chapter 48; Ventricular Septal Defect, Chapter 35; and Ventricular Septal Defect with Pulmonary Stenosis or Atresia, Chapter 38).

### Historical Note

The ductus arteriosus apparently was first described by Galen (born AD 129). It was rediscovered by Botallo in the 16th century, although some attribute the description of its postnatal closure to Acierno and Harvey. In 1888, Munro demonstrated in an infant cadaver the feasibility of dissecting and ligating a PDA. In 1900, Gibson described the characteristic continuous murmur of this anomaly. However, it was not until 1937 that Strieder in Boston attempted to close a PDA surgically in a patient with fulminating infective endarteritis; the patient died on the fourth postoperative day with gastric distention and aspiration of vomitus.

Cardiac surgery received a great impetus on August 26, 1938, when Gross successfully ligated the PDA of a 7-year-old girl at Boston Children’s Hospital. Subsequently, he

### Morphology and Morphogenesis

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**Early Results**

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**Indications for Operation**

**Percutaneous (Catheter) Closure of Patent Ductus Arteriosus**

**Thoracoscopic Closure of Patent Ductus Arteriosus**

### Definitions

- Patent ductus arteriosus (PDA) is abnormal persistence of a patent lumen in the fetal ductus arteriosus, which usually connects the upper descending thoracic aorta with the proximal portion of the left pulmonary artery (LPA). When the aortic arch is right-sided, the ductus usually connects to the proximal right pulmonary artery. The ductus may at times connect to the adjacent subclavian or brachiocephalic artery rather than to the upper descending thoracic aorta.

- This chapter is primarily concerned with isolated PDA. PDA associated with other anomalies is discussed briefly here and in more detail in other chapters (Coarctation of the Aorta and Interrupted Aortic Arch, Chapter 48; Ventricular Septal Defect, Chapter 35; and Ventricular Septal Defect with Pulmonary Stenosis or Atresia, Chapter 38).
The ductus arteriosus is completely closed by 8 weeks of age in 88% of infants with a normal cardiovascular system. When the process is delayed, the term *prolonged patency* of the ductus arteriosus is appropriate; when the process ultimately fails, *persistent patency* of the ductus arteriosus is the appropriate term. Ductus closure or patency is mediated by release of vasoactive substances (acetylcholine, bradykinin, endogenous catecholamines, and probably others), by variations in pH, but chiefly by oxygen tension and prostaglandins (PGF₂α, PGE₂, and prostacyclin PGL₂). Oxygen tension and prostaglandins act in opposite directions, with an increasing PO₂ constricting the ductus and prostaglandins relaxing it; the potency of each varies at different gestational ages. Thus, the ductus is considerably more sensitive to PO₂ in the mature fetus and to prostaglandins (specifically, PGE₂) in the immature fetus. The complex interplay of these factors is the reason prolonged patency of the ductus is more common in premature than term infants, particularly when there is associated respiratory distress syndrome (see *Special Situations and Controversies* later in this chapter). *Intermittent patency* of the ductus arteriosus has been documented, particularly when the ductus is long and narrow.

**Position and Absence**

At birth, usually in subjects with other cardiac anomalies, the ductus may be unilateral, bilateral, or (rarely) completely absent. It is absent in 35% of autopsy specimens with tetralogy of Fallot with pulmonary stenosis, in 40% of those with tetralogy of Fallot with pulmonary atresia, in almost all patients with tetralogy of Fallot and absent pulmonary valve (see Chapter 38), and in truncus arteriosus (see Chapter 43). It is rarely absent in patients with pulmonary atresia and intact ventricular septum (4%) (see Chapter 40) or in those with pulmonary atresia and other complex anomalies (15%).

**Isolated Patent Ductus Arteriosus**

The usual isolated PDA connects to the upper descending thoracic aorta 2 to 10 mm beyond the aortic origin of the left subclavian artery (Fig. 37-1). From the aorta, it passes centrally toward the origin of the LPA from the pulmonary trunk, either directly or angling superiority and hugging the undersurface of the distal aortic arch. When, as in the normally developing heart, the ductus delivers approximately 55% of the combined ventricular output into the descending aorta, the ductus meets the aorta at a proximal acute angle (<40 degrees) and a distal obtuse angle (110 to 160 degrees, mean 134 degrees) (Table 37-1; see also Fig. 37-1).

The PDA is generally 5 to 10 mm in length (in autopsy specimens, 2.5–8 mm), with a wide aortic orifice (4–12 mm) and a considerably narrower pulmonary orifice, and it is restrictive to flow. The PDA may be longer or shorter than this and may have a wide pulmonary as well as aortic orifice.

**Patent Ductus Arteriosus as a Coexisting Anomaly**

When other cardiac anomalies are present, orientation of the ductus to the aortic arch varies, as does the flow pattern in fetal life. When there is pulmonary atresia and the pulmonary circulation is ductus dependent, with ductal flow in utero occurring from the aorta to the pulmonary artery, the ductus becomes a downwardly directed branch of the distal aortic arch. The proximal angle is much less acute and often...
Figure 37-1 Specimen of isolated patent ductus arteriosus (D) in an infant. Ductus passes from junction of pulmonary trunk (PT) and left pulmonary artery (LPA) in an inferior and lateral direction to join descending aorta (Ao). Angle between superior border of ductus (asterisk) and aorta (proximal angle) is acute, and that between the lower border and aorta (arrow) (distal angle) is obtuse. Key: LAA, left atrial appendage; RAA, right atrial appendage; RV, right ventricle. (From Calder and colleagues.\textsuperscript{C1})

Table 37-1 Morphologic Features of Ductus Arteriosus in Fixed Autopsy Specimens

<table>
<thead>
<tr>
<th>Cardiac Diagnosis</th>
<th>n</th>
<th>Range</th>
<th>Median</th>
<th>Open</th>
<th>Closed</th>
<th>Average Length (mm)</th>
<th>Average Width (mm)</th>
<th>Average Prox Angle\textsuperscript{a} (°)</th>
<th>Average Distal Angle\textsuperscript{a} (°)</th>
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<td>Normal\textsuperscript{b}</td>
<td>13</td>
<td>SB-5 mo</td>
<td>2 d</td>
<td>10</td>
<td>3</td>
<td>8</td>
<td>5.9</td>
<td>29</td>
<td>134</td>
</tr>
<tr>
<td>Pulmonary atresia</td>
<td>32</td>
<td>SB-11 mo</td>
<td>8 d</td>
<td>13</td>
<td>19</td>
<td>9.7</td>
<td>3.7</td>
<td>83\textsuperscript{c}</td>
<td>90\textsuperscript{c}</td>
</tr>
<tr>
<td>Aortic atresia</td>
<td>13</td>
<td>2 d-11 wk</td>
<td>4 d</td>
<td>12</td>
<td>11</td>
<td>7.9</td>
<td>7.2</td>
<td>70\textsuperscript{c}</td>
<td>127</td>
</tr>
<tr>
<td>Coarctation</td>
<td>14</td>
<td>3 d-6 mo</td>
<td>14 d</td>
<td>8</td>
<td>6</td>
<td>5.6</td>
<td>6.0</td>
<td>70\textsuperscript{c}</td>
<td>139</td>
</tr>
<tr>
<td>Miscellaneous CHD</td>
<td>37</td>
<td>1 d-8 mo</td>
<td>23 d</td>
<td>18</td>
<td>19</td>
<td>7.1</td>
<td>4.6</td>
<td>52</td>
<td>124</td>
</tr>
</tbody>
</table>

Data from Calder and colleagues.\textsuperscript{C1}
\textsuperscript{a}Angle between ductus and descending aorta.
\textsuperscript{b}Normal hearts except for open ductus arteriosus.
\textsuperscript{c}Difference from normal: $P < .001$.
Key: CHD, Congenital heart disease; d, days; mo, months; prox, proximal; SB, stillborn; wk, weeks.

Uncommonly, in the presence of a left aortic arch, the ductus may arise from an aortic diverticulum (thought to represent persistence of the most distal portion of the right fourth branchial arch) that projects from the medial aspect of the left arch just distal to the origin of the left subclavian artery.\textsuperscript{G9} In rare cases in which the ductus is bilateral, the right-sided PDA connects the right pulmonary artery to the brachiocephalic artery. In the presence of a right aortic arch, a left-sided ductus is still more common than a right-sided ductus. When there is mirror-image branching of the right arch, the left PDA arises from the distal brachiocephalic (or proximal left
subclavian) artery (see Chapter 38). Much less commonly, the right PDA persists in mirror image to the normal, passing from the right arch beyond the right subclavian artery to the right pulmonary artery origin. A PDA (or ligamentum arteriosum) arising from an aortic diverticulum or from an aberrant left subclavian artery is one form of vascular ring (see Chapter 51).

Histology

Histology of a persistent PDA is different from that of simple prolonged patency of the ductus. It is also different from that of the adjoining great arteries. A persistent PDA has a relatively thick intima with an unfragmented elastic lamina separating it from the media, an additional and pronounced wavy unfragmented subendothelial elastic lamina, and variable mucoid material in the media where there is an intricate helicoid spiral muscular arrangement. The media contains variable amounts of elastic material that may form conspicuous lamellae, making the ductus wall resemble the wall of the aorta (aortification).

Aneurysms of Ductus Arteriosus

Aneurysms of the ductus arteriosus, which are rare lesions, appear to be of two types. One is the spontaneous infantile ductal aneurysm, which is present at birth or develops shortly thereafter. The other develops in childhood or adult life.

Presence of the first type may not be detected until autopsy after death from other causes. The aneurysm involves the entire length of the ductus arteriosus and is usually associated with occlusion of the pulmonary artery and a relatively narrow but patent aortic end. It generally contains thrombus and is occasionally a site of infection and embolism. Rarely, it may be a true dissecting aneurysm of the ductal wall. This rare lesion manifests most often in newborns with a history of respiratory difficulties. It produces a tumor-like shadow of variable size that projects beyond the mediastinum adjacent to the aortic knob in the posteroanterior chest radiograph. The aneurysm usually regresses spontaneously within weeks or months, presumably as a result of complete thrombosis and organization, but progressive enlargement or onset of hoarseness from recurrent laryngeal nerve involvement is an indication for surgical exploration and excision. Less marked dilatation of the ductus can be seen on the plain chest radiograph as a fusiform shadow between 6 and 18 hours after birth, disappearing by 24 to 48 hours of age. It has been called the ductus bump.

The second type of ductal aneurysm is thought to be unrelated to the infantile form. The ductus may be patent at both ends, but usually the pulmonary artery end is closed. There is a tendency for progressive enlargement, and death may occur from rupture.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Symptoms and signs of a PDA are the consequence of left-to-right shunting, with the magnitude of the shunt dependent upon size of the communication and relationship between systemic and pulmonary vascular resistances. In this regard, it is similar to other types of high-pressure shunts, which include those across the ventricular septum and others from the aorta.

Large Patent Ductus Arteriosus

Aortic and pulmonary artery pressures are essentially equal when the PDA is large, and the magnitude and direction of shunting are dependent on changes in pulmonary vascular resistance, because systemic vascular resistance remains fairly constant after birth. As neonatal pulmonary vascular resistance decreases, left-to-right shunting increases and severe heart failure develops within a month or so of birth. There is tachypnea, tachycardia, sweating, irritability, poor feeding, and slow weight gain. Pulmonary edema and pneumonia or less severe, and recurrent respiratory infection may occur.

On examination, there is an overactive precordium, sometimes with a systolic thrill, and evidence of cardiac enlargement with a thumping left ventricular apical impulse. The pulse is jerky or frankly collapsing, and the pulse pressure is correspondingly wide. These features become more obvious when heart failure is medically controlled. On auscultation, there is a systolic murmur maximal in the pulmonary area, with late systolic accentuation and minimal spillover into diastole. Occasionally the murmur is continuous, but sometimes with severe heart failure, no murmur is heard. The first and second heart sounds are accentuated, and there is a third sound at the apex or a prominent mid-diastolic mitral flow murmur. The liver enlarges and jugular venous pressure rises; frequently, rales are heard in the lung bases.

The electrocardiogram (ECG) shows left ventricular enlargement with deep Q and tall R waves in the left ventricular leads. There may be evidence of right ventricular hypertrophy with upright T waves in the right precordial leads and evidence of left atrial enlargement with widened P waves. The chest radiograph shows marked cardiomegaly and plethora with or without interstitial or alveolar pulmonary edema. The pulmonary trunk is enlarged, as is the ascending aorta. The echocardiogram shows left atrial enlargement. The ductus may be visualized with two-dimensional echocardiography.

In some infants with a large PDA, heart failure may be less marked, presumably because pulmonary vascular resistance does not fall to the usual level. Histologic changes of pulmonary vascular disease may develop within the first few months of life. These changes may occur in infants in whom heart failure is controlled medically and the ductus is not closed by intervention. These patients become asymptomatic, and the left-to-right shunt diminishes. The murmur becomes purely systolic, the pulmonary component of the second heart sound is markedly accentuated, the apical mid-diastolic murmur disappears, and the pulse loses its jerky quality. Right ventricular hypertrophy becomes dominant in the ECG, the heart becomes smaller on the chest radiograph, and pulmonary plethora disappears. Cyanosis develops as pulmonary vascular resistance increases above systemic vascular resistance (Eisenmenger syndrome), typically earlier than with ventricular septal defect (see Chapter 35). Differential cyanosis may be noted, with blueness of the feet and sometimes the left hand, but not of the face or right hand.

Moderate-Sized Patent Ductus Arteriosus

Left-to-right shunt in moderate-sized PDA is regulated by size of the ductus arteriosus. In this setting, pulmonary artery
pressure is only moderately elevated. As neonatal pulmonary vascular resistance declines, the shunt increases and heart failure may occur. By the second or third month of life, however, compensatory left ventricular hypertrophy is usually associated with clinical improvement and stabilization of symptoms. Physical development may be somewhat retarded, and breathlessness and fatigue may occur, but many patients with moderate-sized PDA remain essentially asymptomatic until the second decade of life or later.

On examination, the pulse is jerky, the precordium is mildly overactive, and the left ventricle is palpable at the apex in association with some cardiac enlargement. The classic continuous murmur is usually heard by age 2 to 3 months, although it varies in intensity. The murmur is generally loud and often masks the heart sounds. It is maximal over the pulmonary artery and radiates upward beneath the mid-third of the clavicle. As described by Gibson in 1900, “it begins after the commencement of the first sound—it persists through the second sound and dies away gradually during the long pause. The murmur is rough and thrilling. It begins softly and increases in intensity so as to reach its acme at or immediately after the occurrence of the second sound, and from that point gradually wanes until its termination.”

Subnormal physical growth is common; Krovetz and Warden found body weight below the third percentile in 26% of 515 surgically proven cases. The ECG may be relatively normal during infancy, but some degree of left ventricular hypertrophy develops in older children. The chest radiograph shows moderate cardiac enlargement and plethora and a prominent ascending aorta (in contrast to findings in patients with a large ventricular or atrial septal defect). In adults, the PDA may be calcified. It is rare for pulmonary vascular resistance to increase, and Eisenmenger syndrome does not develop.

Small Patent Ductus Arteriosus

Left-to-right shunt is small in early life, and pulmonary vascular resistance decreases rapidly to normal after birth.

Left ventricular failure does not occur, and symptoms are absent in infancy and childhood. They may appear later in life, but usually attention is drawn to the condition by a murmur detected on physical examination. Physical development is normal unless there is maternal rubella. The pulse is normal and the precordium is not overactive. By age 2 to 3 months, a short systolic murmur is usually replaced by one that spills over into diastole, or it may be continuous in the second left intercostal space but less intense, and with less radiation than when the ductus is moderate in size. The continuous murmur varies greatly in intensity between patients and sometimes is detectable only when the patient is sitting or standing upright. The ECG and chest radiograph are normal or nearly so.

Special Investigations

Most children and young adults with a PDA and a continuous murmur that is maximal in the second left intercostal space do not need preoperative invasive studies unless other defects are suspected; such studies may be necessary for diagnosis in atypical cases. Instead, two-dimensional echocardiography is usually performed and will image the ductus arteriosus. It has identified so-called silent ductus (a PDA without auscultatory findings). Managing patients with isolated silent ductus remains controversial, although endarteritis has been reported and may be an indication for closure. Cardiac catheterization and angiography are indicated if the echocardiogram suggests elevated pulmonary vascular resistance or associated cardiac anomalies.

NATURAL HISTORY

Isolated PDA in term infants occurs in approximately 1 in 2000 live births and accounts for 5% to 10% of all types of congenital heart disease. It is twice as common in females and may occur in siblings, suggesting a genetic factor. It is particularly common when the mother contracts rubella during the first trimester of pregnancy and may then be associated with multiple peripheral pulmonary artery stenoses and renal artery stenosis.

Because of the early introduction of surgical treatment of PDA, which antedated methods for establishing the diagnosis, its natural history is not completely documented.

Spontaneous Closure

Campbell’s study concluded that spontaneous closure of isolated PDA occurs in 0.6% of patients per year and that this rate is fairly constant through the first 4 decades of life. If this is accepted, it means that in approximately 20% of patients, the PDA will have closed by age 40. His study involved only patients diagnosed beyond age 12 months and was based entirely on clinical findings, closure being assumed to have occurred when a typical murmur was no longer audible, regardless of size of the ductus or initial right-to-left shunt. Other experience suggests that the closure rate is much lower, and it is generally agreed that spontaneous closure is uncommon beyond age 3 to 5 months in full-term infants. Delayed closure of the ductus arteriosus in preterm infants is, however, common (see Special Situations and Controversies later in this chapter).

Pulmonary Vascular Disease

Prevalence and type of pulmonary vascular disease in patients with large PDA are similar to those in patients with large ventricular septal defect (see “Pulmonary Vascular Disease” under Morphology in Section I of Chapter 35).

Rupture

Rupture of both non-aneurysmal and aneurysmal PDA has been reported.

Death

Mortality with untreated PDA in infancy is high, and it has been estimated that, particularly in earlier eras, 30% of patients born with an isolated PDA died within the first year. Risk of death is highest in the first few months of life (see “Patent Ductus Arteriosus in Preterm Infants” under Special Situations and Controversies later in this chapter).

After infancy, the annual death rate of patients with untreated PDA decreases dramatically to approximately 0.5% per year. By the third decade, the death rate has increased to about 1% per year; by the fourth decade, 1.8% per year; and in subsequent decades, as high as 4% per year. As a
result, approximately 60% of patients with PDA die by age 45. Most of the deaths in older patients are related to development of intractable left ventricular failure secondary to long-standing volume overload.

Modes of Death

In infants with a large PDA, mode of death is usually heart failure. Recurrent respiratory infection terminating in pneumonia is a less common mode. In those with a large PDA who survive infancy, death is usually due to acute or chronic right heart failure secondary to development of severe pulmonary vascular disease by the second or third decade of life.

In patients with a moderate-sized PDA, mode of death from the third and fourth decades onward is heart failure. Excluding infants and deaths from pulmonary vascular disease, Campbell estimated that heart failure was the cause of death in 30% of patients.25

Infected endarteritis occurs mainly as a complication of small and moderate-sized PDA. It rarely occurs when the ductus is large. In the preantibiotic era, endarteritis was responsible for approximately 45% of deaths in patients with surgically untreated PDA. A2,C2,K2 After the advent of antibiotics, few patients died from this cause, although they remained subject to recurrent infection. In the current era, risk of infective endarteritis is extremely low.24

TECHNIQUE OF OPERATION

Closure of Patent Ductus Arteriosus

Unless the patient is an infant in severe heart failure or elderly, an intraaerial monitoring catheter is usually unnecessary. After the usual induction of anesthesia and preparations for operation (see Chapter 4), the patient is positioned on the right side (Fig. 37-3, A). A small roll or pillow is placed under the mid-chest. The patient is positioned near the surgeon’s side of the table, but not so much so that the first assistant across the table from the surgeon cannot see into the field well and work comfortably.

Posterolateral Thoracotomy

A curving skin incision is made, centered about 1 to 2 cm below the tip of the scapula. In infants and young children, the incision is really a lateral one, because only the latissimus dorsi and posterior part of the serratus anterior are divided. In older children, the incision is posterolateral, extending posterolaterally to overlie the lower 1 or 2 cm of the trapezius, which is also incised. In patients who are in the second decade of life or older, the incision extends from the anterior axillary line around the scapula and up midway between the spine and posterior scapular border over the lower 3 to 4 cm of the trapezius.

After incising the latissimus dorsi (and trapezius if indicated), the scapula is elevated with a retractor and the ribs are cut from the top down to the fifth rib. Identifying the appropriate rib or intercostal space requires an accurate point of reference. There are three possible points of reference (the second and third are often more reliable than the first):

- First rib: The surgeon passes his or her left hand under the serratus and identifies the first rib by palpation.
- Second rib: The serratus anterior attaches superiorly to the second rib. The surgeon identifies this attachment using upward traction on the scapular retractor, which makes the prominent posterior border of this muscle taut.
- Second intercostal space: This is usually appreciably wider than the third intercostal space.

Counting down from the reference point, the fifth rib is identified and scored. Only then are the posterior and midportions of the serratus anterior divided so that the muscle incision may be directly over the fifth rib. The fourth intercostal space may be opened with a knife or cautery or the chest may be entered through the superior part of the bed of the nonresected fifth rib. With the latter method, the periostecum over the rib is incised, and its superior portion is elevated from the front and back with a periosteal elevator.

After the incision in the rib cage is extended anteriorly and posteriorly, the rib retractor is placed with the ratched portion anteriorly (Fig. 37-3, B). The retractor is opened only partially at first, but as the operation proceeds, it is gradually opened further to obtain adequate exposure.

A retractor is gently placed on the lung, and a vertical incision is made in the mediastinal pleura over the proximal descending thoracic aorta (see Fig. 37-3, B).1 Traction sutures are placed on the anterior and posterior pleural flaps. The lung retractor is removed, moist gauze is placed over the lung, and the anterior pleural traction sutures are pulled taut and anchored to the retractor or drapes. The vein that traverses the aorta obliquely on its anterior surface is divided. The PDA is completely dissected from the surrounding tissue (Fig. 37-3, C-E). In small infants, particular care is taken to be certain that the structure identified as the PDA connects the aorta and pulmonary artery, and that it is not the LPA or distal aortic arch. As dissection proceeds, the left recurrent laryngeal nerve is not isolated, although it should be clearly visualized behind the aortic tissue over the LPA, just inferior and posterior to the PDA (see Fig. 37-3, C).

When the PDA is an uncomplicated one, either division or ligation may be performed. Both techniques, when done properly, ensure complete closure with low risk.

Division When division is elected and the patient is an infant or young child, one straight and two angled fine-toothed Potts ductus clamps are selected. In teenagers and adults, longer-handled vascular clamps are used. At this time, and particularly in older children and adults, the anesthesiologist reduces arterial blood pressure (see Chapter 4) and maintains it below baseline level until the clamps are removed.

The straight clamp is placed completely across the aortic end of the PDA, making sure that its tip does not grasp the recurrent laryngeal nerve or other soft tissue posterior to the ductus. The clamp is placed in the surgeon’s left hand and is gently pulled anteriorly. One angled ductus clamp is placed on the aortic side of the straight clamp and usually on the aorta contiguous with the PDA rather than on the ductus itself. The straight clamp is removed. With the clamp on the aortic origin of the PDA, which is held in the surgeon’s right hand, the other angled clamp is placed with the left hand on

Gross made an anterolateral thoracotomy incision, placed the pleural incision midway between the phrenic and vagus nerves, and retracted the vagus nerve posteriorly.211-214 Exposure is probably less optimal with this approach, although it may be appropriate in small patients and those with variations of situs such as mesocardia and dextrocardia.
the pulmonary end of the ductus. To avoid dislodgment from the clamp and retraction into the pericardial cavity, the clamp must grasp only the ductus and not any of the lappet of pericardium or other tissue. This clamp, like the one on the aortic end, is “squeezed” onto the pulmonary artery as much as possible when it is being placed to give added length to the ductus. The ductus is divided midway between these clamps by Potts scissors or a scalpel (Fig. 37-3, F).

The aortic end of the PDA is oversewn with two rows of 5-0 or 6-0 polypropylene suture placed as a whip stitch (Fig. 37-3, G). The pulmonary end is similarly closed. Although accurate suturing is of obvious importance, the key to a safe repair is separating the clamps widely enough so that a substantial cuff of ductus remains beyond them after the ductus is divided. This permits placing additional sutures for hemostasis.
After anterior surface of ductus has been freed far enough medially so that junction of PDA with left pulmonary artery is visible, superior and inferior surfaces are similarly dissected. Right-angled clamp is passed behind ductus. Clamp stretches areolar tissue behind ductus, which is then grasped with forceps and cut away. This maneuver is repeated several times and creates a space behind ductus. Clamps are placed at aortic and pulmonary ends of ductus (see text), and it is divided midway between them. Aortic end of ductus is oversewn with two rows of 5-0 or 6-0 polypropylene suture. Clamp on aortic end of ductus is generally kept in place following closure and provides traction to expose pulmonary end, which is then oversewn in a similar fashion. Clamps are then released.
The clamp on the pulmonary end of the divided ductus generally is removed first. The clamp on the aortic end is then removed, and a sponge is placed between the divided ends and held in place with pressure for several minutes. Unless the original placement of the clamps has been faulty or the suture closure is inadequate, the bleeding that occurs when the clamps are released usually stops within this period. If not, and if there is no major bleeding that would require replacing one or both clamps, a 5-0 polypropylene suture approximating the adventitia from both sides of the suture line usually controls the bleeding. A pledget of absorbable porcine gelatin sponge is left between the divided ends of the ductus to prevent the suture lines from rubbing against each other.

**Ligation** If the situation is uncomplicated and the PDA is pliable, it may be ligated rather than divided. The technique is basically that described by Blalock in 1946. The operation proceeds exactly as described for ductal division until the PDA is completely dissected. Using a double-armed 5-0 or 6-0 polypropylene suture, adventitial stitches are placed into the accessible superior, inferior, and anterior aspects of the aortic wall contiguous with the PDA (Fig. 37-4, A). One end of the suture is passed beneath the ductus, and the ends are held. A similar stitch is placed on the pulmonary end of the ductus (Fig. 37-4, B). The aortic stitch is pulled up and snugly tied, and then the suture at the pulmonary end is tied. This leaves a long length of ductus between the tied sutures. Finally, a transfixion ligation of 5-0 or 6-0 polypropylene is placed at the middle of the ductus, and the ends are passed in the opposite direction around the ductus and tied to complete the ligation (Figs. 37-4, C to F).

The mediastinal pleura is closed with interrupted sutures, leaving a small opening at each end. In the unlikely event that there is substantial bleeding from the suture lines after operation, this closure will contain it and may be lifesaving.

The rib retractor is removed, a small catheter is inserted into the posterior part of the pleural space through a stab wound in the sixth or seventh intercostal space at the midaxillary line, and suction of 15 to 25 cm water is placed on it. The ribs on either side of the incision are approximated with interrupted sutures. The muscles are individually sutured with a slowly absorbable synthetic material (polyglycolic acid), and the skin edges are approximated with a subcutaneous stitch. In infants, the chest tube may be removed in the immediate postoperative period. A 3- to 4-cm incision is made over the third intercostal space in the axilla. The serratus anterior is reflected inferiorly and laterally, and the pectoralis major is reflected anteriorly. A 3- to 4-cm incision is made over the third intercostal space in the axilla. The serratus anterior is reflected inferiorly and laterally, and the pectoralis major is reflected anteriorly.

**Transaxillary Muscle-Sparing Lateral Thoracotomy**

A 3- to 4-cm incision is made over the third intercostal space in the axilla. The serratus anterior is reflected inferiorly and laterally, and the pectoralis major is reflected anteriorly. The third intercostal space is entered and a rib retractor inserted. The lung is retracted anteriorly, and the pleura overlying the descending thoracic aorta is incised. The PDA is identified at its junction with the aorta, and the recurrent laryngeal nerve is identified and protected. The PDA is dissected circumferentially and is divided or ligated using the techniques just described. Alternatively, it may be occluded with a medium-sized surgical clip. The lung is inflated as the chest is closed.

Fluid and air can be aspirated as the chest wall is closed with interrupted pericostal sutures, making a chest tube unnecessary. The muscle and soft tissue layers are approximated with a slowly absorbable synthetic suture (polyglycolic acid), and the skin edges are approximated with a subcutaneous stitch. This technique is applicable to premature infants, neonates, older children, and adults.

**Closure of Patent Ductus Arteriosus in Association with Repair of Intracardiac Lesions**

Closure of a PDA may be required during operations to correct intracardiac anomalies that require the use of cardiopulmonary bypass (CPB). This occurs in two distinct clinical situations. When the PDA is an incidental finding and relatively small and restrictive, such as with a large ventricular septal defect, dissection of the ductus is usually performed after CPB has been established, because exposure of the adjacent aorta and pulmonary artery is facilitated when the heart is decompressed, and injury to the ductus or surrounding structures can be avoided. The technique for closure of the PDA under these circumstances is described in Technique of Operation in Chapter 35. In the second situation, as can occur in the neonate with transposition of the great arteries with intact ventricular septum, the ductus is large. It must be exposed and controlled before initiating CPB so that it can be ligated immediately after bypass is established.

**Closure of Patent Ductus Arteriosus in Older Adults**

When a PDA requires closure in older adults, the aortic end is often calcified and the ductus very short. A technique using CPB described by Goncalves-Estella and colleagues and later by O’Donovan and Beck is appropriate in this circumstance.

With the usual preparations (see Chapter 2), a median sternotomy is performed and the usual stay sutures and purse-string sutures placed. The aorta and pulmonary trunk are dissected apart. CPB is established with a single venous cannula, and cooling of the patient by the perfusate is begun. The head of the table is lowered to place the patient in a moderate Trendelenburg position. As the heart begins to slow from the cold perfusion, the ductus is obliterated by compressing the front wall of the LPA against it with the index finger. This is essential because otherwise ductal flow into the pulmonary artery will overdistend the pulmonary vascular bed and the right ventricle (this does not occur when the heart is ejecting adequately). When the nasopharyngeal temperature reaches 20°C to 22°C, the aorta is clamped and cold cardioplegic solution is infused into the aortic root or retrogradely into the coronary sinus (see “Technique of Retrograde Infusion” in Chapter 3). The perfusion temperature is stabilized at 20°C to 22°C, and flow is reduced to 0.5 L · min⁻¹ · m⁻². The finger is removed, the distal pulmonary trunk is opened anteriorly and longitudinally, and the incision is continued into the LPA opposite the ductus. (If external pressure on the LPA does not control ductal flow during CPB cooling, perfusion is temporarily reduced to a low level, and the pulmonary artery incision is made such that the finger can be placed directly over the ostium of the ductus to control flow from it into the LPA. CPB flow rate is then increased until cooling is completed.)

The intracardiac sucker is positioned within the LPA beyond the ductus to aspirate blood entering it. The ductal orifice is closed by placing and tying one or more pledgeted
Figure 37-4  Closure of patent ductus arteriosus by ligation. A, Dissection has been completed as shown in Fig. 37-3. Adventitial purse-string suture of 5-0 or 6-0 polypropylene is placed around aortic end of ductus. B, Similar purse-string suture is placed around pulmonary end of ductus. C, The two purse-string sutures are snugly tied. Transfixion suture is placed through ductus. One end is passed beneath ductus. D, Other end of suture is passed beneath ductus in opposite direction, and the two ends are tied on anterior surface. E, Cross-sectional diagram showing scheme for passing ends of suture. F, Transfixion suture has been tied, leaving a space between it and other sutures.

mattress sutures of 3-0 or 4-0 polypropylene. This is usually readily accomplished because the pulmonary artery end of the ductus is rarely calcified, and the pulmonary artery tissues are strong enough to hold sutures well. If the orifice of the pulmonary artery end of the PDA is too large or immobile for this technique, an impervious patch of bovine pericardium, woven polyester, or polytetrafluorethylene can be used to close it, sewing the patch in place with continuous 4-0 or 5-0 polypropylene suture. Flows are then restored, the table leveled, and rewarming of the patient with the perfusate begun. Any leak from the ductus closure site is secured with additional sutures. The pulmonary arteriotomy is closed with a running stitch of fine polypropylene.

With strong suction on a venting catheter or needle that has been placed in the aortic root, the aortic clamp is released. The remainder of the operation is completed in the usual fashion (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).
Closure of Patent Ductus Arteriosus in Premature Infants

Perioperative management and technique of operation are different when surgical closure of the ductus is indicated in the premature infant, most of whom weigh approximately 1000 g and some as little as 400 g. Precise management of ventilation, fluid administration, and body temperature, as well as a precise surgical technique, are essential for success.

Operation is usually performed in the neonatal intensive care unit. This simplifies the logistics and, when properly organized, can provide outcomes as good as those obtained in a conventional operating room.10,12,14

If the procedure is to be performed in the operating room, the infant is intubated in the neonatal nursery, and proper position of the tube is verified by a chest radiograph. The patient, covered by a plastic wrap blanket and cloth cap, is transported to the operating room in a prewarmed (37°C) transport isolette. The room is prewarmed to approximately 30°C, and the patient is placed on the right side on an infant operating table with overhead servocontrolled radiant warmers set at 37°C.

After preparation and draping, a left lateral incision of approximately 2.5 cm is made, cutting or reflecting the latisimus dorsi and posterior aspect of the serratus anterior. The chest is entered through the third or fourth interspace, and a small rib retractor is put into place. With a narrow malleable retractor, the lung is held forward by the first assistant. The ductus is usually large but is variable in position. It may course superiorly as well as anteriorly from the aorta and be immediately adjacent to the distal aortic arch. In this location it can be easily mistaken for the arch. It may course directly anteriorly and be well inferior to the arch.

The friable vascular tissue makes the usual complete dissection of the ductus inadvisable.15,16,71,76 The mediastinal pleura is incised with fine scissors just superior to the aortic end of the ductus and then just inferior to it. The tissue plane is developed by gently spreading fine scissors. As the inferior tissue plane is developed, the back wall (or right side) of the ductus is seen; no attempt is made to pass an instrument around it. The ductus is temporarily and lightly occluded with a fine forceps, and a pulse oximeter on the foot confirms that it is the ductus, not aorta, and that the aortic arch is intact without interruption or coarctation. A medium-sized hemoclip on a holder is positioned well across the ductus at its aortic end; the tip of the clip must be beyond the ductus posteriorly. The adventitia of the aorta may be grasped and gently retracted toward the surgeon as the clip is placed. By closing the holder the ductus is closed.

A 12F catheter is brought out through a stab wound in the chest wall and placed on suction. Placing a chest tube is usually not necessary. The chest wall is closed with two pericostal sutures. The muscles are closed with a continuous fine absorbable suture (polyglycolic acid), and the closure is completed with a subcuticular stitch of fine absorbable sutures. When the procedure is performed in the operating room, the infant is transferred back to the neonatal intensive care unit in a prewarmed transfer isolette.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Care after division or ligation of PDA is simple and follows the principles described in Chapter 5. The patient is usually extubated and the drainage catheter removed in the operating room or within a few hours of leaving it. When the transaxillary muscle-sparing technique is used, most patients can be discharged from the hospital within 24 hours.13,14 When the operation is done with CPB, care is also simple and usual (see Chapter 5).

RESULTS

Early (Hospital) Death

Within 10 years of Gross and Hubbard’s first successful case, hospital mortality for surgical closure of uncomplicated PDA had become very low. In 1951, Gross and Longino reported eight deaths (1.9%; CL 1%-3%) among their first 412 surgically treated cases.14 In 1955, Ash and Fischer reported no deaths (0%; CL 0%-6%) among 116 consecutive children (ages 4 months to 14 years) undergoing surgical closure.15 Other similar experiences reinforce the idea that the operation is safe and that hospital mortality approaches zero.16

Incremental Risk Factors for Early Death

No risk factors for early death can be consistently identified. Operation in infancy or childhood, associated congenital anomalies, pulmonary hypertension, and mild or moderate increase of pulmonary vascular resistance do not increase the risk of hospital death, nor does the surgical technique used. However, by considering the entire span of time since Gross first successfully closed a PDA in 1938, certain situations can be presumed to increase risk.

When pulmonary vascular disease is severe and the shunt is bidirectional or dominantly right to left, risk is high; 5 of 14 such patients (36%; CL 21%-53%) died in the hospital in the early Mayo Clinic experience.15 Death was due to hemorrhage during operation (from the pulmonary artery suture line, because pulmonary artery pressure after closure was higher than systemic arterial pressure and the pulmonary artery was large and thin walled), or it occurred suddenly some days later without any demonstrable cause.15 However, no distinction with regard to reactivity of the pulmonary vascular bed was made in these patients. Thus, it is likely that with preoperative provocative testing, a subgroup of patients could be identified that would have lower operative risk.

When pulmonary vascular disease is mild or moderate, and thus when a large left-to-right shunt is present, there is no increased risk. Even in the early era, 16 among 271 patients undergoing repair of PDA at the Mayo Clinic had severe pulmonary hypertension but only mild or moderate pulmonary vascular disease and a large left-to-right shunt, and there were no (0%; CL 0%-11%) early or late deaths.15

Older age minimally increases risk of surgical closure even in the absence of severe pulmonary vascular disease. This increase is principally from the technical problems posed by the friable and often calcified ductal wall in older patients, and the tendency of the long-standing volume overload of the left ventricle to predispose them to fatal arrhythmias. The mildly increased risk in the older age group is illustrated by the report of Black and Goldman in 1972, which described one death (2%; CL 0.2%-6%) in 53 adults (aged 14-55 years) undergoing surgical closure of a PDA. Death occurred at early reoperation for postoperative bleeding from a tear in the aorta.17 In recent years, the technical problems in older
patients have been eased by use of an open technique (see “Technique of Operation” earlier in this chapter).

Time-Related Survival

Life expectancy is normal after surgical closure of an uncomplicated PDA in infancy or childhood. When moderate or severe pulmonary vascular disease has developed preoperatively, late deaths may result from its progression, as is the case in children with ventricular septal defect (see “Pulmonary Hypertension” under Results in Section I of Chapter 35).

When the operation is performed in adults with advanced chronic heart failure, premature late death is at times unavoidable. This is because the cardiomyopathy secondary to longstanding left ventricular volume overload is irreversible in some patients, in a way entirely analogous to the situation in patients with long-standing aortic valve regurgitation (see “Left Ventricular Structure and Function” under Results in Chapter 12).

Symptomatic and Functional Status

Disappearance of the signs and symptoms of heart failure is dramatic after surgical closure of a large PDA. Ash and Fischer recount that the marked hepatomegaly and splenomegaly in a 3-year-old girl with cardiac cachexia and advanced heart failure were no longer detectable 3 hours after surgical closure of the ductus, and cardiac size on chest radiography had returned to near normal within 4 months. It has been presumed that when a large isolated PDA is closed in infancy, growth pattern becomes normal. However, growth retardation, particularly in regard to height, tends to persist, particularly when the operation is delayed beyond infancy or if the child has a rubella syndrome. The same may occur after repair of ventricular septal defect (see “Physical Development” under Results in Section I of Chapter 35).

Recurrence of Ductal Patency

Currently, prevalence of recurrent or persistent ductal patency approaches zero when division or appropriate ligation techniques are used. In an earlier era, it did occur. In 1965, Jones reported 12 patients (20%; CL 14%-26%) with recurrent or persistent ductal patency out of 61 patients who had ductal ligation with heavy tape. Later, it became less common; Panagopoulos and colleagues reported only four cases (0.4%; CL 0.2%-0.8%) among 936 patients undergoing ductal closure, mostly by ligation. Tripested and Efksind reported 20 among 639 traced cases (3.1%; CL 2.4%-4.0%).

False Aneurysm

False aneurysm is a rare complication of surgical ductal closure that usually occurs after ligation rather than division. Only rare cases of false aneurysm have been reported after ductal division, and these probably resulted from technical errors or infection. Development of a false aneurysm is an indication for urgent reoperation.

Left Vocal Cord Paralysis

Transient and occasionally permanent left vocal cord paralysis resulting from manipulation or injury of the left recurrent laryngeal nerve occurs in 1% to 4% of patients following division or ligation of a PDA. Prevalence is higher among infants with low birth weight.

Phrenic Nerve Paralysis

Phrenic nerve paralysis with elevation of the hemidiaphragm after PDA closure occurs in approximately 4% of patients. It usually occurs on the left side, usually in infants, and most frequently in preterm babies. It is not necessarily due to surgical damage to the phrenic nerve, because it may develop on the right side. It often regresses spontaneously but may persist for many months or indefinitely.

Chylothorax

Chylothorax is a rare complication of surgical ductal closure. Its management is discussed in Section II of Chapter 5.

INDICATIONS FOR OPERATION

Persistent PDA is an indication for closure, and the optimal age for operating is during the first year of life. Patients, either term or preterm, with prolonged PDA require closure in early life only when a large left-to-right shunt results in heart failure. In practice, this means that in term infants in the first month of life, PDA closure is indicated only when symptoms of heart failure are present. (For a discussion of the special situation in preterm infants, see “Patent Ductus Arteriosus in Preterm Infants” under Special Situations and Controversies later in this chapter.)

Beyond the first month of life, prophylactic closure of the PDA is indicated. In the absence of symptoms, operation may be delayed until about age 6 months. However, closure is indicated at any time before this when symptoms of heart failure or failure to thrive persist despite intense medical treatment. Older age is not a contraindication to closure of an isolated PDA in the absence of severe pulmonary vascular disease.

Severe pulmonary vascular disease is a contraindication to closure. The criteria of inoperability in this setting are the same as described for patients with ventricular septal defect (see Indications for Operation in Section I of Chapter 35). In the case of patients with PDA, the ductus may be temporarily occluded at operation; if pulmonary artery pressure does not decrease but remains severely elevated with no increase in aortic pressure, the shunt is not dominantly left to right. Closure of the ductus, therefore, will not reduce pulmonary artery pressure or left atrial pressure and therefore cannot trigger a favorable change in pulmonary vascular resistance. Repair is contraindicated in this situation. With preoperative provocative testing, abandoning closure in the operating room should be uncommon.

Until recently, indications for closure of PDA were indications for operative closure. This is probably still true in many institutions, but percutaneous closure must also be considered (see “Percutaneous [Catheter] Closure of Patent Ductus Arteriosus” under Special Situations and Controversies later in this chapter).
SPECIAL SITUATIONS AND CONTROVERSIES

Patent Ductus Arteriosus in Preterm Infants

Historical Note
In 1963, both Powell and de Cancq, independently, were apparently the first to close a PDA in a preterm infant by operation.13,37 Subsequent improvement in the cardiovascular status of preterm infants after surgical closure of a PDA has been clearly demonstrated.38,41

Clinical Features and Diagnostic Criteria
The preterm infant with a PDA may have a continuous murmur, and under these circumstances diagnosis is made with confidence.48,66 The shunt is considered large enough to be important if there is pulmonary plethora and cardiomegaly on the chest radiograph, if peripheral pulses are bounding, or if by echocardiography, the left atrial–aortic ratio is 1.5 or greater and Doppler color flow interrogation demonstrates a large left-to-right shunt.34

A systolic murmur is less specific for PDA, but the diagnosis is made clinically if the murmur is associated with a hyperactive precordium, increased pulse pressure, or positive chest radiograph or echocardiogram. A few preterm infants have these positive clinical and laboratory findings of PDA without a murmur.48,71

Natural History
A high proportion of preterm infants have prolonged patency of the ductus arteriosus after birth. The frequency increases with decreasing gestational age and decreasing birth weight.12 Sassi and colleagues reported the presence of a PDA (based on presence of a long sputum murmur) in 77% of premature infants with a gestational age of 28 to 30 weeks, 44% with a gestational age of 31 to 33 weeks, and 21% with a gestational age of 34 to 36 weeks.83 Birth weights of less than 1000 g, 1000 to 1500 g, and 1500 to 2000 g were associated with a PDA prevalence of 83%, 47%, and 27%, respectively. Frequency of hemodynamically important PDA is less, however: approximately 40% when the birth weight is less than 1000 g and 10% when it is less than 1750 g.26,42

A PDA has the same hemodynamic effects in preterm infants as in term infants, as evidenced by collapsing pulses and radiographic evidence of increased pulmonary blood flow, left atrial enlargement, and cardiomegaly. Furthermore, experimental studies in preterm lambs have shown that the left-to-right shunt through the open ductus is associated with reduced effective systemic blood flow and organ hypoperfusion.84 This has led to the hypothesis that necrotizing enterocolitis in preterm infants may be associated with a large PDA, which is supported by results of a randomized trial of ductal closure in preterm babies and by other studies.33,62

A strong correlation exists between patency of the ductus arteriosus and idiopathic respiratory distress syndrome, although these may not be causally related.31,82,77 There is also an association between fluid administration and ductal patency; thus, PDA is less frequent in neonatal units that restrict fluids in preterm infants.85

Technique of Operation
See Technique of Operation earlier in this chapter.

Special Features of Postoperative Care
Because surgical closure of a PDA is only one facet of care of a preterm infant, the patient is returned to the care of the neonatologist in the neonatal intensive care unit. The drainage catheter may be left until mechanical ventilation is no longer necessary, because pneumothorax occasionally develops in preterm infants maintained on a ventilator.

Early Results
Hospital mortality is approximately 10% to 20%.12,41,51,59,79 It is not related to the interval between birth and operation, but, as in other circumstances in preterm infants, it is probably related to birth weight and gestational age. Death may be from continuing respiratory distress, intracranial hemorrhage, necrotizing enterocolitis, or a diffuse coagulopathy, but it rarely occurs during the immediate perioperative period. In low-birth-weight preterm neonates, postoperative morbidity includes bronchopulmonary dysplasia, intraventricular hemorrhage, necrotizing enterocolitis, and retinopathy.93 There is no clear evidence that prevalence of intracranial hemorrhage is increased by surgical closure of the ductus.94 Whether ligation of the PDA is causally linked to these adverse outcomes remains to be determined.94

Cardiac status usually improves immediately, and left atrial size is promptly reduced.110 At least one randomized study indicates overall benefit of early surgical closure of a PDA in preterm infants weighing less than 1500 g and requiring mechanical ventilation.51 Another randomized study of infants weighing 1000 g or less and requiring supplemental oxygen demonstrated reduction (P = .001) in necrotizing enterocolitis among those treated by early ligation.53

Late Results
Among preterm infants requiring PDA closure, only half the hospital survivors are well 1 to 5 years later.110,124 About one third have bronchopulmonary dysplasia on chest radiograph, with variable clinical findings. About one sixth have more severe complications, such as retrolental fibroplasia, blindness, and cerebral palsy.110,124

Indications for Operation
Recent publications have questioned the efficacy of PDA closure in preterm infants, whether by surgery or by pharmacologic therapy.36,62 The analyses performed in these publications rely on review and meta-analysis of existing historical literature pertaining to management of PDA in premature infants. The retrospective nature of these analyses incorporates major assumptions and limits the veracity of the conclusions. The authors of these studies acknowledge that there currently are no randomized controlled prospective trials evaluating surgical closure, pharmacologic closure, and conservative medical management not aimed at closure, and that such studies are the only way to resolve this question definitively. Notwithstanding these opinions, the overwhelming consensus is that closure should be actively pursued in preterm infants with hemodynamically important PDA. Indications for operative closure of a PDA include respiratory distress (ventilator dependency and need for high FiO2 in the absence of important shunt) and demonstration of a large PDA (collapsing pulses, left atrial enlargement by echocardiography, and a large Qp/Qs by radionucleotide scanning). In many centers, closure is reserved for infants who do not respond to medical management, including a course of indomethacin or...
ibuprofen therapy, and for infants in whom pharmacologic therapy is contraindicated. Failure of indomethacin treatment may approach 40% to 50%, particularly in low-birth-weight infants (<800 g). Surgical ligation should be considered the primary form of treatment in small preterm infants who have persistent cardiopulmonary compromise after pharmacologic therapy or an increased risk for development of complications from this therapy.

Percutaneous (Catheter) Closure of Patent Ductus Arteriosus

Technical improvements and operator experience have made percutaneous closure of PDA an intervention of proven efficacy. Percutaneous closure is generally contraindicated in patients weighing less than 6 kg. Device closure was effective in 58 patients weighing 3.6 to 6.0 kg, but complication rates led these authors to conclude that surgical closure is first-line therapy. Two case reports document device closure in infants weighing 2.2 and 1.7 kg, but it is not recommended. In earlier years, approximately 65% of patients had complete ablation of the shunt with this technique. Currently, closure can be achieved in a high percentage of patients with umbrella or button coils or plugs. Effective occlusion (no or trivial residual shunt) can be accomplished in up to 94% of patients. Procedures are performed under local anesthesia and on an outpatient basis in many centers. Procedural mortality has been extremely low (1 of 1640 procedures [0.061%; CL 0.01%-0.21%] reviewed by Fortes and colleagues). In this group of patients, embolization of the closure device occurred in 80 patients (4.9%; CL 4.3%-5.5%) and was successfully retrieved in 70. Aortic or LPA narrowing not requiring intervention occurred in 32 patients (2.0%; CL 1.6%-2.4%), significant hemolysis in 12 (0.73%; CL 0.52%-1.0%), and inguinal pseudoaneurysm or loss of pulse in 18 (1.1%; CL 0.82%-1.4%). Overall occurrence of minor complications was 8.8%. Procedural failure did not occur when PDA size was smaller than 1.5 mm. Infective endarteritis occurred in one patient, but follow-up to date is limited and variable in the reviewed studies. It is thus impossible to estimate the true risk of infective endarteritis with these techniques.

The ultimate role of outpatient closure of a PDA will be determined by its costs compared with those of operative closure, reproducibility of the results obtained, prevalence of complete and permanent closure, and occurrence of late complications resulting from a device residing in the ductus arteriosus. Currently in patients with a PDA of large diameter or short length, surgical closure is advisable.

Thoracoscopic Closure of Patent Ductus Arteriosus

An alternative to percutaneous catheter closure of a PDA is thoracoscopic closure without thoracotomy. It is performed under general anesthesia using three or four incisions 3 to 7 mm in length in the left hemithorax. The surgical field is viewed on a video screen. Once the ductus is dissected from the surrounding tissue, one or more clips are applied to close it. The technique has been used in neonates, children of all ages, and adults. In the experience of Laborde and colleagues with 332 consecutive pediatric patients, mortality was zero (CL 0%-0.57%) and morbidity minimal. Three patients with persistent ductal patency required surgical closure. Subsequent series have confirmed the safety of the procedure, with no operative deaths. When compared with open operation, more complications, particularly recurrent laryngeal nerve injury, occurred with the thoracoscopic technique.

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Section I  Tetralogy of Fallot with Pulmonary Stenosis

DEFINITION

Tetralogy of Fallot (TF) is a congenital cardiac malformation characterized by underdevelopment of the right ventricular (RV) infundibulum, with anterior and leftward displacement of the infundibular (conal, outlet) septum and its parietal extension. Displacement (malalignment) of the infundibular septum is associated with RV outflow (pulmonary) stenosis (in extreme forms, atresia) and a large ventricular septal defect (VSD). Typically, the VSD is subaortic in position, but it may be beneath both the aorta and pulmonary trunk (juxta-arterial VSD) when the infundibular septum is absent. The RV and left ventricle (LV) are of equal thickness, and their systolic pressures are usually the same. The atrioventricular connection is concordant, and the aorta is biventricular in origin, overriding onto the RV. The amount of override varies widely. Importantly, there is fibrous continuity between the aortic and mitral valves (i.e., there is no subaortic infundibulum). This aorto-mitral fibrous continuity is the distinguishing morphologic characteristic separating TF from double outlet right ventricle with subaortic VSD (see Chapter 53). This section considers only TF with pulmonary stenosis.

HISTORICAL NOTE

TF was first treated surgically by Blalock and Taussig in 1945, when they performed a palliative subclavian–pulmonary arterial shunt. Other types of systemic–pulmonary arterial shunts were introduced by Potts and colleagues in 1946, Waterston in 1962, Kliner in 1961, Davidson in 1955, Laks and Castaneda in 1975, and de Leval and colleagues in 1981, among others. Palliation by direct relief of pulmonary stenosis with a closed technique was introduced by Sellors and Brock in 1948. TF was first successfully repaired by Lillehei and colleagues at the University of Minnesota in 1954 using controlled cross-circulation with another person serving as oxygenator. The first successful repair of TF using a pump-oxygenator was done by Kirklin and colleagues in 1955. Waterston in 1962, Kliner in 1961, Davidson in 1955, Laks and Castaneda in 1975, and de Leval and colleagues in 1981, among others. Palliation by direct relief of pulmonary stenosis with a closed technique was introduced by Sellors and Brock in 1948.

TF with pulmonary stenosis encompasses a wide spectrum of morphologic subsets that vary primarily in details of RV outflow obstruction, VSD, and aortic overriding. All four major components of TF—RV outflow obstruction, VSD, overriding aorta, and RV hypertrophy—are linked embryologically. Van Praagh has advanced the concept of TF being the result of a “monology.” The concept is that a small-volume subpulmonary infundibulum is the basic anomaly, resulting in pulmonary outflow tract obstruction (stenosis or atresia). There is a VSD because the small-volume infundibulum cannot fill the space above the trabecula septomarginalis (septal band; TSM) and the ventricular septum. The infundibular septum is malaligned anterosuperiorly above the RV outflow tract floor—the infundibular septum—fails to expand in a rightward, posterior, and inferior direction, thereby helping to close the interventricular foramen. Failure of this normal morphogenetic movement of the infundibular septum results in aortic overriding. Because the infundibular septum is abnormally anterosuperiorly malaligned above the RV, so too is the aortic valve, which is attached to what should be the LV outflow tract surface of the infundibulum septum. RV hypertrophy is a secondary response to resulting RV overload.

Thus, Van Praagh posits that embryologically, TF is a conotruncal malformation in which conotruncal septation is complete, but the infundibular septum is displaced. This anterior displacement is responsible for all of the morphologic characteristics of TF: crowding of the RV outflow tract and obstruction, overriding of the aorta, malalignment VSD, and RV hypertrophy.

Anderson, in contrast, argues that the “monology” concept is an oversimplification. His studies suggest two morphologic abnormalities that he considers pathognomonic for the lesion. (1) There is anterocephalad deviation of the outlet septum, but for obstruction of the RV outflow tract to occur, there must additionally be (2) an associated malformation of the septoparietal trabeculations, the muscular bars that reinforce the parietal wall of the RV. The squeeze produced between the malaligned outlet septum and the abnormally arranged septoparietal trabeculations identify the morphologic entity of tetralogy of Fallot.
Right Ventricular Outflow Tract

Infundibulum

Infundibular stenosis associated with specific alterations in position of the infundibular septum is the hallmark of TF. Specifically, the septal (leftward) end of the infundibular septum is displaced anteriorly, inserting in front of the left anterior division of the TSM (septal band) (Fig. 38-1)\(^{A12,VS}\) rather than between its two divisions, as in the normal heart (see Chapter 1, Fig. 1-5). In addition, the parietal (rightward) end of the infundibular septum is rotated anteriorly and passes anteriorly and inferiorly to reach the free wall of the RV (Fig. 38-2), so that the infundibular septum and its parietal extension may come to lie almost in a sagittal rather than the usual coronal (frontal) plane. Parietal and septal ends of the infundibular septum give rise to prominent muscle bands that attach to the right and left sides of the anterior RV free wall.\(^{A12}\) The anterior free wall may show additional trabeculations or moderate thickening.

There is frequently a localized narrowing, the os infundibulum, which in 72% of cases lies in a transverse plane at the lower infundibular septal edge (see Fig. 38-2). This sitting means that when the infundibular septum is well developed, there is a large infundibular chamber (or “third ventricle”; see Fig. 38-2), which in older patients occasionally becomes aneurysmal. In older patients, however, the os infundibulum is surrounded by fibrosis, which, when the chamber is small or absent, may extend into the RV–pulmonary trunk junction (pulmonary “anulus”). Less commonly (about 15% of cases), the major stenotic zone at the lower infundibular septal edge lies almost in a coronal plane, extending inferiorly from the lower infundibular septal edge. This occurs when hypertrophied muscle bands at the parietal end of the infundibular septum pass more inferiorly to join the free wall nearer to the RV apex, while on the septal (medial or leftward) aspect, there are not only inferiorly directed additional trabeculae, but also often an undue prominence and hypertrophy of TSM. Under these circumstances the inferior boundary of the os infundibulum may be formed by a prominent superiorly displaced moderator band.\(^{A12}\) (When this type of low-lying infundibular stenosis is associated with a small or moderate-sized VSD, it is not termed TF; see Section V.) Both transverse and coronal plane stenoses are occasionally present.

When an infundibular chamber is present, its walls laterally and medially consist of numerous trabeculated spaces, some of which may form prominent blind recesses that do not lead directly to the valve “anulus,” and occasionally an accessory opening is present. Endocardial fibrosis is not seen during the first 6 to 9 months of life and is seldom marked before age 2 years.\(^{C23}\) Later, fibrosis seems to progress, which may lead to acquired infundibular atresia.

Generally, the infundibulum is somewhat longer, relative to total RV length, than it is in normal hearts.\(^{B3,H29}\) When the infundibular septum is short (hypoplastic), infundibular stenosis reaches the pulmonary valve “anulus” without an intervening chamber. When the infundibular septum is absent, the VSD is juxta-arterial (doubly committed), extending superiorly to reach the pulmonary valve; infundibular stenosis is absent, and the posterior aspect of the RV outflow tract is formed by the VSD (Fig. 38-3).\(^{B30}\) The pulmonary valve and sometimes its “anulus” are the main sites of the usually moderate stenosis in these hearts. However, once a VSD patch is in position, the hypertrophied RV walls and dextroposed aorta may combine with the patch to form severe subvalvular stenosis.

The infundibulum may be diffusely narrowed and hypoplastic. This is usually associated with severe cyanosis at birth or shortly thereafter. There is no localized os infundibulum (Fig. 38-4) nor increased trabeculations, nor important muscular hypertrophy. Nevertheless, stenosis is usually severe because narrowing occurs throughout the outflow tract (Fig. 38-5). Length of the stenosis in this morphologic variant is determined by length of the infundibular septum (see Fig. 38-4).

Pulmonary Valve

The pulmonary valve is stenotic to some degree in 75% of patients with TF. Approximately two thirds of stenotic valves are bicuspid (Table 38-1).\(^{B9,N21}\) A three-cusp configuration occurs more commonly in nonstenotic valves. Even when nonstenotic, valve area is usually smaller than that of the
Figure 38-2  Autopsy specimen of tetralogy of Fallot with low-lying infundibular stenosis. Death occurred without surgical correction at age 3 years. A, Isolated infundibular stenosis viewed from below through opened right ventricle. B, Stenosis viewed from above after removing anterior wall of large infundibular chamber and opening front of pulmonary trunk. Stenosis is localized at lower border of infundibular septum (os infundibulum). Note that lateral (parietal) end of the septum is deviated anteriorly into almost a sagittal plane. Posterosuperior angle of ventricular septal defect is well seen (arrow), as is its proximity to right aortic cusp. Infundibular chamber is dilated and thin walled in association with the low, transversely placed infundibular stenosis. Pulmonary valve is tricuspid and not stenotic. Key: Ao, aorta; IS, infundibular septum; Osinf, os infundibulum; PT, pulmonary trunk; PV, pulmonary valve; RAA, right atrial appendage; RC, right coronary cusp; RV, right ventricle; TV, tricuspid valve; VSD, ventricular septal defect.

Aortic valve, which is the reverse of normal. The difference in size of these two valves is partly because the pulmonary valve is small and partly because the aortic valve is larger than normal.

**Stenotic valve cusps** are usually thickened, frequently severely so, a feature that increases the amount of obstruction at the valve level (Fig. 38-6). In approximately 10% of cases, cusps are replaced by sessile nubbins of fibromyxomatous tissue that offer little obstruction. Such vestigial valves are usually associated with a stenotic pulmonary “anulus.” When the “anulus” is not severely narrowed and the valve is vesti
gial, severe pulmonary regurgitation results, a condition called **TF with absent pulmonary valve** (see Section III).

Pulmonary valve stenosis is usually caused by cusp tethering rather than by severe commissural fusion (see Table 38-1). The free edge of tethered cusps is considerably shorter than the diameter of the pulmonary trunk, so the valve cannot open adequately, and the pulmonary trunk is pulled inward at the point of commissural attachment. This produces a localized narrowing or corseting of the trunk at distal valve level. Thus, both the valve and trunk are tethered (see Fig. 38-6). In this situation the sinuses of Valsalva are frequently well formed, but entry into them between the cusp edge and pulmonary trunk wall is often also stenotic, resulting in slow filling of the sinuses with contrast medium on cineangiography. Cusps of a tethered valve may be fused for a short distance. Tethering is more common in a bicuspid valve, but can occur in a three-cusp valve.

Less commonly, the dominant morphology is thickened cusps associated with congenital commissural fusion, resulting in a concentric or eccentric stenotic orifice. An eccentric orifice can also result from a unicuspid configuration.
Figure 38-3  Autopsy specimen of tetralogy of Fallot with juxta-arterial ventricular septal defect (VSD). A, Viewed from opened right ventricle (RV) with incision carried across right cusp of aortic valve. B, Viewed after opening RV across pulmonary valve and trunk. Infundibular septum appears to be absent, and VSD is bounded superiorly by fused aortic and pulmonary valve “anuli.” Trabecula septomarginalis (septal band) and RV free wall are severely hypertrophied. There is marked narrowing of pulmonary “anulus” and trunk and thickening and tethering of the valve cusps. Key: Ao, Aorta; FW, right ventricular free wall; L, left coronary cusp; LA, left anterior division at septal band; LC, left coronary aortic cusp; NC, noncoronary aortic cusp; PT, pulmonary trunk; PV, pulmonary valve; RC, right coronary aortic cusp; RP, right posterior division of septal band; TSM, trabecula septomarginalis (septal band); TV, tricuspid valve.

Figure 38-4  Autopsy specimen of tetralogy of Fallot with diffuse right ventricular (RV) outflow hypoplasia (same specimen as in Fig. 38-1). View is through opened RV. Stenotic infundibulum (arrow) is relatively short with a well-formed anteriorly displaced infundibular septum. There is no os infundibulum, but rather diffuse outflow tract narrowing without increased trabeculation or free wall thickening. Ventricular septal defect is conoventricular and perimembranous. Key: IS, Infundibular septum; TV, tricuspid valve; VSD, ventricular septal defect.
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cases, it is variably obstructive. It is small and obstructive when there is diffuse infundibular hypoplasia, resulting in diffuse RV outflow hypoplasia.

Pulmonary Trunk

Like the pulmonary valve and “anulus,” the pulmonary trunk is nearly always smaller than normal, and smaller than the aorta. Reduction is most marked when there is diffuse RV outflow hypoplasia. Then, the pulmonary trunk is less than half the aortic diameter and is short (see Fig. 38-6), directed sharply posterior to its bifurcation. It is thus largely hidden from view at operation by the prominent aorta, which also displaces the origin of the trunk leftward and posteriorly.

When the pulmonary valve is markedly tethered, the pulmonary trunk is also tethered or corseted at its commissural attachments (see Fig. 38-6), and it may be very angulated or kinked at this point. This is the usual mechanism of supravalvar narrowing, and it is not associated with wall thickening. Rarely, however, there may be a discrete supravalvar narrowing beyond commissural level with diffuse wall thickening.

Pulmonary Trunk Bifurcation

The left pulmonary artery (LPA) is usually a direct continuation of the pulmonary trunk, with the right pulmonary artery (RPA) arising almost at right angles and close to it, but this pattern varies (Fig. 38-7). Uncommonly, the distal pulmonary trunk and origin of the RPA and LPA are moderately or severely narrowed (bifurcation stenosis), and in this situation the bifurcation may have a Y shape. A Y-shaped bifurcation is more common when the ductus arteriosus is absent (see “Aortic Arch and Ductus Arteriosus” later in this section).

Right Ventricular–Pulmonary Trunk Junction

The RV–pulmonary trunk junction is normally a muscular structure and, like the infundibulum, varies in diameter during the cardiac cycle. In TF, it is almost always smaller in diameter than the aortic “anulus” (the reverse of normal), and smaller than the normal junction. It is less likely to be stenotic when infundibular stenosis is low lying. The pulmonary “anulus” may become thick from fibrosis, which is usually an extension of endocardial thickening surrounding an intermediate- or high-level infundibular stenosis; in such cases, it is variably obstructive. It is small and obstructive when there is diffuse infundibular hypoplasia, resulting in diffuse RV outflow hypoplasia.

Right and Left Pulmonary Arteries

Anomalies of the RPA and LPA are common in TF with pulmonary atresia (see Section II) but uncommon in TF with pulmonary stenosis, although any of the anomalies present in pulmonary atresia may occur in patients with
Chapter 38 Ventricular Septal Defect with Pulmonary Stenosis or Atresia

Figure 38-6 Specimen of tetralogy of Fallot showing thickened stenotic pulmonary valve (PV), and right ventricular (RV) cineangiograms in the right anterior oblique projection showing same feature. A, Specimen showing stenotic PV viewed through opened pulmonary trunk (PT). There are two thickened nonfused cusps, but PT wall is drawn inward where commissures attach (tethering). B, Early systolic frame. PV stenosis is due to valve tethering. Cusps are thickened and form a dome in systole from their attachments to pulmonary “anulus” (small arrow). Supravalvar PT narrowing (large arrow) is localized to region between pulmonary sinuses and PT. C, Diastolic frame. Distal edges of thickened cusps remain approximated to narrowed PT wall, and the prominent sinuses may be slow to fill with contrast. Note shortness of PT. Key: A, Aortic valve; Ao, aorta; L, left pulmonary artery; R, right pulmonary artery; RAA, right atrial appendage. (From Calder and colleagues.)

pulmonary stenosis (Table 38-2). Fellows and colleagues found pulmonary artery anomalies in 30% of infants having TF with pulmonary stenosis presenting in the first year of life. In particular, proximal LPA stenosis or hypoplasia, or both, can occur when certain configurations of the ductus arteriosus are present (see “Aortic Arch and Ductus Arteriosus” later in this section).

Distal Pulmonary Arteries and Veins

Pulmonary arteries and veins beyond the hilar positions are about normal in size in most patients. Intraacinar arteries are smaller than normal, and their media are thinner. In addition, lung volume, alveolar size, and total alveolar number tend to be reduced.

Dimensions of Right Ventricular Outflow Tract and Pulmonary Arteries

Hypoplasia of the RV outflow tract and pulmonary arteries in patients having TF with pulmonary stenosis is most marked centrally in the RV infundibulum and pulmonary trunk. On average, the RPA and LPA and their branches are not abnormally small. This does not deny the occasional existence of severe narrowing at the origin of the LPA or RPA (see Fig. 38-7). Elzenga and colleagues found juxtaductal proximal
Figure 38-7  Cineangiograms after right ventricular injection showing stenoses at origins of pulmonary arteries in tetralogy of Fallot with pulmonary stenosis. A, Stenosis at origin of left pulmonary artery (LPA) in region of ductus arteriosus, which is closed at its aortic end. B, Stenosis at origin of LPA. This arrangement is unusual in that the LPA comes off at right angles. C, Bifurcation stenosis. Note that, as usual, the right pulmonary artery comes off at right angles to pulmonary trunk. D, Severe narrowing of distal pulmonary trunk. Note that first portion of LPA appears to be a continuation of pulmonary trunk.

stenoses of the LPA in 10% of patients having TF with pulmonary stenosis. There is great variability in these dimensions, however, making their careful pre-repair study important.

Convenient Morphologic Categories of Right Ventricular Outflow Obstruction

The nearly infinitely variable spectrum of RV outflow obstruction in TF can be conveniently categorized in a way that is surgically useful because it relates to difficulty in obtaining good relief of the pulmonary stenosis and therefore to surgical techniques and mortality (Box 38-1). This supplements earlier discussion of patterns of the infundibular portion of the obstruction. It might be inferred that transanular patching to relieve outflow tract obstruction would be more frequently required in those with “anulus” stenosis or diffuse hypoplasia, but a blanket rule is probably inappropriate.

Iatrogenic Pulmonary Arterial Problems

A transanular patch may later produce severe stenosis at the origin of the LPA or, less commonly, of the RPA.
Collateral Pulmonary Arterial Blood Flow

Patients virtually always have increased collateral pulmonary arterial blood flow, primarily from true bronchial arteries. Occasionally (less than 5% of patients), large aortopulmonary (AP) collateral arteries are present (see detailed discussion in “Alternative Sources of Pulmonary Blood Flow” in Section II).
septum (see Fig. 38-4). The septum may support part or most of the right aortic cusp, depending on the degree of aorta overriding the RV (see Fig. 38-1). Because of the anterior and leftward deviation of the parietal end (parietal extension) of the infundibular septum, the posterosuperior angle of the defect extends higher than that of the usual isolated conoventricular VSD (see Fig. 38-2, A) and can be more difficult to expose surgically, particularly if the parietal band is not fully mobilized (transected). When the infundibular septum is hypoplastic, the defect is larger and extends closer to the pulmonary valve; when the infundibular septum is absent, the VSD becomes juxtapulmonary (and juxta-arterial).

Posterosuperiorly, the VSD is bounded by muscle (the ventriculoinfundibular fold) adjacent to the rightward edge of the noncoronary aortic cusp (Fig. 38-8). This cusp may override considerably onto the RV (Fig. 38-9); then, the LV-aortic junction adjacent to the noncoronary cusp forms this boundary.

The posterior margin is variable. It is related to the base of the tricuspid anteroseptal leaflet commissure and to the right fibrous trigone (central fibrous body) at the nadir of the noncoronary aortic cusp. There is tricuspid-aortic-mitral fibrous continuity at this margin, and the membranous septum is absent—characteristics of a true perimembranous VSD. In some hearts the VSD extends inferiorly beneath the tricuspid septal leaflet more than usual, described as “inlet extension” of the VSD. When there is marked clockwise rotation of the overriding aortic root, the right trigone may form the posterosuperior angle of the defect, and the bundle of His (which perforates at this point) is exposed along the edge of the defect (Fig. 38-10). Occasionally the posterior margin may be formed by a remnant of fibrous tissue.

![Figure 38-8](image1)

**Figure 38-8** Specimen of tetralogy of Fallot demonstrating ventricular septal defect (VSD) and position of bundle of His. A narrow muscular bridge separates VSD from anterior tricuspid leaflet and tricuspid anulus. Right ventricle (RV) has been opened and the incision carried across infundibular septum and right coronary cusp (RC) out into the ascending aorta, as shown in Fig. 38-1. Narrow muscular bridge separating VSD from tricuspid valve is the continuity between right posterior division of trabecula septomarginalis and ventriculoinfundibular fold (VI). VI joins the undersurface of the parietal end of infundibular septum. Sutures can be passed safely into this ridge along dashed line (or, alternatively, in base of tricuspid leaflet), but the margin for error is small because the course of the bundle of His (dotted line) is not far removed. Note marked RV overriding of RC. Key: IS, Infundibular septum; NC, noncoronary cusp; RP, right posterior division of trabecula septomarginalis (septal band); RV, right ventricle; T, anterior tricuspid leaflet.

![Figure 38-9](image2)

**Figure 38-9** Specimen of tetralogy of Fallot with right ventricle and pulmonary trunk opened with an anterior incision and infundibular septum divided to expose ventricular septal defect. Accessory prominent muscular trabeculations are present in front of septal attachment of infundibular septum (arrows), contributing to stenosis. Pulmonary valve is bicuspid and tethered, with mild cusp thickening. Marked overriding of aorta is visible, involving rightward margin of noncoronary cusp. Key: Ao, Aorta; IS, infundibular septum; N, noncoronary cusp; PT, pulmonary trunk; PV, pulmonary valve; TSM, trabecula septomarginalis; TV, tricuspid valve; VSD, ventricular septal defect.
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The inferior margin of the VSD is formed by the TSM as it cradles the VSD between its limbs. The papillary muscle of the conus (or corresponding chordae only) arises from the right posterior division of the TSM at the anteroinferior angle of the defect. Anomalous tricuspid chordal attachments to other margins of the defect are rare, in contrast to the situation in isolated perimembranous VSD.

The anterior margin of the VSD is formed by the leftward anterior division of the TSM as it becomes continuous with the inferior margin of the infundibular septum. When the TSM is poorly developed, the defect extends further anteriorly, and the VSD is described as having “anterior extension.”

When the infundibular septum is absent, the VSD is juxta-arterial and is described as having “outlet extension.” Posteriorly, this type of VSD is commonly separated from the tricuspid anulus by a 2- to 5-mm strip of muscle, but it may extend to the anulus. Aortic and pulmonary valve “anuli” are contiguous over about one third of their circumferences, being separated at this point by only a thin fibrous ridge where the infundibular septum would have been, if present (see Fig. 38-3). The two valves are often side by side, with the aorta more than usually dextroposed.

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TF with this type of VSD is morphologically similar to double outlet RV with a doubly committed (juxta-arterial) VSD (see Chapter 53), with the important distinction that in TF, fibrous continuity is maintained between the aortic valve and the central fibrous body, whereas in double outlet RV there is infundibular muscle beneath the aortic valve, and thus there is fibrous discontinuity between the aortic valve and central fibrous body.

In 3% to 15% of patients (see Table 38-2), one or more additional VSDs coexist with the typical juxta-arterial one (Fig. 38-12). Usually the additional VSD is muscular, and multiple muscular defects sometimes occur. It may also be in the inlet septum, either as an inlet septal VSD or a muscular defect (see “Inlet Septal Ventricular Septal Defect” under Morphology in Section I of Chapter 35).

Figure 38-10  Two specimens of tetralogy of Fallot with perimembranous ventricular septal defect (VSD), opened as in Fig. 38-8. There is tricuspid-aortic-mitral fibrous continuity at the posterior margin (leftward in the photograph) of the VSD. A, Right fibrous trigone at nadir of noncoronary aortic cusp has been perforated by a pin passed from right atrial side at point of penetration of bundle of His; bundle extends from this point forward and slightly leftward along margin of VSD (dotted line). White arrow points to this area. VSD patch suture line must pass into base of septal tricuspid leaflet (dashed line) and not along lower VSD margin. B, Position of right fibrous trigone when there is important clockwise rotation of aortic root and right ventricular overriding of noncoronary and right aortic cusps. Bundle position is shown by dotted line and position of VSD suture line (passing into base of anterior tricuspid leaflet) by dashed line. Key: IS, Infundibular septum; NC, noncoronary cusp; T, tricuspid valve.

Figure 38-11  In this heart with tetralogy of Fallot, posterior muscular bridge is bulky and entirely hides right trigone that lies several millimeters caudal and leftward of margin of ventricular septal defect. His bundle will not be damaged by sutures passed into ridge along dashed line. Key: IS, Infundibular septum; NC, noncoronary cusp; T, tricuspid valve.
By contrast, the bundle of His does not lie on the VSD margin when a muscle ridge is present (see Figs. 38-8 and 38-11) because the ridge projects superiorly above the right fibrous trigone; when the ridge is bulky, sutures can be safely placed into it.

Aorta

The aorta is biventricular in origin and more anteriorly placed than normal, often almost obscuring the smaller pulmonary trunk from view at operation. These changes are due to RV overriding, rotation, and enlargement of the aortic root. The proportion of aorta lying above the RV varies between 30% and 90%. Generally, about 50% of the aortic orifice is over the RV.

Aortic overriding is associated with a variable degree of clockwise rotation of the aortic root (as viewed from below). This rotation moves the base of the noncoronary cusp rightward and superiorly onto the posteroseptal margin of the VSD and away from the base of the anterior mitral leaflet so that in extreme cases, it may no longer be continuous with this structure. This cusp may then lie in part just beneath the extension of the infundibular septum. Rightward rotation of the left aortic cusp results in more of it becoming continuous with the anterior mitral leaflet. Simultaneously, the superiorly positioned right cusp moves to the left, and in extreme examples it may be just beneath the uppermost extension of the left anterior division of the trabecula septomarginalis at the anteroseptal VSD margin. An important point is that, despite the degree of aortic rotation, continuity of some portion of the aortic “anulus” and the anterior mitral leaflet is always maintained. As a result the VSD is always related to the aorta in TF. The VSD may also be related to the pulmonary valve when the infundibular septum is absent (see “Ventricular Septal Defect” in this section).

Degree of overriding and clockwise rotation of the aortic root relates to degree of underdevelopment of the RV outflow tract and to deviation (malalignment) of the infundibular septum. When these are minimal, as seen with isolated low-lying infundibular stenosis, the aorta is minimally affected; when there is diffuse RV outflow tract hypoplasia in association with a small, markedly deviated infundibular septum and posterior and leftward movement of the pulmonary trunk origin, the aorta is markedly rotated and dextroposed.

In patients with severe TF, the aortic root is larger than normal, even in infants. Occasionally in adults, it is greatly dilated. This may result in aortic valve regurgitation.

Aortic Arch and Ductus Arteriosus

The ductus arteriosus is absent in about 30% of patients born with TF. This does not mean a closed ductus (ligamentum arteriosum), but rather complete absence of any ductal structure. Absence of the ductus or ligamentum is about twice as common when there is a right, rather than left, aortic arch. The pulmonary artery bifurcation often takes on a Y-shaped configuration, also described as the “staghorn” or “seagull” configuration, in this setting. In the other 70% of patients in whom a ductal structure is present, it is patent at birth and closes over a normal time course unless pharmacologically maintained with PGE1 for therapeutic reasons (cyanosis). The configuration of the ductus can vary from normal (an extension of the pulmonary trunk, creating an arch that somewhat

Conduction System

The sinus and atrioventricular nodes are in their normal locations (see “Conduction System” in Chapter 1), and the bundle of His follows the same general course as in patients with isolated perimembranous VSDs (see “Location in Septum and Relationship to Conduction System” under Morphology in Section I of Chapter 35). Thus, the His bundle emerges through the right fibrous trigone at the base of the noncoronary cusp of the aortic valve and courses forward toward the papillary muscle of the conus along the inferior VSD margin or slightly to the left side of the defect edge. In hearts showing marked clockwise rotation of the aortic root with RV overriding, the right trigone (and along with it the penetrating portion of the His bundle) is carried more rightward and superiorly and directly onto VSD margins (see Fig. 38-10).
Chapter 38  Ventricular Septal Defect with Pulmonary Stenosis or Atresia

A left aortic arch is present in about 75% of patients. In these, arch branching pattern is usually normal.

A right aortic arch is present in about 25% of patients. In 90% of these, there is mirror-image branching of the arch. Should a patent ductus arteriosus be present, it usually arises from the brachiocephalic or proximal left subclavian artery and joins the LPA. Rarely, there may be a right-sided ductus arteriosus to the RPA, usually arising from the upper descending thoracic aorta. In about 10% of patients, there is an aberrant left subclavian artery, analogous to the aberrant right subclavian artery of dysphagia lusoria in left aortic arch (see “Right Aortic Arch with Aberrant Left Subclavian Artery” in Section I of Chapter 51). In right aortic arch with aberrant left subclavian artery, the subclavian artery may arise directly from the descending aorta or from an aortic diverticulum. Thus, a ductus arteriosus may arise from the aortic diverticulum and pass to the left behind the esophagus to join the LPA.

Rarely, the left subclavian artery is sequestered or isolated from its aortic arch origin, but remains connected to the LPA by a patent ductus arteriosus. Often in these circumstances, there is vertebral steal, and on angiography the subclavian artery fills with contrast from the vertebral artery.

Right Ventricle

External dimensions of the sinus (inflow) portion of the RV are larger than normal due to hypertrophy, so the interven- tricular groove is displaced leftward and the LV lies more posteriorly than usual (clockwise rotation of ventricles). The RV sinus may be clearly separated from the infundibulum during systole by a transverse depression representing the site of maximal infundibular stenosis inferior to an infundibular chamber. RV wall thickness equals that of the LV and is therefore never excessive unless the large VSD is made restrictive by a fibrous flap valve on its right side (see Section IV). Normal trabeculations are, however, bulky and prominent. RV end-diastolic volume may be reduced and ejection fraction mildly depressed, typically in older children without TF repair, possibly the result of chronic hypoxia. Rarely (1.5% of cases), the sinus portion of the RV and tricuspid valve are underdeveloped, and rarely this may be so severe (end-diastolic volume < 30 mL · m−2) as to contraindicate primary repair.

The physiologic contributors to LV size are complex. The small pulmonary and thus left atrial blood flow tend to result in a small left atrium and LV. However, the RV ejects blood into the LV as well as the aorta, and this tends to increase LV size. Mild or moderate degrees of LV hypoplasia may result from these physiologic factors, but true hypoplasia is of morphologic rather than functional origin. LV systolic function is normal at birth but may become mildly reduced in older patients who have not undergone repair, particularly in severely cyanotic patients, presumably because of chronic hypoxia.
**Table 38-3** Minor Associated Cardiac Anomalies in Patients Undergoing Repair of Tetralogy of Fallot with Pulmonary Stenosis or Atresia (n = 836)\(^4\)

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>n</th>
<th>% of 836</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial septal defect</td>
<td>75</td>
<td>9</td>
</tr>
<tr>
<td>Persistent left superior vena cava</td>
<td>68</td>
<td>8</td>
</tr>
<tr>
<td>Anomalous origin of LAD from RCA</td>
<td>34</td>
<td>4</td>
</tr>
<tr>
<td>Aberrant origin of right subclavian artery</td>
<td>2</td>
<td>0.3</td>
</tr>
<tr>
<td>Absent right superior vena cava</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Azygos extension of inferior vena cava</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Congenital heart block</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Juxtaposition of atrial appendages</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Vascular ring</td>
<td>1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

\(^4\)UAB experience (1967 to July 1982).  
Key: LAD, left anterior descending coronary artery; RCA, right coronary artery.

Coronary Arteries
As in other cyanotic conditions, the coronary arteries become dilated and tortuous in children and adults. A large conal branch of the right coronary artery (RCA) usually courses obliquely across the free wall of the RV, and the presence of this vessel should be noted at the time of surgical repair.

The left anterior descending coronary artery (LAD) arises anomalously from the RCA in about 5% of patients (Table 38-3).\(^1\)\(^-\)\(^4\)\(^,\)\(^5\) The entire LAD may originate from the RCA and cross the anterior wall of the infundibulum a variable distance from the pulmonary valve, or only the distal part of the LAD may arise anomalously, in this case usually from the large conal branch of the RCA.

Rarely, the RCA originates from the left coronary artery, and equally uncommonly, there is anomalous origin of the left coronary artery from the pulmonary trunk (see Section II of Chapter 46).\(^4\)\(^4\)

Major Associated Cardiac Anomalies
Major associated cardiac anomalies are relatively uncommon (see Table 38-2). Patent ductus arteriosus, multiple VSDs, and complete atrioventricular septal defect\(^6\)\(^,\)\(^7\) are most often seen.

Rarely, the RPA\(^8\)\(^9\) or LPA\(^10\)\(^11\) arises anomalously from the ascending aorta\(^12\)\(^,\)\(^13\) (see Chapter 45). This complicates the pathophysiology and repair, because the lung supplied by the pulmonary artery arising from the aorta usually has overcirculation, and the other usually has restricted flow due to the intracardiac anatomy.

Infrequently, aortic valve regurgitation coexists. This may be from typical cusp prolapse in TF with subarterial VSD (see Section II in Chapter 35).\(^14\)\(^15\) A bicuspid aortic valve occurs rarely in TF and may result in aortic regurgitation.\(^16\)\(^,\)\(^17\) Occasionally, ill patients with TF in the second decade of life or older develop aortic regurgitation from endocarditis.\(^18\)\(^,\)\(^19\)\(^,\)\(^20\) Massive dilatation of the aortic root from anuloaortic ectasia may result in aortic valve regurgitation,\(^21\) particularly in patients with large natural or surgically created systemic–pulmonary arterial shunts (see “Anastomotic” under Morphology in Chapter 26).

Minor Associated Cardiac Anomalies
Most infants undergoing repair of TF have a patent foramen ovale (PFO); when all ages are considered, a true atrial septal defect is found at operation in about 10%. Other minor associated cardiac anomalies are listed in Table 38-3.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

**Clinical Presentation**
The hallmark clinical sign of TF is cyanosis. The severity of cyanosis and its variability depend on the specific morphology of the RV outflow tract. Infants with diffuse RV outflow hypoplasia, severe infundibular plus valvar plus anular stenosis, or severe infundibular plus valvar stenosis (see Box 38-1) are deeply cyanotic from birth and do not develop heart failure. They are breathless on feeding or other exertion. Hypoxic spells are rare, the cyanosis being constant and gradually worsening. It is seldom lessened by propranolol.

This situation contrasts with that in infants having dominant infundibular stenosis, in which onset of cyanosis is delayed and hypoxic (cyanotic) spells due to infundibular spasm may occur. These spells are often prevented or lessened in frequency by propranolol. Characteristically, they become less frequent with age, presumably because stenosis becomes fixed as a result of acquired endocardial fibrosis and thickening.

In up to 10% of patients who require surgical relief in infancy, presentation is initially as a large VSD with pulmonary plethora and sometimes heart failure at age 2 to 3 months, followed by gradually increasing cyanosis, frequently with cyanotic spells, at about age 6 months. In this group, stenosis is purely infundibular.

A minority of patients are acyanotic at rest and only mildly cyanotic during exercise because pulmonary stenosis is mild and right-to-left shunting minimal. In some the shunt is predominately left to right. These individuals may remain acyanotic without spells and present at any age within the first or second decades of life with gradually increasing cyanosis and breathlessness as stenosis slowly increases in severity.

In patients with severe cyanosis and polycythemia, cerebral thrombosis may precipitate hemiplegia at any age (particularly in association with dehydration), or hemiplegia may follow paradoxical embolism or a brain abscess. The latter is heralded by fever, headache, and sometimes seizures. Massive hemoptysis may occur in older patients who are severely cyanotic, presumably from rupture of bronchial collateral vessels.

Cyanosis is always accompanied by effort dyspnea that is sometimes the dominant symptom, and as the child begins to walk (frequently much later than for a healthy child), cyanosis is often accompanied by squatting, which lessens its severity.\(^22\) There may be increased occurrence of respiratory infection, but not to the same extent as in patients with large isolated VSD; failure to thrive is also less striking.

**Physical Examination**
Cyanosis of variable degree is generally evident. Deeply cyanotic infants are often obese (in contrast to infants with isolated VSD). Severe symmetric clubbing of the fingers and toes is often present in children and adults, but not in infants.
Older patients may also have marked acne of the face and anterior chest. Jugular venous pressure is normal. The heart is not enlarged and is relatively quiet with an unimpressive RV lift. In those few patients with increased Qp, the lift may be more marked than usual.

A precordial systolic thrill is rare. There is a moderate-intensity middiastolic pulmonary (ejection) murmur maximal in the second and third left intercostal spaces that becomes less prominent or even disappears when the stenosis is severe. When there is still a reasonable blood flow in the presence of moderate pulmonary stenosis, the systolic murmur is well heard posteriorly and in the axilla. In the presence of important cyanosis and low Qp, the second heart sound is single, but in acyanotic patients it may be finely split with a low-intensity pulmonary component. Splitting is also present in moderately cyanotic patients with only a mildly reduced Qp when there are important pulmonary artery origin stenoses.

Signs of heart failure with venous pressure elevation and liver enlargement occur in patients with a systemic-to-pulmonary arterial shunt that is too large, or in a neonate on PGE1 to maintain ductal patency. Heart failure may also appear in untreated severely cyanotic adults in the fourth or fifth decade of life, presumably secondary to myocardial fibrosis or in association with systemic hypertension or aortic regurgitation.

Laboratory Studies

Neonates or young infants who have severe TF with pulmonary stenosis usually present with marked reduction of arterial oxygen pressure (\(\text{PaO}_2\)) and saturation (\(\text{SaO}_2\)) and sometimes with metabolic acidosis. Polycythemia is rarely present, and, in fact, such infants are often anemic.

In older infants and children, red blood cell count and hematocrit are usually elevated, and degree of elevation is correlated with degree of arterial desaturation and thus with severity of the pulmonary stenosis. In older patients, hematocrit may reach 90%.

Most cyanotic patients have depressed platelet count and prolongation of most coagulation tests.

Chest Radiography

Chest radiographs in children usually show the typical boot-shaped heart of TF. In neonates and young infants the heart may be strikingly small, with an absent pulmonary artery segment along the left upper cardiac border and oligemic lung fields. In older patients, there may be a prominence of the left upper cardiac border caused by a large infundibular chamber. Large AP collaterals may alter the pulmonary blood flow pattern in one or both lungs. Plethora of one lung and oligemia of the other suggest anomalous origin of a pulmonary artery from the ascending aorta (see Chapter 45).

If there is a right aortic arch, posterior indentation of the shadow of the barium-filled esophagus results from an aberrant left or right subclavian artery.

Rib notching of the upper ipsilateral ribs may develop in the presence of a long-standing classic Blalock-Taussig (B-T) shunt, secondary to development of a rich collateral blood flow to the arm. This situation is rarely encountered in the current era because the classic B-T shunt is not commonly performed. Presumably, the same pathophysiology could develop after a modified B-T shunt if the subclavian artery were severely stenotic or occluded. Rarely, collaterals from the pleura to the lung may be sufficiently large, especially after poudrage or pleural stripping procedures, to result in bilateral rib notching in the lower half of the thorax. Patients in the second or third decade of life may show progressive kyphoscoliosis.

Electrocardiography

Electrocardiography (ECG) shows moderate RV hypertrophy consistent with RV pressure that is equal to but not greater than systemic pressure (in contrast to flap valve VSD; see Section IV). Occasionally, there is minimal RV hypertrophy, and in these circumstances RV underdevelopment should be suspected, although it may not be present. Left precordial leads are characterized by absent Q waves and low-voltage R waves. Occasionally the frontal plane vectorcardiographic pattern characteristic of atroventricular septal defect is found in patients with typical TF.

Echocardiography

ECG is considered the definitive diagnostic procedure of choice in neonates and infants. The VSD, atrial septal status, aortic overriding, narrowing of the RV infundibulum, pulmonary valve, pulmonary trunk and bifurcation into the branch pulmonary arteries, and the ductus arteriosus, if present, can usually be seen with ECG (Fig. 38-14). Also, in experienced hands, two-dimensional (2D) echocardiography with Doppler color-flow interrogation has the same sensitivity and specificity for multiple VSDs in TF as does cineangiography. However, morphologic details of distal pulmonary artery branches as they approach the hilum may not be reliably visualized. Additional imaging is indicated when important abnormalities of the branch pulmonary arteries are identified, such as hypoplasia, discontinuity, or stenosis, and when abnormal arterial signals on Doppler interrogation are identified in the central and posterior mediastinum, suggestive of major AP collaterals.

Color Doppler imaging can also provide important physiologic information. Accurate estimates of the severity of obstruction across the RV outflow tract, as well as the site of obstruction (infundibular, valvar, supravalvar), can be obtained. Flow characteristics across the VSD and LV outflow tract can be used to confirm that pressures in the RV and LV are equal. Systolic function of the ventricles and competency of the inlet valves are also easily assessed, and flow patterns across the inlet valves in diastole can provide important information about ventricular diastolic function. In most cases the coronary artery pattern can be characterized, and anomalous patterns, such as the LAD arising from the RCA, can be identified.

Newer modalities of echocardiography, such as 3D echo, tissue Doppler, and strain rate imaging, hold further promise as noninvasive tools for improved morphologic and functional evaluation.\(^{32}\) Echocardiography can effectively diagnose TF in the fetus,\(^{35}\) and can be helpful in planning early surgical intervention and in parental counseling.\(^{327}\)

In patients who have undergone operation for TF, whether palliative procedures or definitive repair, and in unoperated TF patients presenting well beyond infancy, echocardiography is an important part of the diagnostic workup; however, it is not definitive. Characterizing pulmonary vascular...
resistance (Rp) and imaging the distal pulmonary arteries require cardiac catheterization.

Cardiac Catheterization and Angiography
Preoperative cardiac catheterization and angiography, although not routinely required when expertly interpreted echocardiography is available, precisely portray the hemodynamic state and morphology, particularly that of the distal pulmonary arteries. Peak pressure in the RV cavity (P_{RV}) is similar to that in the left (P_{LV}), and pulmonary artery pressure (P_{PA}) is below normal. A systolic pressure gradient is demonstrable at infundibular and valvar levels when both zones are stenotic, but rarely at a more peripheral site. When proximal stenoses are severe, however, it may be impossible to enter the pulmonary trunk with a catheter.

There is right-to-left shunting at ventricular level and low Qp, the severity of which reflect severity of stenosis. In acyanotic patients, there is minimal right-to-left shunting at rest or even a slight increase in Qp, but in most patients, right-to-left shunting occurs on exercise. In severely cyanotic patients, P_{PA} and Rp are not elevated preoperatively, even in the presence of important peripheral pulmonary artery stenosis or thrombosis, because of low Qp. P_{PA} may be elevated when there is a large Qp and an increase in Rp.

Biplane cineangiography demonstrates all the morphologic features of the malformation as well as morphology and dimensions of the RV–pulmonary trunk junction, pulmonary trunk, and RPA and LPA and their branches. Oblique and angled views are used. Configuration of the RV sinus and infundibulum and degree and morphology of the RV outflow tract obstruction are studied. Morphology of the pulmonary valve and any tethering or narrowing of the pulmonary trunk at the level of the commissural attachments of the valve or beyond are noted. Bifurcation of the pulmonary trunk and origins of the LPA and RPA are studied with particular care because the surgeon cannot accurately assess presence or severity of stenoses in this area during operation. The
diagnostic test and in patients after palliative surgery or reparative surgery. It can define the branch and peripheral pulmonary arteries accurately and has replaced conventional angiography for many clinical indications (Fig. 38-16). The chief advantage is that it requires only peripheral intravenous access for contrast injection, thereby removing the risk of catheter-induced complications. Furthermore, CT images are 3D and amenable to image postprocessing (Fig. 38-17), whereas images from conventional angiography are projectional and overlapping vessels can be difficult to interpret. Conventional angiography has better spatial resolution, and
selective branch injections may reveal flow dynamics in collateral branches better than CTA.

At the present time, when echocardiography is not sufficient to allay concerns about peripheral pulmonary artery abnormalities, CTA may be indicated to clarify the morphologic details. The decision to use conventional versus CTA is partly based on institutional expertise and preference; however, if hemodynamic information is required, or if major AP collaterals are suspected, catheterization is necessary.

In neonates and infants with suspected branch pulmonary artery abnormalities on echocardiography, in whom there is usually little concern about abnormal Rp, CTA is an excellent method for defining pulmonary artery stenoses and arborization abnormalities. In patients with systemic to pulmonary artery shunts, in whom concerns about Rp abnormalities are not present, CTA can define the morphologic details of the peripheral pulmonary arteries, systemic-pulmonary collateral vessels, and their pulmonary distributions. Cardiac-gated CTA can also reveal unanticipated coronary artery anomalies associated with TF (see Fig. 38-17). In postrepair TF patients with residual RV outflow tract abnormalities, CT can accurately characterize the morphology from the infundibulum to the peripheral pulmonary arteries and help detect native stenosis and conduit stenosis (Fig. 38-18) and aneurysm or pseudoaneurysm (Fig. 38-19).

**Magnetic Resonance Imaging**

Magnetic resonance imaging (MRI) is also used selectively in TF. Generally speaking, CTA has higher spatial resolution than MRI, and therefore CT is preferred when finely detailed peripheral pulmonary vascular morphologic information is required. MRI can accurately define the anatomy of the RV outflow tract and branch pulmonary arteries (Figs. 38-20 and 38-21). MRI has the advantage that it does not use ionization radiation and is a good choice in larger patients and when repeated studies are anticipated. In neonates and infants, preoperative echocardiography is usually adequate and MRI is rarely indicated.

The major indication for MRI is in postrepair TF patients with chronic pulmonary regurgitation. RV volume, pulmonary valve regurgitant fraction, coexisting pulmonary stenosis, and tricuspid valve regurgitant fraction can all be assessed quantitatively (Fig. 38-22). Serial examinations can accurately define trends in the values of these variables over time, and these trends can be helpful in determining the timing of reoperation. RV end-diastolic volume greater than 150 mL · m$^{-2}$ in children has been identified as a threshold above which the RV is likely not to normalize its volume even after placement of a pulmonary valve prosthesis.

When pacemakers or defibrillators are present, MRI is contraindicated. Under these conditions, CTA can be an excellent alternative.

**NATURAL HISTORY**

The natural history of patients having TF with pulmonary stenosis without major associated cardiac anomalies is variable and is determined primarily by severity of RV and pulmonary arterial outflow obstruction.
Symptoms and Survival

Twenty-five percent of surgically untreated infants die in the first year of life, but uncommonly in the first month (Fig. 38-23, A and B). These are the patients with the most severe obstruction to pulmonary blood flow. Forty percent are dead by age 3, 70% by age 10, and 95% by age 40. Instantaneous risk of death (hazard function) is greatest in the first year of life (Fig. 38-23, C). Risk then stays constant until about age 25, when it begins again to increase.

Hypoxic spells in the first few years of life are related to hyperactivity of the infundibulum. This and contraction of the infundibular septum and its parietal extension earlier in systole than in normal subjects produce variable and sometimes severe episodes of RV outflow tract obstruction and symptoms. Any sudden reduction of systemic vascular resistance also may precipitate a hypoxic spell.

About 25% of patients are acyanotic at birth and become cyanotic in the ensuing weeks, months, or years as pulmonary stenosis increases. Progression of arterial desaturation, cyanosis, and polycythemia is variable and is furthered not only by increasing pulmonary stenosis but also by widespread tendency to thrombosis of the smaller pulmonary arteries, with progressive reduction in Qp. As part of this same tendency, death may result from cerebral thromboses or abscesses.

In those few patients surviving into the fourth and fifth decades of life, death is commonly from chronic heart failure due to secondary cardiomyopathy that results from RV pressure overload and chronic hypoxia and polycythemia.

Pulmonary Artery Thromboses

In severely cyanotic and polycythemic patients, diffuse pulmonary arterial thrombosis can occur. This is initially visible only microscopically, but rarely it progresses to occlusion of a lobar pulmonary artery or even an entire RPA or LPA. Usually, Rp is not importantly increased by this process, but rarely the thrombosis is so widespread and severe as to be a
Figure 38-22  Right ventricular outflow tract cardiovascular magnetic resonance study of a patient with repaired tetralogy of Fallot with important late pulmonary regurgitation. A, Cine image. Red dotted line illustrates through-plane in which a non–breath-hold phase encoded velocity map was acquired. B, Flow curve obtained from same patient. Through integrating areas containing forward and reverse flow, a pulmonary regurgitation fraction of 34% was calculated. (From Shinebourne and colleagues.)

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Figure 38-23  Natural history of surgically untreated patients having tetralogy of Fallot with pulmonary stenosis or pulmonary atresia. A, Survival to age 60 years. Smooth lines represent survival of each group, and dashed lines enclose 70% confidence limits. B, Survival to age 10 years (expanded time scale). C, Hazard function according to age. (From Bertranou and colleagues.)
cause of immediate and sometimes fatal pulmonary hypertension and RV failure following repair.

Pulmonary Vascular Disease

Pulmonary vascular disease rarely develops in surgically untreated patients. It may develop following too large a systemic to pulmonary arterial shunt (see “Interim Results after Classic Shunting Operations” later in this section). When a surgical shunt appears to be the cause, it is possible that preexistent pulmonary arterial thrombosis has compounded the problem.

Genetic History

Offspring of a parent who has TF are more likely to have the anomaly than offspring of parents without congenital heart disease. It is estimated that about 0.1% of live births have TF under the latter circumstances and about 1.5% under the former.29

TECHNIQUE OF OPERATION

General Plan and Details of Repair Common to All Approaches

Surgical Evaluation

Outcome of repair of TF depends mainly on relief of pulmonary stenosis, whether infundibular, valvar, pulmonary arterial, or (as is usual) a combination of these. Therefore, the surgeon must come to the operating room with a clear mental image of the morphology as it has been displayed in the preoperative imaging studies, particularly as it relates to the RV and pulmonary arterial outflow obstruction.

After median sternotomy, external anatomy of the heart is studied, with particular attention to RV and pulmonary artery anatomy and configuration of coronary arteries crossing the RV. The preoperative imaging studies are mentally reviewed; these and observation of the heart determine the incision and details of repair.

Conceptual Approach to Surgery

The idealized goal of repair is to eliminate intracardiac shunting, reduce RV pressure and volume load to normal, and preserve normal myocardial function. This is accomplished by complete closure of the VSD (and atrial septal defect if present) and complete relief of the RV outflow tract obstruction while maintaining a competent pulmonary valve. This ideal is achieved in only a minority of patients, generally those with the most favorable RV outflow morphology, consisting of a normal or nearly normal pulmonary “anulus” and functioning pulmonary valve cusps (see discussion of variability of RV outflow tract morphology under Morphology in this section). In all other cases, the repair will fall short of ideal. Thus, in most cases, a number of important morphologically driven decisions must be made during repair, and these decisions will determine how closely the repair will approach the ideal. The decisions listed here (and discussed further in text that follows) often involve both technical and conceptual elements:

- Performing a transanular patch and determining width of the patch
- Preserving or sacrificing RCA branches
- Managing the RV outflow tract when an anomalous LAD is present
- Technically approaching abnormal pulmonary valve cusps, and preserving cusps when transanular patching is performed
- Managing atrial septal defects and PFOs
- Managing the tricuspid valve when septal leaflet function is compromised at VSD closure
- Dividing or resecting obstructing septal and parietal muscle bands in the RV outflow tract.

Approach

Surgical access to the VSD and RV outflow tract through a right atriotomy, supplemented by evaluating the pulmonary valve via a pulmonary arteriography in most cases, is advocated by some.123,111 This approach makes sense when a well-developed infundibulum is present; however, if there is diffuse hypoplasia of the RV outflow tract, and a full-length transanular patch is anticipated, this approach makes little sense. Additionally, if a small tricuspid valve is present, exposure through the right atrium may be difficult, especially in small infants, and more damage than good may result from traction on the myocardium and tricuspid valve. Nevertheless, initial approach through the pulmonary artery and right atrium is preferred in all situations by some.

Transanular Patch

The question of whether to use a transanular patch arises in many cases, and this decision is now known to have far-reaching implications for long-term outcome. Recent publications continue to emphasize the detrimental effects of large transanular incisions.822,1314 A transanular patch creates obligatory pulmonary regurgitation, and when this is long-standing and severe, important RV dysfunction will inevitably occur (see Results later in this section). Degree of narrowing of the “anulus” can be expressed quantitatively by a z value—that is, the number of standard deviations (usually smaller) from normal. When the z value has been determined from echocardiography, corrected and transformed cineangiographic measurements, or MRI or CTA to be larger than −3, the surgeon’s bias should be that a transanular patch is probably unnecessary (Fig. 38-24); when it is −3 or smaller, a patch is probably required. The surgeon’s bias should also be that even with a transanular patch, when the z value of the “anulus” is less than −7 (<10% of cases), postrepair ratio of peak pressure in the RV to that in the LV (P_{RV/LV}) may be I or higher, even with a properly placed transanular patch (Fig. 38-25). It can be inferred from the findings outlined in Fig. 38-24 that the extremely small pulmonary valve “anulus” may in some cases be associated with diffuse hypoplasia of the distal pulmonary arteries. Thus, when a very small “anulus” is noted, preoperative evaluation of the distal pulmonary vasculature and Rp should be undertaken. If distal hypoplasia, elevated Rp, or both are observed, a reparative operation should be avoided (at least temporarily) in favor of a shunt procedure. It must be emphasized that the z value is used only as a guideline. The pulmonary valve cusp configuration—number, thickness, and fusion—will influence the eventual gradient across the RV outflow tract after repair, and because of these variables, different gradients may result despite similar z values. Thus, the actual gradient should always be assessed after separation.
from cardiopulmonary bypass (CPB), at a minimum by intraoperative echocardiography, and preferably by direct pressure measurement.

**Right Coronary Artery Branches** As a general principle, visible-to-the-eye RV coronary artery branches should be preserved whenever possible. Occasionally visible branches must be transected to achieve acceptable RV outflow obstruction relief. Before transecting a branch, its course should be fully examined. Those that traverse the body of the RV, and even those smaller branches that supply muscle farther down on the RV infundibulum than the lower margin of the infundibular incision, should be preserved. When necessary, small transverse infundibular branches, with distal perfusion that stays above the lower margin of the infundibular incision, can be sacrificed.

**Anomalous Left Anterior Descending Coronary Artery** When an anomalous LAD arises from the RCA, modifying RV outflow tract management is often, but not always, necessary. Key factors are the exact course of the coronary artery and morphology of the infundibulum. In cases with a LAD that crosses high in the infundibulum near the valve anulus, and with low infundibular obstruction and a well-developed distal infundibular chamber, the obstruction can be addressed without endangering the coronary artery. On the other hand, when severe diffuse infundibular hypoplasia is present and the obstruction can be addressed only by placing a conduit from the RV to the pulmonary trunk, the RV-conduit anastomosis should be placed proximal to the coronary vessel. Occasionally the anomalous LAD is intramyocardial. This should be suspected when the left aortic sinus gives rise to an isolated circumflex coronary artery.

**Pulmonary Valve** The pulmonary valve cusps should be assessed carefully, especially when a transanular patch is necessary. There is a high likelihood of bicuspid valve when a transanular patch is needed (small anulus). Orientation of the two commissures may be directly anterior and posterior, directly left and right, or any position in between. With the exception of the direct lateral orientation, the transanular incision can be designed to cross the anulus precisely through the most anterior commissure, thereby preserving the function of both cusps. This maneuver minimizes the severity of pulmonary regurgitation that results from the transanular patching.

**Atrial Septal Communications** Managing the atrial septum can be essential to repair, particularly in neonates and infants. The combination of a transanular patch and high Rp can lead to postoperative RV failure. If the foramen ovale is patent under these conditions, it should be left patent. If the PFO has naturally closed, it can be reopened using a blunt instrument in most young infants. If a true atrial septal defect is present, it should be subtotally closed using a patch, leaving a small open flap that overlaps the edge of the limbus, to function like a PFO. The resulting cyanosis of atrial right to left shunting is well tolerated postoperatively, because chronic cyanosis is typically present preoperatively. In patients who do not receive a transanular patch, the atrial septum can typically be completely closed.

**Tricuspid Valve** Careful attention to the tricuspid valve during VSD closure is essential, particularly in small infants. Tethering of the septal leaflet and distortion of chordal structures during VSD closure is sometimes inevitable. Valve competency should be tested routinely after VSD closure. If regurgitation is present, tricuspid valve repair should be performed. Partial closure of the anterior septal leaflet commissure is effective in restoring tricuspid valve competency when septal leaflet tethering is present. A competent tricuspid valve is critical to achieving excellent outcome, especially if a transanular patch is used.

**Right Ventricular Muscle Bundles** Surgical myotomy or myectomy to manage obstructing septal, parietal, and free-wall muscle bundles in the infundibulum can have both short- and long-term implications for RV function. Despite its necessity, it remains one of the most destructive procedures in all of pediatric cardiac surgery. A minimalist approach is recommended in most cases. In neonates and infants, in whom fibrosis and excessive hypertrophy are not yet present, incision of obstructing septal and/or parietal bands without excision is all that is necessary. In many cases,
if these muscle bundles are not obstructive, patching of the longitudinal infundibular incision is all that is needed to relieve infundibular obstruction. In older patients, when important fibrosis, hypertrophy, or both are present, simple incision may not relieve the obstruction, and excision may be required.

Preparations for Cardiopulmonary Bypass
Before establishing CPB, the ascending aorta is dissected free from the pulmonary trunk so that when the aortic clamp is in position, the pulmonary trunk and RPA are undistorted. Unless it is clear from preoperative imaging studies that the pulmonary trunk bifurcation and central and hilar portions of the LPA and RPA are free of stenoses or diffuse hypoplasia, these too are mobilized. On the left side, this is aided by cutting the pericardium down to the LPA, dissecting away and preserving the left phrenic nerve. The ligamentum (or ductus) arteriosum, if present, is dissected, ligated, and divided. Division of the ligamentum (or ductus) will prevent tethering of the proximal LPA, which can cause late kinking and obstruction, especially when a transanular patch is used at repair. On the right side the aorta is retracted anterior and to the left, and the RPA is dissected completely away from it out to the superior vena cava and beneath it if necessary.

Any surgically created shunts are at least partially dissected before establishing CPB (see later sections on repair after various shunts).

Technical Details of Repair
Immediately after CPB is established, all surgically created shunts are ligated or divided, and the ductus (if present) ligated and divided if this has not been accomplished prior to establishing CPB. Thereafter, once the heart is arrested, the right ventriculotomy or right atriotomy is made and the internal anatomy further visualized and conceptualized. The plan is to:

- Dissect and resect the infundibular stenosis (recalling that this may be at several levels).
- Visualize the pulmonary valve and open it if necessary.
- Estimate dimensions of the outflow tract, valve, and anulus with a Hegar dilator, and decide whether a transanular patch is needed.
- Repair the VSD.
- Evaluate the atrial septum and make a decision about closing any defects or leaving a PFO.
- Evaluate residual RV outflow tract obstruction following separation from CPB.

Repair is similar whether an RV or right atrial approach is chosen and is represented in Figs. 38-26 through 38-29, which should be studied in parallel with this text to obtain the most complete understanding of the pathologic anatomy and its repair.

Infundibular Dissection In patients presenting for surgery beyond early infancy, considerable RV infundibular muscle hypertrophy and fibrosis are typical, requiring a number of maneuvers during the infundibular dissection. The parietal extension of the infundibular septum is dissected away from the RV free wall and ventriculoinfundibular fold and is divided transversely 5 mm or so to the right of the attachment of the right coronary cusp of the aortic valve to the undersurface of the infundibular septum. This increases diameter of the infundibulum at its rightward end and improves exposure of the VSD from the RV approach. Any obstructive trabeculae along the left side of the outflow tract are also incised and partially removed. The aim is to increase the circumference of the infundibulum by enlarging each lateral recess in front of the infundibular septum. An obstruction at a low level (coronal plane) is relieved by dividing anomalous trabeculae above the moderator band while protecting adjacent papillary muscles; the moderator band is divided only when necessary to relieve the obstruction. When an os infundibulum is present at the level of the inferior edge of the infundibular septum, the fibrous thickening all around the ostial orifice is excised, as is any fibrous obstruction extending upstream toward the pulmonary valve. If the infundibular resection is performed using an RV infundibular incision, the...
Figure 38-27  Repair of tetralogy of Fallot via right ventricular (RV) approach using vertical incision. **A,** Superiorly, incision stops short of pulmonary valve “anulus” and may vary according to presence and direction of a large conal branch of right coronary artery. **B,** RV incision is spread widely by retraction sutures. Parietal extension of infundibular septum is transected where it begins to fuse with RV free wall, dissected away from ventriculoinfundibular fold, and then amputated from infundibular septum. This uncovers the ventricular septal defect (VSD) and tricuspid valve. Ventriculoinfundibular fold remains unseen because it is overhung by the tricuspid valve anterior leaflet. **C,** Parietal extension has been mobilized (divided and partially amputated). Septal extension is likewise mobilized to maximize circumference of infundibular outflow tract.
Figure 38-27, cont’d  

D, Pledgeted mattress suture is placed from right atrial side through base of commissural tissue between septal and posterior tricuspid leaflets and through patch. A few more stitches are taken, working posteriorly between base of septal leaflet and patch, followed by stitches through ventriculoinfundibular fold and patch.  

E, Suturing is continued onto parietal extension and infundibular septum, visualizing and staying close to aortic valve leaflets to avoid leaving a hole between muscular bands. Suture is then held. With other arm of suture, a few stitches are taken, working anteriorly between septal tricuspid leaflet and patch, weaving beneath any chordae crossing the VSD. When this has taken the suture line about 5 mm inferior to edge of the VSD, stitches are taken in septum, well back from VSD edge.  

F, Repair of VSD is completed. Note that suture line is away from bundle of His and its branches, except where it crosses the right bundle branch anteroinferiorly. Crista supraventricularis is pulled downward by the patch, which helps increase infundibular outflow circumference. Key: LAD, Left anterior descending coronary artery; RBB, right bundle branch; RCA, right coronary artery; TSM, trabecula septomarginalis.
Figure 38-28  Anatomy of tetralogy of Fallot from perspective of right atrial approach, shown as if right atrial free wall and tricuspid valve were translucent. The striking difference from the right ventricular (RV) perspective (see Fig. 38-27) is apparent position of parietal extension. From right atrial perspective, the surgeon is looking beneath this, as parietal extension arches over the RV outflow tract. Ventriculoinfundibular fold is easily seen through tricuspid valve. Key: AV, Atrioventricular; IVC, inferior vena cava; SVC, superior vena cava; TV, tricuspid valve; VSD, ventricular septal defect.

Figure 38-29  Repair of tetralogy of Fallot, right atrial approach. A, A high right atrial incision made close to the atrioventricular groove aids exposure. Ventricular septal defect (VSD) is located beneath anteroseptal commissure, indicated by dashed line. B, VSD is closed before amputating parietal extension. A pledged double-armed suture is begun at the anteroinferior aspect of VSD about 5 mm away from rim to avoid conduction fibers.

Incision is closed with a patch of glutaraldehyde-treated autologous pericardium or other material (see “Decision and Technique for Transanular Patching” later in this section). Direct closure could narrow the outflow tract. When a transanular patch is needed, a glutaraldehyde-treated or untreated pericardial patch is inserted after extending the infundibular incision across the pulmonary “anulus.”

This type of anatomic dissection is not possible in the presence of diffuse RV outflow hypoplasia and is often not possible when there is combined infundibular, valvar, and anular stenosis. These structures are all hypoplastic, a situation frequently encountered in patients who have become importantly symptomatic, as neonates or infants, and patch graft enlargement is often all that can be accomplished. In any event, particularly in infants, resection or even transection of RV muscle bundles that are not obstructive must be avoided because this unnecessarily impairs RV function.

Pulmonary Valvotomy If pulmonary valvotomy is needed, a vertical incision is made in the pulmonary trunk, taking care to avoid damaging the valve commissures (Fig. 38-30). The
pulmonary arteriotomy is not made through a commissure between the cusps, because placing a patch in such an incision renders the valve regurgitant. Rarely can an adequate valvotomy be performed by simply dividing one or more sites of commissural fusion, because fusion is present in only 20% of stenotic valves and is almost always associated with important cusp thickening, particularly at the cusp free edge (see Morphology earlier in this section). After valvotomy, therefore, the surgeon may elect to excise the thickened cusp edge to relieve the stenosis, although some pulmonary valve regurgitation results. When there is cusp tethering only, the most common situation, the cusp edge may be cut from its attachment to the pulmonary artery wall over about 3 mm. This is done to one cusp at each commissure. Here, too, excising thickened cusp tissue may be required. Regurgitation from minor detachment of a cusp may be less than that from a transanular patch. If considerable cusp incision and detachment are required, regurgitation results; if there is also important residual narrowing, it is preferable to excise the cusps and place a transanular patch after completing the intraventricular part of the repair. If a transanular patch is not needed (see “Decision and Technique for Transanular Patching” later in this section), the pulmonary arteriotomy is closed, usually with a pericardial patch.

**VSD Closure** In children and adults, the VSD is closed with a filamentous polyester or polytetrafluoroethylene...
Figure 38-30  Repair of tetralogy of Fallot with separate infundibular and pulmonary arterial patches. **A,** Pulmonary trunk incision is shown extending to but not into pulmonary valve “anulus” (dashed line). Vertical ventriculotomy is also shown. **Inset,** Stenotic pulmonary valve seen through pulmonary arteriotomy. Fused commissures are incised with a knife to the pulmonary trunk wall. Fine tissue forceps steady the cusps on each side of commissure and provide even tension as incision is made. **B,** Unless pulmonary trunk is of normal width, which is uncommon, incision is closed with an oval pericardial or polytetrafluoroethylene patch. Patch is cut in the form shown, and its dimensions ensure that it is convex rather than flat.

(PTFE) patch; in neonates and infants, glutaraldehyde-treated pericardium works well. The patch is trimmed to be slightly larger than the VSD. Exposure may be obtained entirely with stay sutures; alternatively, the VSD is exposed through the right ventriculotomy by the assistant using two small curved retractors, one beneath both ends of the infundibular septum, which are pulled upward and apart. A third retractor is positioned in the lower margin of the ventriculotomy for gentle inferior traction. Sequencing of the suturing depends on whether the repair is from the right atrium or RV and is similar to that used for isolated VSD (see Figs. 38-26 through 38-29; see also Chapter 35 and Figs. 35-24 and 35-25). For example, through the RV it is usual to begin the continuous suture at the base of the tricuspid septal leaflet at the posterior-inferior aspect of the VSD. Via the right atrial approach, the suture is often begun anterior to the insertion of the medial papillary muscle (muscle of Lancisi).

**Decision and Technique for Transanular Patching** Preoperative imaging, usually by echocardiography and occasionally by cineangiography, is used to estimate the diameter of the pulmonary “anulus,” and this information is used to assess the likelihood of whether a transanular patch will be
necessary. In extreme cases (of both large and small “anuli”), this measurement can be highly predictive of whether or not a transanular patch will be needed. In many less extreme cases (z values between −2 and −4), intraoperative information will be used to decide when to place a transanular patch. The surgeon’s bias regarding transanular patching is that it generally should not be necessary when the pulmonary “anulus” z value is larger than −3 as measured on the preoperative echocardiogram or cineangiogram. This is based on the high probability under these circumstances that the postrepair $P_{RV/LV}$ will be less than about 0.7, and on the anticipated increased need for insertion of a pulmonary valve very late postoperatively when a transanular patch has been placed. Generally, a transanular patch should not be placed when the z value is larger than −3. Otherwise, the incision is carried across the “anulus,” the pulmonary valve excised, and the patch inserted.

When the patient has TF with subarterial VSD, the “Asian” variant of TF, the surgeon’s bias is that there is a three in four chance a transanular patch will be necessary. Reassessment after closing the VSD is accomplished by estimating the diameter of the “anulus” with a Hegar dilator that passes snugly but not tightly through it. This provides one more precise estimate in borderline situations. This diameter is transformed to a z value as described in Chapter 1, Appendix Fig. 1D-1; generally this finding is similar to that obtained from the cineangiogram (but slightly smaller when the body surface area of the patient is less than 0.7 m² and slightly larger in patients with a body surface area greater than about 0.7 m²). Generally, a transanular patch should not be placed when the z value is larger than −3. Otherwise, the incision is carried across the “anulus,” the pulmonary valve excised, and the patch inserted (Fig. 38-31). If the situation is borderline, the lesser risk lies with inserting a transanular patch.
essentially unchanged and be at the junction of the patch and distal pulmonary trunk. In some patients the distal pulmonary trunk is narrower than the anulus; in these cases the incision is extended into the LPA, which usually continues in the same general direction as the pulmonary trunk and is usually proportionally larger than the distal pulmonary trunk. If the origin of the LPA is proportionally no larger than the distal pulmonary trunk, the incision and patch reconstruction should be carried into the midportion of the LPA, which is nearly always wider than the origin. Care must be taken to not damage the left phrenic nerve or left superior pulmonary vein. In neonates with a patent ductus, especially if they are on PGE, it is difficult to assess the proximal LPA, and patching that extends beyond the ductus onto the distal LPA should be performed.

The transanular patch may be of glutaraldehyde-treated or untreated autologous pericardium, processed bovine pericardium, or cut from a cylinder of preclotted double-vessel woven polyester, collagen-impregnated knitted polyester, or PTFE. In neonates and young infants, autologous pericardium should be used exclusively. In older patients, collagen-impregnated polyester provides the benefit of precise sizing of the patch (an important consideration), and when properly trimmed, its convexity is ensured, as is a relatively “square cut” of its distal end (see Fig. 38-31, B). Glutaraldehyde-treated pericardium has significant advantages. When a polyester tube is used, one is selected whose diameter corresponds to a z value of 0 to +2. Too large a transanular patch increases postoperative pulmonary regurgitation.

When the time comes for inserting the patch and the distal end of the incision is on the pulmonary trunk, the polyester tube is stretched slightly and cut to the length of the incision, cutting both ends squarely (see Fig. 38-31). The corrugated (crimped) nature of the tube provides sufficient length that it is convex longitudinally; the curve makes it a convex “roof” transversely. The tube is then cut longitudinally so that about three fifths of the circumference remains as the roof. Only the corners are trimmed at the distal end, leaving it very broad, while the proximal (RV) end is tapered. It is then sewn into place with a continuous 5-0 polypropylene suture (see Fig. 38-31, B).

When the incision has been carried onto the LPA, a slightly different technique is used, in the belief that the result is more apt to be geometrically correct. For this, a rectangular piece of pericardium is cut about 1.5 times wider than the apparent diameter of the LPA and about 1.5 times longer than the incision in the LPA. It is sewn into place with continuous 6-0 polypropylene sutures placed slightly farther apart in the patch than in the wall of the LPA. A polyester tube is used for the remainder of the reconstruction (Fig. 38-33). Alternatively, glutaraldehyde-treated pericardium can be used for both the transanular patch and the extension onto the LPA. Its length can be determined by measuring length of the incision from the RV to the pulmonary artery, and its maximum width is determined visually by holding the edges of the incision open at valve level and judging the size of the roof required to create a new pulmonary “anulus” whose diameter is no larger than three fourths the diameter of the ascending aorta. Alternatively, in infants, an 8-, 9-, or 10-mm Hegar dilator can be placed through the divided “anulus” and the width of the patch required to complete the roof over it measured. Both ends are cut almost transversely to create a blunt patch, particularly distally, and the patch is positioned using continuous 6-0 or 7-0 polypropylene sutures commencing at the distal end of the incision. The suture is placed using a running over-and-over technique, placing the first two or three throws along each side before pulling the pericardial patch into position as the suture is tightened. Suturing is continued down each side to anulus level, then the remainder of the right ventriculotomy is closed by incorporating the pericardial patch into it with continuous sutures. Deep bites of muscle are taken down each side and at the angle.

A monocusp may be attached to the pericardial roofing patch. The cusp diameter is fashioned somewhat larger than the planned rooved RV outflow. It is cut more or less circular and sutured to the patch when the latter suturing from distally reaches the valve “anulus.”

### Assessing Postrepair Right Ventricular Outflow Tract Obstruction

#### Measuring Postrepair (Operating Room [OR]) \( P_{RV/LV} \)

In older infants and beyond, the \( P_{RV/LV} \) is helpful in assessing important residual RV outflow tract obstruction. After repair and separation from CPB, and preferably with the cannulae for CPB still in place, postrepair (OR) \( P_{RV/LV} \) is obtained. The peripheral systemic systolic blood pressure can be used to estimate the \( P_{LV} \). A polyvinyl catheter is placed through the right atrial wall and passed across the tricuspid valve into the RV to measure \( P_{RV} \).

If a transanular patch has not been placed and postrepair (OR) \( P_{RV/LV} \) is greater than 0.7, CPB should be reestablished and a transanular patch placed.

When a transanular patch has been placed and the ratio is greater than about 0.8, localizing the site of the gradient is vigorously pursued by pressure manometry or transesophageal echocardiography. If pressure gradient or localized obstruction is identified between the sinus portion of the RV
Figure 38-33  Repair of tetralogy of Fallot in neonates.  
A, A transanular right ventricular–pulmonary trunk incision is almost always used, keeping ventricular portion as cephalad as practicable.  B, Pulmonary valve is incised fully to arterial wall and, if grossly distorted, resected fully. Parietal and septal extensions of the trabecula septomarginalis are incised at their origins from the infundibular septum, but resection of muscle is kept to a minimum. Ventricular septal defect (VSD) is closed as for the right ventricular approach (see Fig. 38-27). Often, pericardium is used for VSD patch.  C, Transanular incision is closed with a polyester, polytetrafluoroethylene, or pericardial patch large enough to attain a mildly convex contour in all directions. Key: LPA, Left pulmonary artery; SVC, superior vena cava.
and distal end of the patch, CPB is reestablished and the situation corrected. If the operation has been properly performed (in which case the gradient is located at the distal end of the patch) and if the patch has been extended into a widened portion of the pulmonary trunk or LPA, little more can be done to relieve the obstruction.

If no correctable cause of the elevation of postrepair (OR) \( P_{RV/LV} \) is found, and if the elevation is not extreme and the patient’s condition is good, the patient should be sent to the intensive care unit (ICU) with continuous monitoring of RV pressure. There, over a few hours, postrepair (ICU) \( P_{RV/LV} \) may fall to reasonable levels (see Special Features of Postoperative Care later in this section). If the patient’s condition in the operating room is not good or if right atrial pressure is considerably elevated above left, then the situation is precarious, although uncommon, and requires action. CPB is reestablished, and a large hole is cut in the VSD patch, usually during a brief period of aortic clamping and through a right atriotomy.

**Measuring Postrepair (OR) Right Ventricular Outflow Tract Pressure Gradient** In neonates and young infants, compared with older patients, the \( P_{RV/LV} \) is less helpful for assessing important residual RV outflow tract obstruction. There are several reasons for this. First, the data used to develop and interpret the ratio are from older patients, so the ratio thresholds predicting poor outcomes have not been validated in neonates. Second, and most important, the physiology in neonates and young infants is substantially different from that in older patients. Especially in the operating room post-CPB, systemic vascular resistance can be quite low, yielding systemic systemic arterial pressure (and thus the \( P_{LV} \)) as low as 50 mmHg. Also, \( R_p \) tends to be higher, so typically the \( P_{RV} \) may be as high as 40 to 45 mmHg without RV outflow tract obstruction. As a result, the \( P_{RV/LV} \) may approach 1.0 without any residual RV outflow tract obstruction.

Nevertheless, assessment of residual obstruction, both when the pulmonary “anulus” is left intact and when a transannular patch is used, should be routinely performed. A polyvinyl catheter is placed in the RV as described in the previous section, to measure \( P_{RV} \). Another catheter is placed in the pulmonary trunk and can be manipulated into the RPA and LPA, to obtain \( P_{RPA}, P_{LPA} \), and \( P_{LPA} \). In a patient with an intact pulmonary valve “anulus,” a gradient of 20 mmHg or more at the valve is an indication for revision with a transannular patch. In a patient with a transannular patch, a gradient of similar magnitude is an indication for revision at the specific site of the residual obstruction.

**Management of Atrial Septum** During repair, a PFO (present in about two thirds of patients) should generally be closed in older infants and children. Rarely, a persistent atrial communication can be the source of paradoxical cerebral emboli late postoperatively. If a true atrial septal defect is not closed, there may be left-to-right shunting at atrial level. In neonates and infants, if a transannular patch is placed or if important pulmonary regurgitation is present, a PFO is left unclosed to allow decompression of any right atrial hypertension caused by acute RV failure. Some arterial desaturation may be present in the first few postoperative days, but it then disappears as the RV remodels to accommodate the physiology of a high-volume, low-pressure circulation, as opposed to the preoperative physiology of a low-volume, high-pressure circulation. In fact, evidence of arterial desaturation is essentially proof that important RV failure is present.

A PFO should be narrowed to a diameter of 3 to 4 mm. This is accomplished by suturing a portion of the free edge of the septum primum to the left side of the limbus (where it would naturally attach if spontaneous closure had occurred) using several 5-0 polypropylene mattress sutures (Fig. 38-34). This will preserve a functioning, but somewhat smaller, PFO. If the pulmonary valve is competent in neonates and infants after repair, important RV failure is unlikely, and the PFO can be closed at repair.

**Repair of Uncomplicated Tetralogy of Fallot with Pulmonary Stenosis via Right Ventricle**

After usual intraoperative preparations (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2), a median sternotomy is performed. Prompt control of major bleeding from collaterals is accomplished with electrocautery. The usual dissections are made (see “General Plan and Details of Repair Common to All Approaches” earlier in this section) and purse-string sutures and tapes placed. A polyester tube (see “Decision and Technique for Transanular Patching” earlier in this section) may be selected and pericardium may be removed and treated with glutaraldehyde.

CPB is established, and the patient’s core temperature is cooled to 24° to 32°C using direct or indirect vena caval cannulation (see “Preparation for Cardiopulmonary Bypass in Section III of Chapter 2”). The colder end of the spectrum...
should be considered in older, very cyanotic patients who may have developed substantial acquired systemic to pulmonary artery collaterals. Two venous cannulae are preferred; however, a single right atrial cannula can be used (see “One versus Two Venous Cannulae” under Special Situations and Controversies in Section III of Chapter 2). The cardioplegic catheter (or needle) is secured into the ascending aorta. An efficient system for venting the left heart is essential for precise repair of TF, because of the potential for high collateral flow return to the left atrium. The left atrial suction line may be inserted through the base of the right superior pulmonary vein through a purse-string suture and advanced across the mitral valve to vent the LV. The aorta is clamped and cold cardioplegic solution injected (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Efflux from the coronary sinus is aspirated and discarded or allowed to escape from the right atrium.

The RV is opened through a vertical (longitudinal) incision, sparing large conal and anterior branches of the RCA that cross the RV. If it is expected that the pulmonary valve will be adequate, the incision is made in the midportion of the RV infundibulum and extended nearly to, but not into, the pulmonary valve superiorly and just into the sinus portion of the RV (see Fig. 41-27, A).311 Two pledgeted stay sutures placed through each side of the incision are placed on traction for exposure (see Fig. 41-27, B). Alternatively, this can be achieved manually using a hand-held retractor.

Infundibular dissection is performed (see “General Plan and Details of Repair Common to All Approaches” earlier in this section and Figs. 38-26 and 38-27, A to C). The pulmonary valve is examined, and if it is stenotic, a valvotomy is performed through a pulmonary arteriotomy (see Fig. 38-30, A). Diameter of the valve anulus is estimated with Hegar dilators. If a transanular patch is considered necessary (see “Decision and Technique for Transanular Patching” earlier in this section), the infundibular incision is carried across the “anulus” before performing the infundibular dissection, paying attention to the position of the pulmonary valve commissures (see Fig. 38-31).

After the RV outflow tract is addressed, the VSD is closed using a patch (see Fig. 38-27, D to F). If the decision earlier in the operation has been not to use a transanular patch, measurements with Hegar dilators are repeated from the RV after VSD closure. If no further narrowing has resulted, the pulmonary arteriotomy and infundibular incision are closed with patches (see Fig. 38-30, B). Similarly, if a transanular incision has been used, it is closed with a patch of appropriate diameter (see “Decision and Technique for Transanular Patching” under Technical Details of Repair earlier in this section). The right atrium is opened and the atrial septum examined. If an atrial septal defect or PFO is present, it is managed as described in “Management of the Atrial Septum” under Technical Details of Repair earlier in this section). The right atriotomy is closed.

Rewarming and myocardial reperfusion (see Chapter 3) can be commenced at any point after VSD closure. Thus, by preference, the RV outflow tract patches can be placed and atrial septum addressed either with the aortic clamp in place or with rewarming and myocardial reperfusion initiated. Separation from CPB is performed in the usual way (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Repair of Uncomplicated Tetralogy of Fallot with Pulmonary Stenosis via Right Atrium

This procedure is identical to repair through the RV up to the point that CPB is established. Aortic cannulation is standard. Bicaval venous cannulation is required. After commencing CPB, cooling is initiated. The left side is vented by placing a cannula through the right upper pulmonary vein across the mitral valve into the LV. Once the desired core temperature is achieved, the aorta is clamped and cardioplegia administered. The caval tapes are snugged, and a long right atriotomy is carried from the base of the appendage well inferiorly, a little anterior to the inferior vena cava cannula site. The right atrium, atrial septum, tricuspid valve, VSD, and RV outflow tract are examined (see Fig. 38-29, A).

With properly placed 6-0 polypropylene traction sutures on the septal and anterior leaflets of the tricuspid valve, edges of the VSD can usually be visualized, although with more difficulty in TF than in isolated VSD because of the leftward and anterior displacement of the infundibular septum and its parietal extension.312 Alternatively, manual retraction by the surgical assistant using delicate instruments can achieve similar, or superior, exposure. The pathway from sinus to outflow portion of the RV is examined. The obstructive nature of the prominent parietal extension of the infundibular septum (see Figs. 38-28 and 38-29, B) is particularly well appreciated from this approach, and the infundibular chamber, if present, is easily visualized. The pulmonary valve can usually also be well seen. The VSD is repaired by sewing into place a patch (autologous glutaraldehyde pericardium or polyester velour) with continuous polypropylene (Fig. 38-29, B to D). It is closed before mobilizing and resecting the parietal band (as illustrated in Fig. 38-29). Often this allows better visualization of the borders of the VSD and, importantly, defines the limit of parietal extension to be resected (see Fig. 38-29, B). The VSD patch protects the aortic valve and crista during subsequent relief of outflow stenosis. Care should be taken not to cut or loosen the continuous patch suture anteriorly when resecting the parietal band. If needed, several interrupted sutures should be placed on this portion of the rim of the VSD patch.

RV outflow tract obstruction is addressed following VSD closure. The parietal extension is deeply incised 2 to 4 mm beyond its origin (toward the free wall) from the infundibular septum and 4 to 5 mm above the aortic cusps, which are visualized as the cut is made (see Fig. 38-29, E). The parietal extension is then dissected away from the ventriculo-infundibular fold (inner curvature of the RV) and from the anterior free wall of the RV and excised. The free wall of the RV is palpated occasionally from outside during this dissection to avoid perforating it. Any hypertrophied and obstructive trabeculae along the left side of the outflow tract are incised and removed together with the fibrous margins of the infundibulum. The infundibular chamber and areas just proximal to the pulmonary valve are examined to determine (in concert with the preoperative imaging studies) whether they need to be widened by an infundibular patch. Generally speaking, if this is the case, the atrial approach should not have been

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1In about 5% of patients, aortic dextroposition is sufficiently severe that the cephalad (superior) borders of the VSD cannot be seen except with extreme traction on the tricuspid valve. In these cases, rather than using such strong traction, the right atrial approach is aborted and the RV approach used.
considered. This is because in TF, the VSD is always easier to expose and close through a ventriculotomy than through an atriotomy. Thus, if a ventriculotomy (infundibulotomy) is required because of a narrow infundibulum, the VSD should be closed through the infundibular incision. It makes little sense to close the VSD through the right atrium if an infundibular incision is required. The pulmonary valve is examined and the diameter of the “anulus” is estimated by passing a Hegar dilator antegrade across the RV outflow tract.

If a pulmonary valvotomy is needed, it is usually done through a vertical incision in the pulmonary trunk (see Fig. 38-30). After valvotomy, RV outflow diameter is again estimated by sizing the pulmonary valve orifice with Hegar dilators. The pulmonary arteriotomy is closed, usually with a pericardial patch. Management of an atrial septal defect or PFO and the remainder of the operation proceed as described for repair through the RV.

Repair of Tetralogy of Fallot in Infancy

A median sternotomy is performed and the heart exposed. A subtotal thymectomy is performed, paying careful attention to the phrenic nerve. If the echocardiogram or cineangiogram indicates that a transanular patch is required, and in borderline cases, the front of the pericardium is removed from where it joins the diaphragm to its most superior reflection from the aorta. This secures a piece of pericardium at least 6 cm long and 3 cm wide, tapering at both ends. The pericardium is stretched with its epicardial surface downward onto moist gauze or cardboard and is set aside for later use. Dissection of the pulmonary trunk, RPA, LPA, and ductus arteriosus or ligamentum arteriosum is easily and rapidly achieved.

CPB is established using aortic cannulation and, preferably, bicaval cannulation; however, single venous cannulation of the right atrium can be used. Standard continuous CPB with cooling to 28° to 32°C and cardioplegic cardiac arrest is preferred. The left heart is vented in standard fashion through the right upper pulmonary vein. Alternatively, hypothermic circulatory arrest can be used and is preferred by some. The ductus arteriosus, if present, is doubly ligated using two 5-0 polypropylene sutures and divided. The suture used to ligate the pulmonary artery end of the ductus should be placed precisely, at least 3 mm distal to the pulmonary artery origin of the ductus, to avoid constriction of the LPA branch or obstruction of the LPA lumen by extrusion of bulky ducal tissue. If a ligamentum is present, it should also be ligated and divided to avoid tethering of the LPA origin, which can cause late kinking and LPA obstruction, especially if pulmonary regurgitation and RV outflow tract dilatation develop. When imaging studies indicate that a transanular patch is not required and when dissection of the pulmonary trunk confirms that it is of adequate diameter, a vertical incision is made into the RV (see Fig. 38-27). The infundibular stenosis is completely relieved. This often involves simple transection of the parietal and septal extensions of the TSM, rather than resection (similar to that shown in Fig. 38-33, B). The pulmonary valve is examined from below and any stenosis relieved in the manner already described. The VSD is closed through the infundibular incision (similar to that shown in Fig. 38-27).

The tricuspid valve is retracted and the atrial septum exposed, looking retrograde from the RV into the right atrium. If a PFO is present, it is often possible to close or modify it from this approach; if not, the right atrium is opened and the PFO is managed through this approach. Or, if there is a more extensive atrial septal defect, the right atrium is opened and the defect closed using a pericardial patch with continuous polypropylene suture. If it has to be reduced in size, it is managed as described in Fig. 38-34. The right atrium is closed. The ventriculotomy is then closed with a narrow patch, also using a continuous suture.

When a transanular patch is indicated, the incision is carried across the “anulus” and out along the pulmonary trunk almost to the origin of the LPA, and a transanular pericardial patch is placed after VSD closure (see Fig. 38-33, A). Should there be LPA origin stenosis, the incision passes beyond this to reach the normal-diameter LPA (Fig. 38-35). If a transanular patch is used in neonates and young infants, the PFO should always be left open.

Repair of Tetralogy of Fallot with Stenosis at Origin of Left Pulmonary Artery

In this situation, there is usually sufficient hypoplasia of the pulmonary anulus and trunk that a transanular patch is also required (see Morphology earlier in this section). Repair is usually accomplished in exactly the manner described for situations in which the incision for placing a transanular patch must be extended onto the LPA (see “Decision and Technique for Transanular Patching” earlier in this section and see Fig. 38-35). In those uncommon instances in which a transanular patch is not needed, an incision is made across the stenosis in the origin of the LPA. A rectangular patch of pericardium is trimmed and sewn into place as described.

When there is virtual or total occlusion of the LPA origin, patch graft enlargement is not satisfactory. Instead, after locating the patent portion of the LPA beyond the zone of occlusion by dissecting along the chord of tissue that still connects it to the pulmonary trunk bifurcation, the patent LPA is opened longitudinally on its anterior surface for a short distance. The opened end is then sutured to the adjacent leftward edge of the pulmonary trunk with a running fine polypropylene suture to create a new posterior wall. The anterior wall is next created by a pericardial patch positioned as for reconstruction of a zone of stenosis (see earlier text). When the LPA is totally disconnected from the pulmonary trunk or is too small for this reconstruction, repair entails locating the LPA close to or adjacent to the lung hilum (usually by intrapleural dissection) and disconnecting it from any vessel, usually the ductus arteriosus, that supplies it. It is then usually possible to anastomose the LPA end to side to the leftward edge of the distal pulmonary trunk (mobilizing the trunk completely so that it will swing more easily to the left). If the LPA is narrowed proximally, however, a technique similar to that described earlier is employed.

Repair of Tetralogy of Fallot with Stenosis at Origin of Right Pulmonary Artery

This situation occurs uncommonly without associated LPA stenosis. In contrast to the LPA, the RPA is usually not an extension of the pulmonary trunk but comes off its side at a right angle. This makes the simple type of repair used for origin stenosis of the LPA less satisfactory, although it can be used when stenosis is not too severe.
Chapter 38 Ventricular Septal Defect with Pulmonary Stenosis or Atresia

Operation proceeds as usual until the VSD has been repaired. Then a small longitudinal incision is made in the pulmonary trunk to visualize the RPA orifice (Fig. 38-36, A). The origin of the RPA is excised from the pulmonary trunk. Lateral incisions are made to enlarge the orifice in the side of the pulmonary trunk (Fig. 38-36, B). The RPA is incised from its narrow orifice back into its wide portion. A rectangular piece of pericardium is trimmed and sewn to the RPA to make a markedly enlarged proximal RPA (Fig. 38-36, C). The proximal end of the reconstructed RPA is then sutured to the enlarged orifice in the side of the pulmonary trunk using continuous 6-0 or 7-0 polypropylene sutures, while taking care to avoid any purse-string effect (Fig. 38-36, D). Alternatively, the posterior edge of the opened RPA is sutured to the back wall of the opened pulmonary trunk; the rectangular piece of pericardium is then sewn to the remaining opening to widen it further.

Transection of the ascending aorta to improve exposure is rarely necessary.

Repair of Tetralogy of Fallot with Bifurcation Stenosis of Pulmonary Trunk

This condition requires appropriate reconstruction based on proper understanding of the morphology, although few papers discuss details of this repair. Both the LPA and RPA ostia are usually stenosed to a similar degree and over a short distance (<15 mm), and the distal pulmonary trunk is often similarly narrowed. The pulmonary trunk may be short, making the bifurcation proximal and more Y-shaped than usual.

In patients 5 years of age or older, the optimal procedure may be to replace the pulmonary valve, trunk, bifurcation, and proximal RPA and LPA with a pulmonary allograft (Fig. 38-37). It is a less desirable operation in infants, however, because the allograft will almost certainly be outgrown and require earlier replacement than when used in older children. However, this procedure has the greatest probability of providing a good hemodynamic result in this complex situation.
Alternatively, and especially in infants, repair rather than replacement is indicated (Fig. 38-38). Complete mobilization of the aorta, pulmonary trunk, RPA, and LPA is required, preferably before CPB. The vertical ventriculotomy is carried across the anulus into the pulmonary trunk and extended to the bifurcation. A second incision is made on the anterior aspect of the branch pulmonary arteries, extending from the normal diameter of the distal LPA, across the stenotic region of the LPA, onto the RPA, and extending across the stenotic region of the RPA to the distal normal-diameter RPA. Thus, the two incisions described create a T shape. Autologous pericardial tissue or allograft pulmonary artery tissue is used to patch-augment the pulmonary trunk and branch pulmonary arteries. Two patches are used, the first to patch the branch pulmonary arteries (Fig. 38-38, A) and the second as the transanular patch, which extends distally to the first patch (Fig. 38-38, B).

Repair of Tetralogy of Fallot with Anomalous Origin of Left Anterior Descending Coronary Artery from Right Coronary Artery

In hearts in which there is a large coronary artery crossing the RV outflow tract close to the pulmonary “anulus” (usually an anomalously arising LAD from the RCA, but sometimes the entire left coronary artery coming from the RCA), relief of pulmonary stenosis must neither divide nor compromise flow through this vessel. Because such a vessel is occasionally

Figure 38-36 One type of repair of stenosis at origin of right pulmonary artery (RPA). Initially, a small incision is made in pulmonary trunk through which stenotic orifice of RPA can be viewed from within. A, Ascending aorta has been mobilized to expose origin of RPA. Proposed incision for disconnecting RPA from pulmonary trunk is shown. B, RPA has been disconnected from pulmonary trunk. Resulting orifice in RPA can be enlarged as shown, but enlargement by incision is preferable. An incision is made down anterior aspect of RPA. C, RPA is enlarged with a pericardial patch. D, Enlarged RPA is reattached to enlarged aperture in pulmonary trunk. (At times, it may be easier to suture posterior wall of RPA to posterior aspect of pulmonary trunk orifice before making pericardial enlargement of RPA.) Key: LPA, Left pulmonary artery; SVC, superior vena cava.
Figure 38-37 Repair of severe pulmonary trunk and bifurcation stenosis using a pulmonary valve allograft and its bifurcation. A, Dissection must be complete. For this, entire ascending aorta is completely freed from its posterior connections and from pulmonary trunk and its bifurcation. B, Superior vena cava is completely mobilized and right and left pulmonary arteries (RPA and LPA) dissected at least to the point where the first branch is visualized; that is, beyond the immediately prebranching level. C, Ascending aorta may be divided, but often the procedure can be performed without this step. Distal anastomoses are made first, taking care to transect the LPA and RPA beyond the narrow areas and to leave some redundancy in allograft bifurcation. D, Completion of the proximal anastomosis, often with a polyester (or pericardial) hood as shown. If transected, aorta is brought together end to end. Importantly, however, if aorta is enlarged and compresses the underlying allograft bifurcation or RPA, a short segment of polyester or polytetrafluoroethylene tube should be interposed between the two ends of the aorta. Key: SVC, Superior vena cava.
This technique may be used by choice, instead of the patch technique, when the infundibulum requires mild or moderate augmentation; it is the only option when marked augmentation is needed.

If the left coronary artery is damaged by the right ventriculotomy, the left internal thoracic artery can be taken down (see “Internal Thoracic Artery” under Technique of Operation in Chapter 7) and anastomosed to the distal left coronary artery. Alternatively, the coronary can be primarily repaired. This procedure can be life saving.

Repair of Tetralogy of Fallot after Blalock-Taussig Shunt or Polytetrafluoroethylene Interposition Shunt

Systemic-to-pulmonary artery shunts will have been created either through a thoracotomy (left or right) or a median sternotomy, and will consist of either a native systemic artery–pulmonary artery anastomosis (classic B-T shunt), or an interposition PTFE graft between the systemic and pulmonary artery. In the modern era, PTFE shunts are used much more commonly than classic B-T shunts, and a median sternotomy approach has commonly been used. However, variation in preferred shunt technique still exists, and older patients may be encountered with shunts placed using techniques rarely used today.

In many centers, median sternotomy has replaced lateral thoracotomy for primary systemic–pulmonary arterial shunts in neonates. Generally, a PTFE tube graft is used, connecting the brachiocephalic artery or brachiocephalic-subclavian junction to a pulmonary artery. In patients with a left aortic arch, the shunt is placed on the right side; with a right arch, it is on the left. At complete repair, access to the shunt is much better than that for all other types of shunts, with the graft positioned intrapericardially and centrally. Right-sided shunts are positioned medial to the superior vena cava and apposed to the lateral aspect of the ascending aorta, and on the left, just leftward of the ascending aorta. The shunt can be dissected prior to institution of CPB in most cases, the only exception being deeply cyanotic patients with a very small shunt. Interruption of the shunt is accomplished as CPB is initiated by placing appropriately sized hemostasis clips securely across the tube graft at the systemic and pulmonary ends. The graft is divided.

Median sternotomy in an older patient with TF and a classic B-T shunt is usually accompanied by profuse bleeding from arteries in front of and behind the sternum that have developed as part of the collateralization that follows subclavian artery ligation. While this bleeding is being controlled, rapid volume replacement should not be made with banked blood. This is because this low-calcium-content and low-pH blood passes directly across the VSD into the aorta and coronary arteries. If this cold, unmodified banked blood is infused rapidly, the heart may slow and even develop asystole. Warmed calcium-enriched blood may be used.

Left thoracotomy has often been used for shunt placement in neonates or small infants with a left aortic arch. Typically, a left PTFE tube graft has been used between the left subclavian artery and LPA. In part this was motivated by the ease with which it can be closed during repair. After sternotomy is performed, hemostasis secured, and sternal retractor inserted, and when the patient’s condition is good, initial dissection is made. Because the graft lies deeply in the left chest, the approach is not beneath the thymus gland but over it, directly into the left pleural space. The few adhesions between the mediastinal pleura and lung are divided with the electrocautery. The PTFE tube graft is somewhat rigid and easily palpated. A small incision is made directly over it and carried down to it. At times a plane of dissection between the graft wall and surrounding tissue is easily established; if so, this dissection is carried out. Otherwise, the pericardium is opened and CPB established. The lungs are collapsed, and a plane of dissection is easily established around the graft. The shunt is clipped at each end and divided. Remainder of the operation is carried out as usual.

When a classic right B-T shunt is present in a patient with a left aortic arch, the pericardium is opened, and as the assistant elevates and retracts the ascending aorta to the left, the RPA is visualized coming from beneath the aorta. The superior vena cava is dissected off it and gently retracted rightward (in a few cases, exposure of the subclavian artery may be easier with the superior vena cava retracted to the left). Possible distortions of the RPA by the shunt are known from preoperative imaging studies, and these are kept in mind as dissection proceeds. Course of the right subclavian artery coming down to the RPA usually can be suspected from observation and palpation of a continuous thrill. The entire circumference of the subclavian artery may be freed along a short length by sharp dissection well superior to the anastomosis, and two heavy ligatures placed loosely around it. The artery is then temporarily occluded, and if vessel identification has been correct, the continuous thrill disappears, systolic and diastolic systemic arterial pressures increase, and pulse

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**Figure 38-38** Repair of left pulmonary artery (LPA) stenosis in tetralogy of Fallot using two-patch technique. A, Typical right ventricular (RV) outflow tract hypoplasia and LPA stenosis present at ductus arteriosus or ligamentum arteriosum. B, Separate RV outflow tract patches and LPA patches are placed using a running monofilament suturing technique. This technique is useful when the angle of take-off of the LPA makes a single patch difficult to position correctly. Key: PA, Pulmonary artery; RPA, right pulmonary artery.
pressure narrows. If these things do not occur, the RPA has been misidentified as the subclavian artery or the shunt is small. The heart is cannulated, CPB is begun, ligatures around the subclavian artery are tied, and the operation proceeds as usual. An alternative preferred method is closure with hemostasis clips, in which case temporary ligatures are not placed.

When a classic left B-T shunt is present in a patient with a left or right aortic arch, the subclavian artery is approached from outside the pericardium. For this, the upper left pericardial stay sutures are placed on strong traction to the patient’s right. Level of the LPA is noted before this maneuver; just cephalad (superior) to this level, the thymus gland and left phrenic nerve are dissected from the pericardium, sharply and over a limited area, because excessive dissection in this region can result in major bleeding that is difficult to control. A narrow retractor is slipped under the thymus, and the region of the subclavian artery is located by gentle palpation and sharp dissection beneath the thymus gland. The subclavian artery is dissected out as described for the right side, and the same tests are made for accuracy of identification. Operation then proceeds as described earlier.

If the left subclavian artery cannot be located by going over the thymus gland and phrenic nerve, an alternative method is used in patients with a right aortic arch. The brachiocephalic artery is identified beneath the brachiocephalic vein and traced distally to the point at which it bifurcates into left subclavian and left common carotid arteries. After identifying the left subclavian artery positively by the maneuvers described and by the fact that the anesthesiologist can feel the left common carotid (or left superficial temporal) pulse when the vessel is temporarily occluded, the operation proceeds as described.

**Repair of Tetralogy of Fallot after Waterston and Potts Shunts**

These shunts are of historical interest only; they are not used in current practice. In previous years, occasional older patients were seen for evaluation and repair who received the shunt many years before. Nearly all such patients have been repaired or have died; thus, it is rare to encounter such a patient currently. TF repair after Waterston or Potts can be performed using well-described techniques, including those in editions 1 through 3 of this book.

**Technique of Shunting Operations**

Fig. 38-39 is a composite illustration of various positions used for systemic–pulmonary arterial shunts for augmenting pulmonary blood flow. General anesthesia with endotracheal intubation and controlled ventilation is used. Monitoring with an intraarterial catheter placed in an artery that will not serve as the systemic source of the shunt is established. Reliable intravenous access is obtained, either centrally or peripherally. Continuous pulse oxymetry is utilized. Details of each type of shunt follow.

**Classic Right Blalock-Taussig Shunt**

This is the original shunt described; however, it is typically not the first choice in modern practice. This is because it has the disadvantages of both sacrificing direct circulation to the right arm and delivering unpredictable flow to the pulmonary arteries. The artery can vary in size initially and can dilate over time. It may have some advantage in extremely small infants.

With the patient in left lateral decubitus position, a right lateral thoracic incision is made (Fig. 38-40, A, inset). The thorax is entered through either the top of the bed of the nonresected fourth rib or the third interspace. A rib spreader is positioned and gradually opened (see Fig. 38-40, A).

The first step in dissection is to securely identify the right superior pulmonary vein as it courses obliquely downward (medially and inferiorly) toward the heart to pierce the pericardium posterior to the phrenic nerve. The vein partially overlies the RPA; however, the RPA, in contrast to the vein, follows a straight course medially. With the lung retracted toward the surgeon, the periarterial sheath over the RPA is incised. Usually the superior branch of the RPA is first freed, in the process of which the main RPA (lying in a slightly different plane of dissection) can be easily overlooked. To find it, the superior surface of the right superior pulmonary vein is cleared, and it and the superior vena cava are elevated (Fig. 38-40, A). Dissection is carried centrally until the proximal RPA is identified as a single vessel, proximal to its first branch. With lateral traction on a loop of heavy suture placed around it, the RPA is dissected in the periarterial tissue plane...
as far centrally as possible. The loop is then removed so that the RPA does not inadvertently become obstructed during the next phase of the operation.

The lung is packed off and retracted inferiorly. An incision is made in the mediastinal pleura over the azygos vein and carried superiorly to the top of the chest, parallel and posterior to the phrenic nerve. The azygos vein is divided between ligatures, and the soft tissue and right paratracheal lymph nodes are divided to provide a free pathway for the turned-down right subclavian artery. Any small veins overlying it are ligated and divided. Vagus and recurrent laryngeal nerves are identified, and the periarterial plane over the right subclavian artery is incised. By grasping only the adventitia of the often delicate subclavian artery, dissection is carried distally in the periarterial plane until the origins of internal thoracic and vertebral arteries are identified. These vessels are divided between ligatures, taking care that the proximal ligature is placed 1 to 2 mm away from the subclavian artery (Fig. 38-40, B). Anomalies in branching of the subclavian artery are frequent. The vagus nerve is gently retracted laterally, and
Chapter 38  Ventricular Septal Defect with Pulmonary Stenosis or Atresia

Figure 38-40, cont’d  C, Subclavian artery has been divided and appropriate occluding devices placed on RPA. Incision in RPA is made on its very superior aspect. D, Anastomosis is made using interrupted or continuous 7-0 polypropylene sutures, starting posteriorly from within vessels. Inset shows completion of anastomosis. Key: SVC, Superior vena cava.

the periarterial plane over the subclavian artery medially is opened and dissected. The subclavian artery is divided between ligatures placed beyond the first two large branches, and a right-angled clamp is passed beneath the vagus nerve from its medial aspect superior to the recurrent laryngeal nerve (Fig. 38-40, C). The subclavian artery beyond the ligature is grasped with the clamp and pulled out from under the vagus nerve. Holding the artery beyond the ligature, dissection is carried centrally in the periarterial plane until the distal portion of the brachiocephalic artery and nearly the entire right common carotid artery are liberated. As dissection proceeds, a small artery is occasionally found arising from the origin of the subclavian from the brachiocephalic artery; this must be ligated and divided. The only thing limiting the turned-down length of the subclavian artery is the common carotid artery. Any obstructing bands in the paratracheal soft tissue are divided so that there is nothing in the pathway of the relocated right subclavian artery.

A light, straight arterial clamp with a handle long enough to allow easy holding by the first assistant is placed across the subclavian artery about 8 mm proximal to the point of final transection. The artery is cut squarely across, just proximal to its first branch. (Rarely the first branch comes off very proximally and the subclavian artery is unusually large beyond it. In such instances, the artery can be transected beyond this branch.) Double-looped elastic ligatures are placed around the upper branch and distal main RPA, snugged, and weighted laterally with heavy Kocher clamps. An appropriate-sized Baumgartner clamp is placed across the very proximal RPA, with the surgeon passing a right-angled clamp beneath the artery for lateral retraction as the first assistant tightens the clamp. A longitudinal incision is made in the very superior surface of the RPA (so that when the occluding devices are removed, there will be no torsion of the RPA).

Anastomosis is made with continuous or interrupted double-armed 7-0 polypropylene or polyester sutures, the continuous suture placed from within the respective arteries posteriorly (Fig. 38-40, D). The first assistant holds the two clamps such that the vessels are in perfect apposition and without tension during the anastomosis. Before placing the last few sutures, the lumina are examined and any tiny thrombi or debris irrigated away. After completing the anastomosis,
in rather rapid succession the two doubly looped elastic ligatures are cut and removed, the clamp on the subclavian artery removed, and the proximal RPA clamp removed. Packing is placed lightly around the anastomosis, any unusual bleeding is controlled digitally, the lung is partially reexpanded, and 5 minutes are allowed to pass. During this time, a palpable continuous thrill should be present in the RPA. When the packs are removed, the field is usually dry. Rarely, an additional adventitial suture is needed.

A small chest catheter is brought out from the posterior gutter through about the seventh intercostal space and attached to gentle suction. The chest wall is closed and the lungs are well inflated before the ribs are brought together with absorbable suture. The wound is closed in layers with continuous fine polyglycolic acid sutures, and the skin approximated with a continuous subcuticular suture.

**Interposition Shunt between Left Subclavian and Left Pulmonary Artery**

This is a commonly performed procedure. It can be performed classically through a left thoracotomy or through a median sternotomy. The procedure performed through a thoracotomy is described.

Thoracotomy is as described for the classic B-T shunt, except on the left side. The LPA is identified and dissected out. The mediastinal pleura is opened over the left subclavian artery and contiguous portion of the aortic arch, and the periarterial sheath over these structures is opened. The subclavian artery is not mobilized.

The diameter of the graft is chosen based on the patient’s weight and other factors. In normal-sized neonates or in the case of a very small LPA, a 3.5- or 4-mm PTFE tube graft is used, despite a possible small reduction in patency (see “Size” under Special Situations and Controversies, Systemic–Pulmonary Arterial Shunt, in Section II of Chapter 41 for discussion of criteria for selecting size of the PTFE tube graft). Before any occluding devices are placed, the proper length of the tube graft is determined. For this, the lung is partially inflated to bring the LPA into its usual position. When the anastomosis is completed, the graft should lie without tension and without redundancy (and thus potential kinking) between the proximal half of the subclavian artery and the superior surface of the LPA. The end of the graft that will be anastomosed to the subclavian artery is beveled (Fig. 38-41), the graft is placed in a temporary position, and the other end is cut square at the point that will make the length to the LPA correct.

A delicate side-biting clamp is placed deeply on the subclavian artery so that its handle lies inferiorly and the clamp occludes the artery both proximally and distally. A longitudinal incision is made in the excluded portion of the delicate subclavian artery, and an adventitial stay suture is placed on the anterior lip. The proximal anastomosis is made with a continuous 6-0 or 7-0 polypropylene suture. The clamp on the subclavian artery is not loosened or removed at this time (see variation in detail under “Systemic–Pulmonary Arterial Shunt” under Technique of Operation in Section II of Chapter 41). Elastic ligatures are looped twice around the upper branch and main LPA and snugged, and heavy Kocher clamps are placed on each for lateral traction. A C-shaped clamp is placed very proximally on the LPA, taking care not to compromise the ductus arteriosus. A longitudinal incision is made in the superior surface of the LPA, making this a little shorter than half the circumference of the PTFE tube graft. The distal anastomosis is made with continuous 6-0 or 7-0 polypropylene suture.

In quick succession, the doubly looped ligatures are cut and removed, the clamp on the subclavian artery is opened and carefully removed from the field, and the LPA clamp is opened and removed. A light pack is placed about each anastomosis, with light digital pressure if needed. A continuous thrill should be present in the LPA. Other evidences of patency include registration of an immediate increase in oxygen saturation (pulse oximeter) and an immediate increase in systolic and diastolic blood pressure when the shunt is briefly occluded with forceps. Five minutes are allowed to pass.

Remainder of the procedure is completed as described for the classic B-T shunt.

The interposition operation as an isolated procedure in patients with left aortic arch can be performed through a right thoracotomy. The PTFE tube graft is anastomosed proximally to the junction of the right subclavian and brachiocephalic arteries, which is in the cupola of the chest. This operation is more difficult than that on the left side. In comparison with the classic B-T anastomosis, the PTFE interposition shunt is a more reliable resistor and is easier to close later.

**Right-Sided Interposition Shunt Through Median Sternotomy**

The preferred systemic–pulmonary arterial shunt in neonates with left aortic arch is a right PTFE interposition shunt performed through a median sternotomy (Fig. 38-42, A). After sternotomy, most of the thymus gland is removed. The pericardium is opened in its superior portion and stay sutures applied. The posterior pericardium is opened over the RPA between the ascending aorta and superior vena cava. A small, fine side-biting (C-shaped) clamp is used to isolate the junction between the brachiocephalic and right subclavian arteries. A longitudinal incision is made, and the end of a beveled 3.5- or 4-mm PTFE tube is anastomosed to the incision (Fig. 38-42, B). A small, fine side-biting clamp is placed on the RPA as it is elevated with fine forceps; the clamp isolates the full width of the RPA. The other end of the PTFE tube graft is anastomosed to this opening (Fig. 38-42, C). Continuous 6-0 or 7-0 polypropylene on a cutting needle is used for both anastomoses. The clamps are removed sequentially, the RPA clamp first. After hemostasis is secured, the pericardium is loosely closed. The remainder of the sternotomy is closed in the usual manner. Although this technique has been used primarily in neonates, it is applicable to infants.

In patients with a right aortic arch, a left-sided PTFE interposition shunt from the left subclavian–brachiocephalic junction to the LPA is preferred. Details of the technique are the same as described for the right-sided shunt.

**Classic Left Blalock-Taussig Shunt (in Patients with Right Aortic Arch)**

Left thoracotomy incision and dissection of the LPA are as described in the preceding text. The left subclavian artery is dissected in the cupula of the chest, and maneuvers for freeing it, bringing it beneath the vagus nerve, and preparing it for anastomosis are those described for the right side (see Fig. 38-40). Occluding devices are placed, the anastomosis performed in the manner already described, and the operation
completed as described. This procedure has the same disadvantages as the right classic B-T shunt.

**Right-Sided Interposition Shunt (in Patients with Right Aortic Arch)**

This procedure in patients with right aortic arch proceeds exactly as the procedure on the left side in patients with left aortic arch (see Fig. 38-41).

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

**Repair**

Management is by the general measures described in Chapter 5. Patients with TF have a particular tendency to increase their interstitial, pleural, and peritoneal fluids early postoperatively. Like other deeply cyanotic individuals, they probably have abnormal systemic and pulmonary capillary membranes, and this may make them particularly sensitive to the damaging effects of CPB (see “Response Variables” in Section II of Chapter 2). Therefore, particular care is taken lest loss of intravascular plasma to extravascular spaces produces undesirable hemoconcentration early postoperatively, and attention is given to the possible development of pleural and peritoneal fluid collections. If these develop, they should be aspirated.

Evaluation is complicated by the fact that in patients convalescing normally after repair of TF, with warm feet and good pedal pulses, arterial blood pressure tends to be as much as 10% lower than that in patients who are acyanotic.
Figure 38-42 Right-sided interposition shunt performed through median sternotomy using a 3.5-, 4-, or 5-mm thin-walled polytetrafluoroethylene (PTFE) tube graft. A, Aorta and superior vena cava are mobilized enough to expose right pulmonary artery (RPA). Brachiocephalic vein is elevated and right subclavian, right carotid, and brachiocephalic arteries are mobilized. Proposed incisions (indicated by dashed lines) are at cephalad aspect of RPA and junction of brachiocephalic and subclavian arteries. B, PTFE tube graft is cut on a bias and sutured to brachiocephalic–subclavian artery junction using continuous 6-0 or 7-0 polypropylene suture, beginning the anastomotic suture from within PTFE tube graft and systemic arteries. C, Shunt is completed after transecting PTFE tube graft squarely and using a suture technique similar to that for the systemic arterial anastomosis. Although not shown, subclavian artery clamp remains in place until RPA anastomosis is completed. Key: SVC, Superior vena cava.

Preoperatively, cardiac index is usually normal for this stage of convalescence, and tendency to hypotension is related to relatively low systemic vascular resistance. In the presence of other signs of normal convalescence, treatment of arterial blood pressure is not indicated.

The hemodynamic state is assessed continuously and management constantly reviewed to be certain of its appropriateness. Measurement of cardiac output is helpful, along with other determinants of adequacy of cardiovascular subsystem function (see “Cardiovascular Subsystem” in Section I of Chapter 5). An important right-to-left or left-to-right shunt must be identified, either by the indicator dilution method (see “Risk Factors for Low Cardiac Output” under Cardiovascular Subsystem in Section I of Chapter 5) or by 2D echocardiography with Doppler color flow interrogation. This is particularly important in neonates and infants, in whom the foramen ovale may have been left open for early postoperative decompression of the right atrium. Arterial desaturation is then the rule in the early hours after operation, and demonstrating right-to-left shunting at atrial level by echocardiography using color Doppler reassures that desaturation is not from pulmonary dysfunction (Fig. 38-43). Desaturation from right-to-left shunting usually decreases within 48 hours as RV function improves.

In the absence of shunting, values of left (PLA) and right (PRA) atrial pressures provide considerable insight into the relative function of the two ventricles. After repair of TF, these are usually similar, but one may be 2 to 4 mmHg higher than the other. Rarely, PLA is 5 to 10 mmHg higher than PRA. When this occurs, a residual left-to-right shunt at ventricular or great artery level must be sought and, if found, promptly closed by reoperation. Even relatively small postoperative residual left-to-right shunts may not be well tolerated in repaired TF patients. An important reason for this is that preoperative physiology in TF is that of a volume-underloaded heart, rather than the volume-overloaded preoperative physiology of lesions that tolerate postoperative small residual left-to-right shunts quite well, such as VSDs, atrioventricular septal defects, or truncus arteriosus. If no shunt is found, elevated PLA indicates LV hypoplasia or severe impairment of
LV systolic or diastolic function, and an inotropic agent and afterload reduction are indicated.

Rarely, PRA is 5 to 10 mmHg higher than PLA, indicating important volume or pressure overload of the RV or severe impairment of RV function. This situation is precarious and requires intense treatment, especially when postrepair \( \frac{P_{RV/LV}}{P_{LV}} \) is greater than about 0.7 (Fig. 38-44). If a transanular patch was not used, generally the patient should promptly be returned to the operating room and a patch placed. If a transanular patch is in place, as complete a repair as possible was obtained, and the patient’s condition is reasonably good on only modest catecholamine support (e.g., 5 \( \mu \)g · kg\(^{-1} \) · min\(^{-1} \) of dopamine or dobutamine), then delay for a few hours is reasonable. If no improvement occurs, and particularly if postrepair \( \frac{P_{RV/LV}}{P_{LV}} \) is 0.8 or greater, risk of death approaches 50% and intervention is indicated. In neonates and young infants, \( \frac{P_{RV/LV}}{P_{LV}} \) may not be as useful as in older patients. Anesthetized postoperative neonates may have low systemic vascular resistance and thus low systemic systolic blood pressure despite excellent cardiac output. In this setting, a relatively normal RV and pulmonary artery pressure may result in a \( \frac{P_{RV/LV}}{P_{LV}} \) as high as 0.8 or 0.9. Under these circumstances, the absolute \( P_{RV} \) should be carefully evaluated. Systolic \( P_{RV} \) over 50 mmHg should be investigated routinely, and that between 40 and 50 mmHg considered for investigation. Regardless of the patient’s age, investigation, when indicated, is the same. A right ventriculogram and determination of site of the gradient by cardiac catheterization is performed. If an appreciable gradient is found in the RV or at the pulmonary “anulus,” or a localized important uncorrected LPA or RPA origin or bifurcation stenosis is found, correction of these areas of residual stenosis at prompt reoperation is indicated.

However, if the original repair was complete, it is likely that none of these will be found. Instead, the gradient will be located at the distal transanular patch suture line. This circumstance is uncommon (1%-2% of patients), limited almost entirely to patients with severe hypoplasia of the “anulus” and pulmonary trunk. In that setting, and particularly without a distal widening (in the distal pulmonary trunk or LPA) into which the transanular patch can be extended, it may be impossible to make a geometrically proper patch.\(^{20,310}\) If evaluation reveals that hypoplasia or discrete stenosis is present in the branch pulmonary arteries with normal distal pulmonary arterial development, then further patch augmentation of the pulmonary arteries is indicated. If the pulmonary artery hypoplasia is diffuse, a large perforation is made in the VSD, preventing the \( P_{RV} \) from becoming suprasystemic, and augmenting systemic output from right-to-left shunting across the VSD.

Particular attention is paid to the possible need for reoperation for bleeding. Preoperative polycythemia and depletion of many clotting factors, extensive collateral circulation, and damaging effects of CPB often combine to produce a considerable bleeding tendency. Intense treatment, particularly with platelet-rich plasma, is indicated. The usual criteria for reoperation are followed (see “Bleeding” in Section II of Chapter 5), and prompt reoperation is advised as soon as they are violated. This practice was one factor contributing to the considerable reduction in risk of operation in the early 1960s. Currently, with careful intraoperative hemostasis and definitive repair at a young age, reoperation for bleeding is rarely necessary.

After the patient leaves the ICU, body weight is followed closely because transient fluid retention is common, particularly when a transanular patch has been used. Pharmacologic management of right-sided heart failure is indicated.

**Systemic–Pulmonary Arterial Shunting**

In neonates and young infants, careful intraoperative and postoperative monitoring and control of \( P_{\text{O}_2} \), pH, and

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**Figures**

**Figure 38-43** Relation of arterial oxygen saturation (\( \text{Sao}_2 \)) on first arrival at intensive care unit after repair of tetralogy of Fallot (horizontal axis) to that present about 48 hours later (vertical axis), emphasizing arterial desaturation present early postoperatively when foramen ovale has been left open. Line of identity is shown. Squares represent patients who died postoperatively, and circles represent survivors. Patients identified by two asterisks had the foramen ovale closed. Key: ICU, Intensive care unit; \( \text{Sao}_2 \), systemic arterial oxygen saturation. (From Di Donato and colleagues.\(^{216}\)

**Figure 38-44** Effect of postrepair (ICU) \( \frac{P_{RV/LV}}{P_{LV}} \) on probability of early (6-month) survival after repair of tetralogy of Fallot. Additional effect of age at operation on this relation is also indicated. (See original paper for data and equations.) Key: ICU, Intensive care unit; \( \frac{P_{RV/LV}}{P_{LV}} \), ratio of peak pressure in right ventricle to that in left ventricle. (From Kirklin and colleagues.\(^{520}\))
buffer base are required (see “Neonates and Infants” in Section II of Chapter 5). The usual intense postoperative care and protocols are applied (see Chapter 5). An intraarterial catheter is used to monitor blood pressure, paying careful attention to the systolic/diastolic difference and absolute diastolic pressure. The patient is returned to the ICU ventilated through an endotracheal tube. A chest radiograph is obtained immediately. Ventilation is controlled postoperatively for at least several hours and up to a full day, until stable hemodynamics and confirmation of balanced systemic-pulmonary blood flow is assured. A combination of $\text{SaO}_2$, diastolic blood pressure and pulse pressure, and various signs that reflect systemic cardiac output are used to estimate the systemic-pulmonary blood flow balance. Assuming normal hematocrit and pulmonary gas exchange, an $\text{SaO}_2$ of about 80% usually reflects well-balanced systemic and pulmonary blood flow. Diastolic blood pressure ideally should be above 30 mmHg. Major diversions from these levels usually indicate an imbalance of systemic-pulmonary blood flow. A repeat chest radiograph should be performed to confirm that a pulmonary parenchymal process, and thus gas exchange, is not responsible. If this is ruled out, intravascular volume, pharmacologic (inotropes), and ventilator manipulation should be initiated to restabilize the balance of flow.

Maintaining an adequate cardiac output and blood pressure is an important factor in assuring shunt patency in the vulnerable period of the first 48 hours after surgery. Some centers use a heparin drip as an additional measure. Additionally, or alternatively, aspirin at 10 mg · kg$^{-1}$ daily may be started and continued for the life of the shunt.

Infrequently, mild renal failure, and rarely, acute renal failure and anuria, develop after a simple shunting procedure. This is related to the renal pathology sometimes present in cyanotic patients with TF and to renal damage by radiopaque dye that may have been used for the cineangiogram a few hours or days before operation. Therefore, urine flow is carefully observed postoperatively.

A surgically created shunt must function. Therefore, auscultation is used to assess its patency during the entire postoperative hospitalization. If doubt develops concerning shunt function, immediate 2D echocardiography, cineangiographic study, or both are indicated. If it is poorly functioning, prompt reoperation is indicated. In older patients with large acquired systemic-to-pulmonary artery collaterals, a continuous murmur is present preoperatively, and therefore simple auscultation is not as useful early postoperatively. In this setting, if cyanosis has not improved, echocardiography and/or cineangiography is indicated.

**RESULTS**

**Survival**

**Early (Hospital) Death**

Although hospital mortality in a few series of heterogeneous groups of patients has been 1% or less, in most series it varies between 2% and 5% (see Section II of Chapter 5). TF repair in patients 90 days of age or younger at 32 centers participating in the Society of Thoracic Surgeons congenital heart database over a 3-year period from 2002 to 2005 was associated with a mortality of 6.1% (CL 3.6%-9.6%). In the same centers, mortality for shunt palliation was 8.3% (CL 5.4%-12%).

Because the early rapidly declining phase of hazard does not flatten out until 3 to 6 months after operation (Fig. 38-46), hospital or 30-day mortality underestimates the risk of death early after repair.

**Time-Related Survival and the Question of “Cure”**

In considering survival after surgical repair, it must be recalled that deaths occurring before repair are not represented. Thus, an institution that delays repair until some specified age may have a few patients who, whether shunted or not, die before repair, whereas an institution that has a policy of one-stage repair in all symptomatic patients, no matter how young, may have an apparently higher mortality while actually saving more lives. Vobecky of Toronto’s Hospital for Sick Children examined this issue in 270 TF patients younger than age 18 months. A few deaths occurred before palliation, between palliation and repair, and after repair (Table 38-4). Major noncardiac anomalies may preclude repair, and major associated malformations may increase operative risk at any age. At present, the data show nearly equal time-related survival for one-stage repair performed at any age and staged operation.

In one analysis, time-related survival after repair in heterogeneous groups of patients at 1 month and 1, 5, 10, and 20 years was about 94%, 92%, 91%, 90%, and 87%, respectively (Fig. 38-47). Patient-specific survivals and those of homogeneous groups of patients vary, with 10- and 20-year values as high as 97% in some circumstances (Fig. 38-48). In another analysis, overall time-related survival was 80% at 40 years. In that study, predicted 40-year survival for patients repaired in the latter part of the experience (operation performed in the year 1985) was 88%.

“Is the patient cured of TF?” This is a critical question that must be examined not only for the entire heterogeneous population of patients undergoing repair but also for specific patients, taking into account the strength and time-relatedness of their various risk factors. For operation to be curative, the hazard function for death after the early postoperative period (3-6 months) must be no greater than that for an age-sex-race-matched general population and have no late increase
Table 38-4  Time of Death of Infants with Isolated Tetralogy of Fallot (n = 237)

<table>
<thead>
<tr>
<th>Timing of Death</th>
<th>No.</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>None</td>
<td>218</td>
<td>92</td>
</tr>
<tr>
<td>Before palliation</td>
<td>3</td>
<td>1.3</td>
</tr>
<tr>
<td>At palliation</td>
<td>2</td>
<td>0.8</td>
</tr>
<tr>
<td>Secondary palliation</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>After palliation/before repair</td>
<td>8</td>
<td>3.4</td>
</tr>
<tr>
<td>At repair</td>
<td>7</td>
<td>3.0</td>
</tr>
<tr>
<td>After repair</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>TOTAL DEATHS</td>
<td>22a</td>
<td>9.3</td>
</tr>
</tbody>
</table>

Data from Vobecky and colleagues.15

*Fourteen deaths occurred before repair (5.9%; CL 4.3%-7.9%).

Figure 38-46  Hazard function for death after repair of tetralogy of Fallot (TF) with pulmonary stenosis from two different studies. In both, the rapidly declining early phase of hazard does not flatten appreciably until 3 to 6 months after repair. A, Hazard function from UAB study (1967 to May 1986; n = 814) with follow-up over 15 years. There is a constant phase of hazard extending for as long as patients were followed. B, Hazard function from combined Boston Children’s Hospital–UAB study (September 1984 to 1989; n = 176), which has no late constant phase.220 Thus, the hazard function at 5 years, and presumably for a considerable period beyond, is the same as that of a matched general population (barely visible as dash-dot-dash line). (From Kirklin and colleagues.220)

Figure 38-47  Survival after repair of tetralogy of Fallot with pulmonary stenosis in the two heterogeneous groups of patients whose hazard functions are depicted in Fig. 38-46. Each circle represents a death estimated by the Kaplan-Meier method. Vertical bars represent 70% confidence limits (CL) of these estimates. Solid line represents parametric estimate of survival, and dashed lines enclose its 70% CLs. Dash-dot-dash line represents survival of an age-sex-race–matched general population. A, Survival after repair in UAB study (1967 to May 1986; n = 814). B, Survival after repair in combined Boston Children’s Hospital–UAB study (September 1984 to 1989; n = 176). (From Kirklin and colleagues.220)
Hospital–UAB data set, most of whom underwent primary (one-stage) repair, is behaving as if the constant hazard phase will be closer to that of a matched general population when they have been followed long enough for this to be identified. The Boston-UAB long-term data suggest that a late rise in the hazard function will not occur within the first 20 to 30 postoperative years (see Fig. 38-46).69,K20

Thus, the inference is that time-related survival of most patients after repair of TF with pulmonary stenosis under proper circumstances is excellent, approaching that of the general population, but that the risk of death throughout life is slightly greater than that of the general population.

Modes of Death

Considering death with multiple subsystem failure to be basically death in subacute heart failure, only half the patients who died in hospital after repair in the combined Boston Children’s Hospital–UAB study died this way. Pulmonary failure, hypermetabolic state, and catastrophic surgical or early postoperative events account for the remainder, a higher percentage than after most kinds of cardiac surgery in adults.275 Pathologic basis of the pulmonary failure has been described by Harms and colleagues,116 who found in their autopsy studies that extensive alveolar and interstitial edema and hemorrhage are characteristic of the lungs of patients dying early after repair of TF. This process is probably caused by the damaging effects of CPB (see Chapter 2),116,K18 to which severely cyanotic and polycythemic patients seem particularly sensitive. Thus, further improvement in results of repair may demand not only improved myocardial management but also lessening of the damaging effects of CPB and improved technical efficiency in the operating room and ICU when repair is being done in very small patients.

Incremental Risk Factors for Death

Incremental risk factors for death early and late after repair have been identified from a number of studies. A typical analysis from a single institution, identifying early hazard phase and late hazard phase risks, is shown in Table 38-5. There are a number of difficulties in definitively identifying risk factors for early death. These difficulties are that some variables were available for one analysis and not for another, that the risk factors may be different if procedural as well as patient characteristics are considered, and that some simultaneously determined “independent” risk factors are highly correlated and thus may be surrogates for one another (see “Variable Selection” in Section IV of Chapter 6). One of the most important difficulties is that in the current era, early mortality is so low that identifying risk factors for that phase is not possible.

Young Age at Repair

Young age at repair2 has been identified as a risk factor for death early after repair.19,C19,C22,M12,P20,W16 There are, however, two important qualifications that accompany this observation. First, young age is not necessarily an immutable risk factor, because the age at which risk increases appreciably has been progressively reduced as experience and knowledge have grown. This improvement is illustrated by the UAB experience, in which risk of hospital death and predicted 20-year survival after repair in a 6-month-old infant improved considerably between 1967 and 1986 (Fig. 38-49). The

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Table 38-5 Incremental Risk Factors for Time-Related Death Following Corrective Repair of Tetralogy of Fallot (n = 1181)

<table>
<thead>
<tr>
<th>Risk Factor for Death</th>
<th>Estimate</th>
<th>P value</th>
<th>Reliability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early hazard phase</td>
<td>-0.06</td>
<td>&lt;0.001</td>
<td>99</td>
</tr>
<tr>
<td>Earlier date of corrective surgery (units = years)</td>
<td>-0.18</td>
<td>&lt;0.001</td>
<td>92</td>
</tr>
<tr>
<td>Classic tetralogy of Fallot</td>
<td>-0.94</td>
<td>&lt;0.001</td>
<td>75</td>
</tr>
<tr>
<td>Coexisting atrioventricular septal defect</td>
<td>+1.21</td>
<td>&lt;0.001</td>
<td>98</td>
</tr>
<tr>
<td>Right aortic arch</td>
<td>+0.57</td>
<td>0.001</td>
<td>78</td>
</tr>
<tr>
<td>Previous central/Potts/Waterston shunt</td>
<td>+0.86</td>
<td>0.002</td>
<td>71</td>
</tr>
<tr>
<td>RV-PT conduit in classic tetralogy of Fallot</td>
<td>+1.05</td>
<td>0.03</td>
<td>—</td>
</tr>
<tr>
<td>Late hazard phase</td>
<td>+2.01</td>
<td>&lt;0.001</td>
<td>72</td>
</tr>
<tr>
<td>Coexisting atrioventricular septal defect</td>
<td>+1.00</td>
<td>0.002</td>
<td>79</td>
</tr>
<tr>
<td>Branch pulmonary artery stenosis</td>
<td>+1.47</td>
<td>0.001</td>
<td>66</td>
</tr>
<tr>
<td>Double-outlet right ventricle variant</td>
<td>+1.33</td>
<td>&lt;0.01</td>
<td>54</td>
</tr>
</tbody>
</table>

Data from Hickey and colleagues.774 Reliability represents the percentage reliability of the P value as determined by percentage of bootstrap resamples for which the variable is included in the parametric model (inclusion threshold P < .1). Key: RV-PT, Right ventricular-pulmonary trunk.
incremental risk of young age in general is currently unapparent until age is younger than 3 months, and in some circumstances younger than 1 month (Fig. 38-50). Second, studies examining young age as a risk factor for early death have the inherent bias that only symptomatic patients were repaired in the neonatal period or early infancy. Because symptoms correlate with less favorable morphology of the RV outflow tract in patients with TF, it follows that patients who underwent repair at a very early age uniformly had less favorable morphology. Thus, there were no patients who underwent very early repair in these series with favorable morphology (asymptomatic). Even with multivariable analysis, it is difficult to overcome this bias.

Reduction of the age at which risk is increased is due in part to increasing technical expertise in intracardiac surgery and early postoperative care in the very young. Further improvements in these areas may completely neutralize the increased risk of young age. Control of the damaging effects of CPB (see Chapter 2) and improvement in the function of the heart early postoperatively, brought about by more effective intraoperative myocardial management, will assist in this effort.

Older Age at Repair
Older age has been identified as a risk factor for death early and late after repair (see Table 38-5). Its effect on survival late after repair is probably truly immutable (Fig. 38-51). This is because the bases of the incremental risk of older age lie in the adverse, and to a considerable extent irreversible, effect of long-standing RV hypertension, cyanosis, and polycythemia on cardiac structure and function. It is in part to prevent these irreversible changes that repair is advisable early in life. A contraindication to early repair may be presence of an anomalous LAD from the RCA. Relative contraindications include complex pulmonary artery anatomy or very small pulmonary arteries. However, independent reports from Reddy, Stellin, Sousa-Uva, Starnes, and Groh and their colleagues document excellent results when early one-stage repair is applied routinely in neonates and infants.

Severity of Right Ventricle–Pulmonary Trunk Junction Hypoplasia
Severe hypoplasia of the RV–pulmonary trunk junction (“anulus”) has been identified as a risk factor for death, at least early after repair (see Fig. 38-50). This may be related in part to the need for a transanular patch when the hypoplasia is severe, and to the correlation between severity of anular hypoplasia and postrepair \( P_{RV/LV} \), even when a transanular patch is used and particularly when there is coexisting hypoplasia of the distal pulmonary trunk (see “Decision and Technique for Transanular Patching” earlier in this section). Thus, severity of anular hypoplasia, use of a transanular patch, and postrepair \( P_{RV/LV} \) are all surrogates for one another in a complex manner that is difficult to quantify (Fig. 38-52).

Small Size of Right and Left Pulmonary Arteries
Important localized or diffuse hypoplasia of the RPA and LPA is uncommon in patients having TF with pulmonary

Figure 38-49 Nomograms illustrating decreasing strength across year of operation of the incremental risk of young age on early and late survival after repair of tetralogy of Fallot with pulmonary stenosis. (Nomogram is specific solution of multivariable risk factor equation from Kirklin and colleagues. Values entered for other variables in equation are in Appendix 38A). A, Predicted 30-day mortality. B, Predicted 20-year survival, including early deaths.

Figure 38-50 Nomogram illustrating incremental risk of young age and of dimension of pulmonary “anulus” on early survival after repair of tetralogy of Fallot with pulmonary stenosis in recent era. Note that effect of young age is stronger and more evident in patients with a very small “anulus” (\( z \) value of –8) than in the others, reflecting the usual incremental effect of one risk factor on another. (From Kirklin and colleagues.)
Transanular patching was not a risk factor late postoperatively in earlier UAB and Mayo Clinic patients. However, the increased chance of needing later reoperation and its attendant risk suggest that in a sufficiently large and well-matched comparison, use of a transanular patch may have a late increased risk. The adverse effect of transanular patching, as noted in earlier studies, is well tolerated acutely and chronically out to about 20 years by the previously hypertrophied RV. However, the natural history of patients with isolated congenital pulmonary valvar regurgitation suggests that by about 40 years after repair, RV dysfunction will have developed in some and could lead to premature death.

**Postrepair \( P_{RV/LV} \)**

Important residual pulmonary stenosis after repair, expressed as postrepair \( P_{RV/LV} \), has been identified as a risk factor for premature death early and late after operation. This is true of postrepair (OR)
P_{RV/LV}, but the ratio as measured in the ICU about 24 hours after operation is a more powerful and precise predictor (see Fig. 38-44). The interaction of young age (or small patient size), small anulus, transanular patching, and postrepair P_{RV/LV} is apparent from these same studies.\textsuperscript{16,20} Although identified as a risk factor, postrepair P_{RV/LV} is inversely correlated with size of the pulmonary valve “anulus” and of the distal pulmonary trunk.

Previous Palliative Operations
A single previously performed classic shunting operation is not a risk factor for death after repair, but more than one palliative operation has been shown to be.\textsuperscript{16} When a pulmonary artery has been importantly distorted by a shunting operation, an unusual occurrence under proper circumstances, risks of repair are increased.

Multiple Ventricular Septal Defects
Multiple VSDs are present in only 1% to 3% of patients having TF with pulmonary stenosis, but they have been identified as a strong risk factor for death in the early hazard phase, as evident in Fig. 38-53.\textsuperscript{20}

Coexisting Related Cardiac Anomalies
Coexisting complete atrioventricular septal defect complicates repair of TF with pulmonary stenosis, and a composite review of outcomes from 50 individual studies reported over a 40-year period imply higher surgical mortality than for simple TF (Table 38-6).\textsuperscript{15} Although mortality improved in the 1990s compared with prior years, it has not improved further and remains substantial. Nevertheless, mortality varied from study to study in this review, with some reports showing only a small incremental risk.\textsuperscript{2}

In one study, Down syndrome, rather than the atrioventricular septal defect itself, appeared to be the incremental risk factor (Table 38-7).\textsuperscript{20}

Historically, large AP collateral arteries were risk factors for death early after repair of TF with pulmonary stenosis.

### Table 38-6
Compilation of All Major Studies Reporting Surgical Mortality for Repair of Tetralogy of Fallot in Association with Complete Atrioventricular Septal Defect between 1965 and 2005

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients</th>
<th>Mortality ((n))</th>
<th>Mortality (%)</th>
<th>CLs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1965-1990</td>
<td>106</td>
<td>21</td>
<td>20</td>
<td>16-25</td>
</tr>
<tr>
<td>1991-1998</td>
<td>120</td>
<td>13</td>
<td>11</td>
<td>7.9-15</td>
</tr>
<tr>
<td>1998-2005</td>
<td>120</td>
<td>12</td>
<td>10</td>
<td>7.2-14</td>
</tr>
</tbody>
</table>

Data from Ricci and colleagues.\textsuperscript{21}

### Table 38-7
Confounding Effects of Down Syndrome and Coexisting Complete Atrioventricular Septal Defects on Non–Risk-Adjusted Survival in Patients with Tetralogy of Fallot

<table>
<thead>
<tr>
<th>Category</th>
<th>Total Deaths after Entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Down syndrome</td>
<td>177</td>
</tr>
<tr>
<td>No AV septal defect</td>
<td>173</td>
</tr>
<tr>
<td>AV septal defect</td>
<td>9</td>
</tr>
<tr>
<td>P (Fisher)</td>
<td>.7</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>19</td>
</tr>
<tr>
<td>No AV septal defect</td>
<td>10</td>
</tr>
<tr>
<td>AV septal defect</td>
<td>9</td>
</tr>
<tr>
<td>P (Fisher)</td>
<td>.3</td>
</tr>
<tr>
<td>P (Normal vs. Down syndrome, (\chi^2))</td>
<td>.001</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues.\textsuperscript{20}

Key: AV, Atrioventricular; CL, 70% confidence limits.

However, this may have been due to the greater frequency of important RPA and LPA hypoplasia in such patients, and of discontinuity between the pulmonary trunk and RPA or LPA.\textsuperscript{20} It is likely that early risk associated with AP collaterals has largely been neutralized, because current surgical mortality for patients with AP collateral arteries and TF with pulmonary atresia is now as low as 2%.\textsuperscript{56}

### Other Risk Factors
Although high hematocrit was frequently observed in an earlier era of delayed surgery, it is uncommon today; when seen, it may be a strong risk factor.\textsuperscript{11,17}

Graham and colleagues proposed that small LV end-diastolic volume (<55% of normal for age) is an important risk factor for early death after repair.\textsuperscript{26} Nomoto and colleagues also reported that small LV volume is a risk factor, with a demonstrable increase in risk when preoperative LV end-diastolic volume is less than about 65% of normal.\textsuperscript{10} Oberhansli and Friedli reported similar findings.\textsuperscript{91}

### Heart Block
Complete heart block is uncommon after repair. It occurred in 7 of 814 patients (0.9%; CL 0.5%-1.3%) from 1967 to May 1986 at UAB, and in 0.6% (CL 0.1%-1.9%) of patients from September 1984 to 1989.\textsuperscript{16,20} Right bundle branch block...
Figure 38-54  New York Heart Association (NYHA) functional class after repair of tetralogy of Fallot with pulmonary stenosis, according to interval between operation and last follow-up. Numbers in parentheses along horizontal axis represent number of patients available for functional class categorization at the odd-numbered interval below which number is positioned. Squares represent proportion of patients in functional class I at each interval; circles, those in class II; and triangles, those in class III. Solid line represents slope of solution of ordinal logistic (longitudinal) regression analysis, although the P value of .2 for the difference from zero slope indicates that change across time in the distribution of patients according to their NYHA functional class could be due to chance alone. (From Kirklin and colleagues.\textsuperscript{19})

Junctional Ectopic Tachycardia

Junctional ectopic tachycardia occurs infrequently after repair of TF. Survival depends on aggressive treatment in the ICU with moderate core cooling and amiodarone (see “Atrial Arrhythmias” in Section I of Chapter 5).\textsuperscript{39} Thereafter, there is probably little risk of complete heart block. Repair by way of the right atrial–pulmonary artery approach may carry a higher risk of junctional ectopic tachycardia; however, there are no firm data to support this.

Functional Status

About 98\% of patients are considered by themselves or their parents to be in New York Heart Association (NYHA) functional class I after repair.\textsuperscript{12,27} Most importantly, this proportion has not declined over time, at least to 20 years (Fig. 38-54).

Some asymptomatic patients have reduced exercise capacity,\textsuperscript{29,89} some have normal functioning capacity as judged by quantitative testing (Table 38-8), and some have the capacity of a trained athlete.\textsuperscript{89} Some patients with normal response to exercise testing have other abnormalities, such as limitation in chronotropic response to exercise.\textsuperscript{12}

Risk factors for impaired exercise tolerance have been identified, and these include older age at repair. Repair in the first 5 years of life results in a normal response to objective exercise testing.\textsuperscript{11,36,12} Patients averaging 12 years of age at operation have subnormal exercise capacity late postoperatively.\textsuperscript{11} Residual RV hypertension, expressed as P\textsubscript{RV}, P\textsubscript{RV/LV}, or RV-to–pulmonary artery gradient, adversely affects functional status late after complete repair.\textsuperscript{39,14,99} Wessel and colleagues suggest that in the absence of other problems, P\textsubscript{RV} greater than 50 mmHg (corresponding roughly to P\textsubscript{RV/LV} > 0.7) is likely to exert this effect (Table 38-9), although P\textsubscript{RV} greater than 70 mmHg may be a more realistic number (indeed, the relation is likely continuous but nonlinear).\textsuperscript{99} Pulmonary valve regurgitation after repair in reduced exercise capacity regardless of RV systolic pressure.\textsuperscript{14,12,12,33,77,99} Consistent with this is the tendency of patients with transanular patches to have larger cardiothoracic ratios and RV volumes\textsuperscript{82} late postoperatively. In patients who have undergone repair without insertion of a valve for TF with absent pulmonary valve (Section III),

| Table 38-8  Exercise Performance Under Standardized Conditions 1 or More Years after Repair of Tetralogy of Fallot |
|-------------------------------------------------|-------------------------------------------------|---------------|
| Characteristic                                  | 10 Highest Performers\textsuperscript{a} | 10 Lowest Performers\textsuperscript{a} | P (for Difference) |
| CT ratio                                        | 0.49                                        | 0.58          | .001 |
| P\textsubscript{RV} (mmHg)                      | 39                                          | 76            | .001 |
| Age at repair (years)                           | 5.83                                        | 10.7          | .001 |
| Pulmonary regurgitation (patients)              | 0/10                                        | 8/10          | .0004 |
| Previous Potts anastomosis (patients)           | 0/10                                        | 4/10          | .04  |

Data from Wessel and colleagues.\textsuperscript{99} \textsuperscript{a}Mean values are given for continuous variables. \textsuperscript{b}Duration of exercise greater than 100\% of normal for age. \textsuperscript{c}Duration of exercise 43\% of normal for age. Key: CT, Cardiothoracic; P\textsubscript{RV}, right ventricular pressure.

| Table 38-9  Exercise Performance Under Standardized Conditions One or More Years after Repair of Tetralogy of Fallot, According to Right Ventricular Pressure and Presence of Pulmonary Regurgitation |
|-------------------------------------------------|-------------------------------------------------|---------------|
| Right Ventricular Pressure Range and Regurgitation | Duration of Exercise (% of Normal Controls) Mean ± SD | P (for Difference) |
| P\textsubscript{RV} < 50 mmHg                   | Pulmonary regurgitation: no                     | 98 ± 20       |               |
|                                                | Pulmonary regurgitation: yes                    | 75 ± 8.9      | <.05          |
| P\textsubscript{RV} > 50 mmHg                  | Pulmonary regurgitation: no                     | 88 ± 16       |               |
|                                                | Pulmonary regurgitation: yes                    | 51 ± 30       | <.02          |

Data from Wessel and colleagues.\textsuperscript{99} Key: P\textsubscript{RV}, Right ventricular pressure; SD, standard deviation. \textsuperscript{a}Exclusive of patients with residual ventricular septal defects.
When the pulmonary valve is regurgitant, RV systolic function and end-diastolic volume are less likely to be normal, and their abnormality correlates with amount of regurgitation. When a transanular patch has been used in the repair, ejection fraction is more likely to be low, and RV end-diastolic volume is increased, often severely so. 

Increased RV wall thickness and consequently decreased ventricular compliance may limit volume expansion and RV enlargement. Reduced compliance may also protect against detrimental effects of pulmonary regurgitation. 

When repair is made at a still older age, the functional result is clearly worse than when it is performed in infancy or early childhood.

Pulmonary regurgitation has its most evident effect on RV function. When a transanular patch has not been used and the pulmonary valve is competent, RV systolic function (ejection fraction) and end-diastolic volume may be normal late postoperatively. Furthermore, large residual or recurrent VSDs (Qp/Qs > 2) strongly predispose the patient to chronic heart failure late postoperatively. 

Maximal oxygen uptake during exercise is only 30% to 40% of normal in patients corrected at an average age of 19.5 years. When repair is made at a still older age, the functional result is clearly worse than when it is performed in infancy or early childhood.

Figure 38-55 Results of serial exercise testing (work capacity above, exercise duration below, expressed as percentage of predicted value for age) after repair of tetralogy of Fallot with absent pulmonary valve. Intracardiac repair was performed without a valve in this patient at age 8.45 years, and exercise and work capacity steadily decreased. An allograft pulmonary valve was inserted when the patient was 19 years old, with subsequent improvement in performance. Key: APV, Allograft pulmonary valve; Ex, Exercise; ICR, intracardiac repair; Pred, predicted; W, work. (From Ilbawi and colleagues.)

Pulmonary regurgitation has its most evident effect on RV function. When a transanular patch has not been used and the pulmonary valve is competent, RV systolic function (ejection fraction) and end-diastolic volume may be normal late postoperatively. However, even in this circumstance, RV ejection fraction may not increase normally with exercise (Fig. 38-56). 

Residual or recurrent VSDs decrease exercise capacity. Furthermore, large residual or recurrent VSDs (Qp/Qs > 2) strongly predispose the patient to chronic heart failure late postoperatively.

Maximal oxygen uptake during exercise is only 30% to 40% of normal in patients corrected at an average age of 19.5 years. When repair is made at a still older age, the functional result is clearly worse than when it is performed in infancy or early childhood.

Figure 38-56 Right ventricular and left ventricular systolic function at rest and during exercise after repair of tetralogy of Fallot. Mean value for each set of data is indicated by open circle. Key: LV, Left ventricular; NS, not significant; RV, right ventricular. (From Reduto and colleagues.)

Figure 38-57 Right ventricular end-diastolic volume late after repair of tetralogy of Fallot. Patients are separated into those with and without a transanular patch. Stippled area represents normal values. Key: RVEDV, Right ventricular end-diastolic volume. (From Graham and colleagues.)

When the pulmonary valve is regurgitant, RV systolic function and end-diastolic volume are less likely to be normal, and their abnormality correlates with amount of regurgitation. When a transanular patch has been used in the repair, ejection fraction is more likely to be low, and RV end-diastolic volume is increased, often severely so. However, it has been suggested that increased RV wall thickness and consequently decreased ventricular compliance may limit volume expansion and RV enlargement. Reduced compliance may also protect against detrimental effects of pulmonary regurgitation.
valve regurgitation. Decrease in ejection fraction is correlated with the increase in end-diastolic volume. Precise measurements of RV end-diastolic volume using MRI and CT imaging suggest that volume over 150 to 170 mL · m⁻² will result in failure of the RV to remodel even after placement of a competent pulmonary valve.

A resting systolic pressure up to 60 to 70 mmHg has little adverse effect on postrepair RV systolic and diastolic function. Higher systolic pressures produce dysfunction, but this is not well quantified.

Other potential determinants of postrepair RV function have not been correlated with it in a quantitative fashion.

**Right Ventricular Aneurysms**

RV aneurysms adversely affect RV function, but they are uncommon. True aneurysm is more common than false aneurysm and is presumably related to excessive thinning or devascularization of the RV free wall, or thinning and bulging of pericardium if it has been used as an infundibular or transanular patch. Most RV aneurysms develop within 6 months of operation, and true aneurysms stabilize and rarely progress. False aneurysm, in contrast, may progress rapidly and rupture.

**Residual Right Ventricular Outflow Obstruction**

Residual narrowing in the infundibulum at the RV–pulmonary trunk junction (with or without a transanular patch) or more distally can result in at least some residual RV outflow obstruction. Magnitude of obstruction is not evident at the end of operation, because both the gradient between the RV and distal pulmonary trunk and the postrepair \( P_{RV/LV} \) are usually somewhat less late postoperatively than when measured in the operating room (Fig. 38-58). Dimensions of the RV–pulmonary junction enlarge proportionally to growth of the child after repair, whether or not a transanular patch was used (Fig. 38-59). However, disproportionate growth (i.e., “catch-up” growth) of the “anulus” does not occur without a transanular patch, and it cannot be expected that an “anulus” that is relatively small preoperatively and intraoperatively will become normal sized late postoperatively (Table 38-10). In some cases when a transanular patch is used, the junction will enlarge far out of proportion to growth of the child. This is caused by the same mechanism proposed for RV aneurysm formation: stretching and thinning of the patch, native tissue, or both.

Progression of originally unimportant residual RV outflow tract obstruction to important obstruction occurs uncommonly. Stiffening, thickening, and eventually even calcification of pulmonary valve cusps may occur and produce increasing RV hypertension, whether they are left in an intact “anulus” or beneath a transanular path. Also, if mild to moderate infundibular obstruction is present immediately after surgery, progressive hypertrophy and fibrosis in the infundibulum may lead to an increase in obstruction. This usually becomes evident within a year of initial repair.

Important residual or recurrent RV outflow obstruction is an indication for reintervention if the obstruction is considered treatable. This is because of its adverse effect on RV function, particularly when considerable pulmonary regurgitation coexists.
Table 38-10  Change in Size of the Right Ventricular–Pulmonary Trunk Junction (“Anulus”) after Repair of Tetralogy of Fallot

<table>
<thead>
<tr>
<th>Type of Repair</th>
<th>Pulmonary “Anulus”</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>z (Preop) Mean ± SD</td>
</tr>
<tr>
<td>No transanular patch or allograft (n = 12)</td>
<td>−2.2 ± 1.5</td>
</tr>
<tr>
<td>Transanular patch (n = 11)</td>
<td>−2.4 ± 1.8</td>
</tr>
</tbody>
</table>

Data from Calder and colleagues.2

| | Change over a 30-month period in 23 infants aged 0.7 to 21 months. |
| Key: | Postop, Postoperative; Preop, preoperative; SD, standard deviation. |

Table 38-11  Reasons for Reintervention after Repair of Tetralogy of Fallot with Pulmonary Stenosis

<table>
<thead>
<tr>
<th>Cause of Reinterventionb</th>
<th>No.</th>
<th>% of 757</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent or recurrent RV outflow obstruction</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>Pulmonary regurgitation</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Residual or recurrent VSD</td>
<td>3</td>
<td>0.3</td>
</tr>
<tr>
<td>Large left-to-right shuntc</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>Valved conduit obstruction</td>
<td>2</td>
<td>0.2</td>
</tr>
<tr>
<td>Miscellaneous (four different categories)</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>32</td>
<td>4</td>
</tr>
</tbody>
</table>

*bBased on follow-up and analysis of 757 hospital survivors (UAB experience, 1967 to May 1986). |
| bObstruction was isolated and in the infundibulum in 4, at anulus in 1, at bifurcation of pulmonary trunk in 2, at origin of one or both pulmonary arteries in 2, and at multiple sites in 4. In one person each, it was associated with a small VSD, a right ventricular aneurysm, a small VSD and a right ventricular aneurysm, and severe tricuspid regurgitation. |
| cThrough a recanalized classic Blalock-Taussig shunt and residual VSD. |

Reoperation and Other Reinterventions for Right Ventricular Outflow Problems

Reoperations are infrequent in the first years after TF repair (Table 38-11), but by 30 years, half of all survivors require reoperation (Fig. 38-60).1,18 Risk of reoperation for RV outflow tract obstruction and pulmonary regurgitation both increase as time passes; however, the pattern is different. Most reoperations for obstruction occur early postoperatively, mostly in the first year, and then the rate slows but persists.1,16 The pattern of reoperation for pulmonary regurgitation varies depending on the study. In one study, the reoperation rate for pulmonary regurgitation was very low in the first years after repair and then increased substantially as time passed.1,16 In a report that covered operations performed between 1967 and 1986 that involved a transanular patch, Kirklin and colleagues reported freedom from reintervention for pulmonary regurgitation of 98% at 10 years and 88% at 20 years.1,16 In a recent (2009) study from Toronto, however, the hazard for pulmonary valve replacement was constant up to 4 decades after repair, at 0.8% per year.1,18 In an earlier (1997) study from Toronto, with follow-up extending to 36 years, only 1.2% of patients underwent reintervention for pulmonary regurgitation.1,18 Furthermore, the study by Kirklin and colleagues identifies use of a transanular patch as a risk factor for subsequent pulmonary valve replacement, but the Toronto study does not. Although Kirklin and colleagues identify transanular patching as a risk factor, few patients in whom a transanular patch was inserted have undergone reoperation unless their postrepair (OR) $P_{RV/LV}$ was greater than about 0.7 (Fig. 38-61). Many of these differences and inconsistencies among studies probably reflect the subjective nature of the decision-making process related to the timing of reintervention for pulmonary regurgitation.

These classic studies notwithstanding, compelling data now exist showing that late serious problems arise in patients with isolated free pulmonary regurgitation; that is, pulmonary...
regurgitation without associated residual elevated RV pressure or residual left-to-right shunting. Free pulmonary regurgitation results in dilatation of the RV, \( \text{RV} \) dilatation correlates with prolonged QRS duration on ECG, and prolonged QRS duration is associated with sudden death. Reoperation as a marker of residual RV outflow tract problems in many analyses presents some difficulties and limitations. There are no accepted, standardized physiologic criteria for reoperation. This is of particular concern when the problem is pulmonary regurgitation. The long-term follow-up studies cited above show varying, but generally low, rates of reoperation for pulmonary regurgitation, even with follow-up of several decades or more. It must be kept in mind, however, that these studies used criteria for reoperation that are both more subjective and less strict than those used today. Also these studies rarely involve patients who originally underwent neonatal or even infant repair. They utilized presence of symptoms, onset of arrhythmias, and progressive tricuspid regurgitation as criteria for reoperation. More recently, a prolonged QRS complex of greater than 180 msec, and RV diastolic volume greater than 150 to 160 mL·m\(^{-2}\) have been added. Several studies using MRI indicate that enlarged RVs above about 150 to 170 mL·m\(^{-2}\) do not remodel to normal volume after a competent pulmonary valve is placed, although substantial volume reduction is observed.

Inserting an allograft aortic or pulmonary valve, or a bioprosthetic valve, are the therapeutic options when intervention is required for pulmonary regurgitation, because they increase RV ejection fraction, decrease RV end-diastolic dimensions, and improve symptomatic status. Survival after pulmonary valve replacement is excellent, with reports of 94% at 20 years. Percutaneous transcatheter pulmonary valve placement is an alternative in selected cases.

Reoperation for residual pulmonary stenosis is uncommon, with 95% of patients being free from it for at least 20 years (Fig. 38-62). Although rate of reoperation is highest early after repair, there is a constant phase of hazard as well, lasting as long as patients have been followed. The higher the postrepair (OR) \( P_{RV/LV} \), the greater the probability of this type of reoperation, and the prevalence increases particularly steeply when the value is greater than about 0.7 (Fig. 38-63).

Early results for pulmonary valve replacement are good, even when additional procedures such as tricuspid valve repair or more complex RV outflow tract reconstruction are also performed. Thirty-day mortality of 2.6% (CL 1.2%-5.1%) has been reported, with 19% occurrence of postoperative arrhythmias, 13% respiratory complications, 13% renal complications, 13% reoperation during admission, and 3% myocardial infarction. Predictors of prolonged hospitalization include age greater than 45 years, number of previous sternotomies, and need for urgent operation.

Left Ventricular Function
LV systolic and diastolic function are variable late after operation. Risk factors for poor LV function include older age at repair, pre-repair status of LV (affected as it is by previous palliative operations), and residual or recurrent defects.

Patients undergoing repair during the first few years of life have normal or near-normal LV function not only at rest but also during stress. Patients who are older at the time of...
repair, often have depressed LV ejection fraction at rest that intensifies during stress. Less satisfactory function in patients undergoing repair at an older age may be due to myocardial damage from chronic preoperative hypoxia and to long-standing LV overload from systemic–pulmonary arterial shunts in most patients who are older at repair. Other potential causes of LV dysfunction include intrinsic aortic root pathology. Aortic root dilatation and reduced aortic elasticity have been linked to aortic regurgitation, and aortic regurgitation to reduced LV function.

The age range at repair within which late postoperative LV function at rest and during exercise can be expected to be normal is not clearly defined. Some studies indicate that it extends to only age 2 to 3 years, others suggest that it extends to as late as age 10 if shunting operations have not been necessary.

Pulmonary Function

Patients with an optimal hemodynamic result from repair of TF in infancy or early childhood (closed VSD, PrV < 50 mmHg, and no pulmonary valve regurgitation) have normal lung volumes and capacities late postoperatively. Conversely, patients with a less than optimal hemodynamic result and those operated on later in life have distinctly subnormal lung function. Postoperative pulmonary valve regurgitation has a particularly adverse effect on late postoperative lung volume and function.

Recurrent (Residual) Ventricular Septal Defects

Important recurrent or residual VSDs are uncommon, with reoperation being necessary in less than 1% of cases. Even small and hemodynamically unimportant leakage is infrequent. Routine left ventriculography done an average of 23 months postoperatively in 23 infants showed a tiny residual VSD in one (4%; CL 0.6%-14%). Others have reported small leakage in up to 10% of patients. When important shunts are present, they are usually from inaccurate repair or dehiscence at the posteroinferior angle of the VSD.

Sudden Death and Important Arrhythmic Events

There has been much discussion about the possibility of sudden or arrhythmic death late after repair of TF with pulmonary stenosis, but there is a lack of information about the circumstances under which this is likely to occur. These events are more likely to occur in patients not operated on in early life and are unlikely when patients are repaired in the first few years of life. Thus, probability of sudden death or an important arrhythmic event (defined as a clearly arrhythmic death, intractable ventricular tachycardia, or insertion of a pacemaker for bradycardia developing late postoperatively) within 20 years of repair has occurred in less than 1% of patients who were younger than age 5 years at operation (Fig. 38-64). When the patient underwent repair in adult life, probability was 5% to 10%. Castaneda and colleagues found no sudden deaths and no important ventricular electrical instability in long-term follow-up of patients undergoing repair in infancy. Others have reported similar experiences with the relation between age and prevalence of sudden death late postoperatively.

When repairs are incomplete, and particularly when this results in postoperative cardiomegaly, prevalence of ventricular arrhythmias and sudden death is higher. During long-term follow-up of the early Mayo Clinic patients, only 2% experienced sudden death; most had important cardiomegaly. Similar findings have been reported by others.

When there is important residual pulmonary stenosis, prevalence of late postoperative arrhythmic events may be somewhat higher, but the correlation is weak. Strong correlation has been demonstrated between pulmonary regurgitation and important ventricular arrhythmias late postoperatively. Prolongation of the ECG QRS complex, which develops with the RV dilatation associated with pulmonary regurgitation, is associated with sudden death.

Rarely, the right ventriculotomy scar may be arrhythmogenic. This should be considered as a possibility in patients with life-threatening ventricular arrhythmias only when cardiomegaly is absent and there is neither important pressure nor volume overload of the RV. Under these circumstances, electrophysiologic mapping is indicated. When the source of the arrhythmia can be localized to the right ventriculotomy scar, excising the scar and inserting a patch graft have been reported to be beneficial. Cryoablation techniques may also be effective in controlling arrhythmogenic foci localized to the ventriculotomy scar.

Infective Endocarditis

Infective endocarditis is rare after repair. No instances were observed with up to 10-year follow-up in two large studies. Interim Results after Classic Shunting Operations

Survival

Classic B-T and PTFE interposition shunts have a hospital mortality approaching zero and 1-month mortality of less than 1%. Other types of shunting operations have a higher hospital mortality; however, they
are rarely used in modern practice and are of historical interest only.\textsuperscript{\text{118}}

Probably the most important risk factor for early death after classic shunting procedures is pulmonary arterial problems.\textsuperscript{\text{113}} Young age adds an increment of risk to shunting operations, but a relatively small one (Fig. 38-65).

**Interim Events**

*Early (<30 days) nonfatal shunt closure* or narrowing occurs uncommonly (7%) in patients undergoing classic B-T or PTFE interposition shunt operations for TF.

*Early and intermediate-term shunt closure* or narrowing requiring reoperation occurs in 3% to 20% of heterogeneous groups of infants and children.\textsuperscript{\text{26,42,44,20,\text{113}}} Closure or important narrowing is considerably more common in neonates and young infants than in older patients (74% vs. 90% freedom at 2 years).\textsuperscript{\text{113}} However, closure may be less common in neonates and young infants when a PTFE interposition graft is used.\textsuperscript{\text{113}} Overall, shunt closure or narrowing results in unsatisfactory palliation within 3 years of shunting in about 40% of patients.\textsuperscript{\text{14}} This prevalence does not seem to differ among patients receiving a classic B-T shunt and those receiving a PTFE interposition graft.\textsuperscript{\text{14}} Use of aspirin seemingly does not increase long-term patency or reduce occurrence of localized shunt stenosis.\textsuperscript{\text{14}}

One manifestation of reduced blood flow in the arm on the side of a classic B-T shunt is that it becomes slightly shorter and smaller during the intermediate term after operation.\textsuperscript{\text{107}} Likewise, strength of the arm on the side of the shunt has been demonstrated to be less than normal, even though the patient is unaware of this.\textsuperscript{\text{73}} When blood flow reduction is more severe than usual, gangrene of the hand can occur, although rarely.

*Sudden death* without explanation or autopsy, and nonfatal brain abscess each occur in about 1% of cases.\textsuperscript{\text{116,22}} Improperly performed shunts of any kind result in a higher prevalence of unsatisfactory interim results, primarily because of iatrogenic pulmonary arterial problems.

Iatrogenic pulmonary arterial problems are reported to be uncommon after classic shunting or PTFE interposition

shunting operations in early series.\textsuperscript{\text{26,22}} However, in the present era, because shunts are performed more frequently in patients with small pulmonary arteries, especially neonates, angiographic evidence of pulmonary artery distortion is fairly common late postoperatively and must be dealt with at the time of repair.\textsuperscript{\text{118}} From a historical perspective, these problems are much less frequent and less severe than those that were seen with obsolete shunts, such as Waterston and Potts shunts.\textsuperscript{\text{111,11,5,13,17,13}}

The key beneficial interim results of shunting procedures are increased $Q_p$, with consequent reduction in cyanosis and polycythemia, and improved functional capacity. NYHA functional class is usually I or II after shunting. $Sao_2$ at rest is usually 80% to 90%, but it always decreases with exercise, at times to as low as 50%.\textsuperscript{\text{47,15}} These benefits are obtained at the expense of increased LV stroke volume, a stimulus to gradual development of LV dysfunction.

Another benefit of classic shunting procedures is the diffuse increase in size of the RPA and LPA.\textsuperscript{\text{22,19}} The response of the valve and pulmonary “anulus” to shunting procedures is unpredictable. Some studies suggest that enlargement of the “anulus” can occur as a result of a shunting procedure.\textsuperscript{\text{47,26,18}} Whereas others indicate that a stenotic valve can progress to atresia after shunting.\textsuperscript{\text{1,28}}

Important pulmonary vascular obstructive disease does not occur with use of PTFE shunts if size of the shunt is chosen appropriately. Historically, vascular disease did develop after other shunts, such as a classic B-T, Waterston, or Potts shunt, but rarely before 5 years had passed.\textsuperscript{\text{25,24}} Beyond this time, the proportion of patients who developed hypertensive pulmonary vascular disease increased with increasing shunt duration.\textsuperscript{\text{24,6,3,21,10}}

**INDICATIONS FOR OPERATION**

Diagnosis of TF is generally an indication for repair. Early repair is advisable because of the unfavorable natural history of the disease, particularly in the first year of life (see Fig. 38-23), advantages of repair before irreversible secondary myocardial and pulmonary changes occur, and low risks of repair in the current era. Yet the timing of repair remains controversial. When severe symptoms develop in the first 1 or 2 months of life, some favor one-stage repair, whereas others prefer an initial shunting operation followed within 12 months by repair.

When diagnosis is made in the neonatal period and the patient is, and remains, essentially asymptomatic or only mildly symptomatic, one-stage repair is typically deferred for a variable period. The ideal period of deferral, if any, is unclear and in current practice ranges from 2 to 24 months. A strong argument can be made that for institutions experienced in complex surgery in small infants, one-stage repair should be performed in the first 2 to 3 months.

Overall results with a two-stage protocol with an initial shunting operation for patients younger than about age 6 months and repair between age 6 and 24 months appear to be similar to those of one-stage repair, although such a protocol is not ideal.\textsuperscript{\text{20}} However, two-stage repair is probably prudent for institutions not well prepared for the intraoperative and early postoperative care required by neonates and small children undergoing intracardiac operations. It is also reasonable for surgeons who are not yet certain of their ability to achieve comparable results with one-stage

![Figure 38-65 Nomogram illustrating effect of age on hospital mortality after repair of tetralogy of Fallot with pulmonary atresia versus pulmonary stenosis in patients with previous classic shunts. (Nomogram is specific solution of multivariable risk factor equation in original publication. Values entered for other variables are also given in original publication.) (From Kirklin and colleagues.\textsuperscript{\text{25}})](image-url)
repair in neonates and infants younger than about age 6 months.

When the LAD arises from the RCA, repair can be accomplished with usual techniques unless a “full-length” transanular patch is required. When a transanular patch is needed, there are two alternatives. One is to perform a systemic-to-pulmonary artery shunt in small symptomatic neonates and infants, deferring repair with a valved conduit for several years. The other is to perform a one-stage repair using a small valved conduit.

Multiplicity of VSDs in very young patients increases the risk of repair. Closure of apical muscular defects can often be accomplished percutaneously (see “Percutaneous Closure of Ventricular Septal Defects” under Special Situations and Controversies in Chapter 35). Thus, an initial shunting operation may be prudent, with subsequent percutaneous closure of muscular VSDs, followed by repair.

SPECIAL SITUATIONS AND CONTROVERSIES

Timing and Type of Initial Surgery

There remains wide variability in the initial surgical approach to TF.4,12,26,72,74 It is becoming increasingly common to follow a protocol that involves only primary repair without use of palliative shunts; however, this approach is not universal4,12 and may not even be the most common. In an analysis of 196 patients undergoing surgery within the first 90 days of life from 32 centers participating in the Society of Thoracic Surgeons congenital heart database, 99 underwent primary repair and 97 shunt palliation.28

Even when primary repair is used exclusively, there is variability in timing of repair. In patients with important symptoms, repair is performed immediately regardless of age.4,44,56,65,72,81 In asymptomatic patients, however, practices vary, ranging from elective repair as early as 8 to 12 weeks of age4,44 up to about 1 year of age.81

Others prefer to perform a palliative shunt in symptomatic patients under a specific age, and primary repair above this age.4,12 The age threshold varies between 4 months and 1 year.

Currently, there is no conclusive evidence that any one of these protocols is superior.

Rationale for Use of Postrepair P_{RV/LV}

P_{RV/LV} is easily measured in the operating room after repair, so when pulmonary artery pressure is known to be low, it is a convenient way of assessing adequacy of relief of pulmonary stenosis. It has the disadvantage of being difficult to measure postoperatively, so in its place the ratio of peak P_{RV} to peak radial, femoral, or aortic pressure is generally used. P_{RV/LV} is neither better nor worse for assessing relief of pulmonary stenosis than is the theoretically more useful gradient between RV and pulmonary artery. Scanty data available concerning the relationship both of postrepair (OR) RV–pulmonary artery gradient to that of the next day or late postoperatively42,44,47 and of the gradient to late results are compatible with information and conclusions drawn from postrepair P_{RV/LV}.

Postrepair P_{RV/LV} is related to pulmonary arteriolar resistance, size of the RPA and LPA,28 presence and severity of localized or segmental stenoses or incomplete distributions of the pulmonary arteries, and residual pulmonary trunk or RV outflow obstructions. It is also related to flow through the RV outflow tract, which may be increased postoperatively by residual left-to-right shunting across the VSD and by pulmonary valve regurgitation, or decreased by right-to-left flow through a PFO.

Postrepair P_{RV/LV} should be interpreted with caution in neonates and small infants. Data correlating this ratio with medium and long-term outcome are based on patients repaired at an older age. Very young patients, especially those sedated and anesthetized perioperatively, may have low systemic vascular resistance and thus low systemic blood pressure. This may result in a P_{RV/LV} that is high, above 0.7, even though the absolute RV systolic pressure is only 30 to 40 mmHg.

Initial Palliative Operations

In most institutions, a PTFE interposition shunt between the brachiocephalic or subclavian artery and pulmonary artery via a median sternotomy is preferred in all age groups. The PTFE shunt, introduced by Gazzaniga and colleagues in 1976,63,64 is reliable even in young infants, with few late occlusions (see “Interim Results after Classic Shunting Operations” earlier in this section). This shunt has for the most part replaced the classic B-T shunt.

Although at one time the Waterston ascending aorta–RPA shunt was popular, most groups find it has higher mortality in infants,64,33 a considerably higher proportion of iatrogenic RPA problems, and a relatively high prevalence of late pulmonary hypertension because of excessive Qp.61 The same disadvantages pertain for the Potts descending aorta–LPA anastomosis.66 In addition, it is more difficult to perform than other shunts and more difficult to close later. These shunts are not performed in modern practice.

A central PTFE shunt between the ascending aorta and pulmonary trunk is another option. It has no proven advantage over a properly performed laterally placed PTFE interposition shunt; however, it will never result in branch pulmonary artery distortion. On the other hand, it may not allow as fine a regulation of pulmonary blood flow as the laterally placed interposition shunt.

Initial Palliation by β-Adrenergic Blockade

The possible advantage of β-adrenergic blockade with, for example, propranolol therapy for severe cyanosis and hypoxic spells in early infancy is that surgery may be deferred. Disadvantages are that propranolol does not always provide good palliation, and risk of repair may be higher in patients who are taking it.

Honey and colleagues showed in 1964 that β-adrenergic blockade usually alleviates paroxysmal hypoxic spells.27,30,31 When doses of about 2.5 mg · kg{}^{-1} · day{}^{-1} of propranolol are used, relief of the hypoxic spells for at least 3 months occurs in 80% of patients.33 However, Garson and colleagues found this regimen to be more effective in patients older than 1 year, when it could be considered unnecessary, and less successful in infants age 6 months or less.35 However, their conclusion was that the drug was effective in very young patients if the dose was adequate (2–6 mg · kg{}^{-1} · day{}^{-1} and serum propranolol levels about 100 ng · mL{}^{-1}).
Initial Palliation by Balloon Valvotomy

Percutaneous balloon dilation of the infundibulum and pulmonary valve, and percutaneous infundibular myectomy, have been reported to provide good relief of cyanosis and symptoms, with little risk, in some small patients. However, the reports are anecdotal, and risks and effectiveness of the procedure in safely deferring repair remain to be clearly defined. Because repair can be performed safely at any age, these procedures are most applicable when extenuating circumstances increase surgical risk.

Monocusp Valves Beneath Transanular Patches

Many informal reports suggest that constructing monocusp valves, usually made of pericardium, beneath a transanular patch, or use of cusp-bearing allograft patches, are of value. They usually support the idea that these valves are competent in the early postrepair period but generally become regurgitant later. Over the long term, they do not appear to result in less pulmonary regurgitation than does a simple transanular patch. Subsequent calcification of the cusp is potentially obstructive. Some enthusiastic formal reports have appeared, but evidence favoring their use is not persuasive.

Timing of Pulmonary Valve Replacement for Pulmonary Regurgitation Late after Repair

When this procedure should be performed to maximize effect and promote longevity of the RV remains unclear. Symptomatic deterioration of exercise ability, onset of clinical arrhythmia, or overt right heart failure from severe pulmonary regurgitation are unequivocal for pulmonary valve replacement. However, it is likely that these criteria represent a degree of hemodynamic deterioration that has progressed beyond the capacity for complete recovery (“reverse remodeling”) after intervention. Therrien and colleagues showed that using these criteria, pulmonary valve replacement failed to provide for satisfactory RV reverse remodeling, with many patients suffering continued RV dilatation and low ejection fraction. Also, QRS duration stabilized (it continued to increase in a control group with similar follow-up duration), but failed to decrease to a normal level as one would have hoped. It can be argued that patients would benefit more if valve replacement were performed before onset of symptoms. However, this approach presents an additional problem. Currently, indications for pulmonary valve replacement in asymptomatic patients are being developed. Degree of RV dilatation, RV ejection fraction, and volume of pulmonary regurgitation can all be measured with precision using MRI, for example, but the need for and timing of pulmonary valve replacement late after TF on the basis of such measurements remain to be firmly established. For example, pulmonary regurgitant fraction and RV diastolic dimensions (as assessed by MRI) were not independently associated with impaired clinical status in long-term survivors of TF repair. However, numerous MRI studies show that recovery of RV function following pulmonary valve replacement was less likely if RV end-diastolic dimension exceeded 150 to 170 mL · m⁻². Similar arguments can be made for asymptomatic patients with prolonged QRS duration on ECG.

Percutaneous Pulmonary Valve Implantation

Percutaneous pulmonary valve implantation is a new option for patients with dysfunctional RV to pulmonary trunk conduits in selected TF patients who meet specific physiologic and anatomic criteria. The device can be used in cases of both RV outflow tract obstruction and pulmonary regurgitation. As of 2008, more than 500 percutaneous valves have been placed worldwide. In Lurz and Bonhoeffer’s experience with 230 of these cases followed for a mean of 28 months, freedom from reoperation was 93% at 10 months and 70% at 70 months. Currently, technology has not been modified to allow implantation in native outflow tracts.

Section II Tetralogy of Fallot with Pulmonary Atresia

DEFINITION

The definition of tetralogy of Fallot with pulmonary stenosis applies to TF with pulmonary atresia, except that in the latter there is no luminal continuity between the RV and pulmonary trunk (or both the RPA and LPA). Atresia is usually congenital but may be acquired.

HISTORICAL NOTE

As noted in Section I, Lillehei and colleagues first successfully repaired TF, and their original paper included a patient with pulmonary atresia. Rastelli and Kirklin reported the first use of an RV–pulmonary trunk extracardiac conduit to repair this anomaly in 1965. Ross and Somerville first reported use of a valved conduit for this purpose in 1966, as did Weldon and colleagues soon thereafter. Enlarging very hypoplastic pulmonary arteries by increasing pulmonary artery pressure and flow using a conduit connecting the RV to pulmonary arteries or by a systemic–pulmonary arterial shunt was reported by McGoon and colleagues and Kirklin and colleagues in 1977.

The important role of large aortopulmonary (AP) collateral arteries in many patients having TF with pulmonary atresia appears to have been first addressed in a constructive manner by Macartney and colleagues. These investigators reported on the hemodynamic characteristics of these arteries in 1973 and again in 1974. They introduced the concept of a multifocal blood supply to the pulmonary circulation through both the central pulmonary arteries and large AP collateral arteries. In 1980, Haworth and Macartney described in detail the large AP collateral arteries supplying blood to some pulmonary arterial segments by end-to-end anastomosis, and to others by end-to-side anastomosis. By then, the UAB group had described, in 1978, the adverse effect of incomplete distribution (arborization) of the pulmonary arteries on survival after repair of TF with pulmonary atresia. In 1981, Haworth, Macartney, and colleagues introduced the concept of unifocalization of pulmonary arterial supply as a first step to repair in patients with multifocal supply and large AP collateral arteries. Subsequently the surgical results of these procedures have accumulated (see...
“Results after Staged Palliative Operations for Unifocalization” later in this section). Systematic one-stage complete repair in infancy, involving bilateral unifocalization and intracardiac repair via median sternotomy, was introduced by Reddy and Hanley in 1992 and reported in 1995. Percutaneous catheter dilatation of localized stenoses in the RPA and LPA was reported by Lock and colleagues in 1983 and closure of large AP collateral arteries using this technique was reported by Yamamoto and colleagues in 1979.

MORPHOLOGY AND MORPHOGENESIS

Tetralogy of Fallot with Congenital Pulmonary Atresia

General morphology of the heart in TF with pulmonary atresia is similar to that in TF with pulmonary stenosis. The most important differences are that in TF with pulmonary atresia:

- No blood passes from RV to lungs; consequently, all pulmonary blood flow arises from the ductus arteriosus, collateral vessels, or fistulae.
- Pulmonary arterial anomalies are common.
- Large AP collateral arteries are common.

Right Ventricular Outflow Tract

Atresia, when congenital, may be in the infundibular area or at the RV–pulmonary trunk junction (“anulus”).

Infundibular atresia is the most severe manifestation of RV outflow atresia in TF, occurring in about 70% of hearts. The RV infundibulum seems to be totally absent in such cases, or the infundibular septal elements may be present but nearly fused with the anterior RV free wall (Fig. 38-66). The VSD is usually large and extends nearly to the free wall of the RV anteriorly, as does the aortic valve. The RV in such hearts is usually massively hypertrophied.

When the atresia is at the RV–pulmonary trunk junction, the infundibulum is usually present, but the pathway is narrowed by marked hypertrophy of the infundibular structures (Fig. 38-67). Obstruction consists of a thick fibrous membrane (analog of the pulmonary valve) above the infundibulum. Length and width of the infundibulum is variable.

Pulmonary Trunk

The pulmonary trunk may be present and of reasonable size, but more commonly it is importantly hypoplastic (Fig. 38-68). Occasionally, it is represented by only a fibrous cord without a lumen. In about 5% of patients with duct-dependent pulmonary blood flow, it appears to be completely absent. In patients with collateral-dependent pulmonary blood flow, the pulmonary trunk as well as the central branch pulmonary arteries are absent in up to 23%.

No clear correlation has been developed between location and type of atresia and morphology of the pulmonary trunk. An unusual variation of pulmonary trunk morphology has been recognized with increasing frequency recently, especially in patients with arborization abnormalities of the pulmonary artery branches. In this variant the pulmonary trunk arises from the proximal coronary artery system. Origins from the left main, right, and circumflex coronaries have all been identified. The true prevalence of this variant is not known, because most cases have been reported in isolation or in small groups; however, when systematically sought in a population of patients with arborization abnormalities of the pulmonary artery branches, it has been found to occur in up to 10%.

Right and Left Pulmonary Arteries

Confluence of Right and Left Pulmonary Arteries About 20% to 30% of patients have nonconfluent RPAs and LPAs (discontinuity). This usually results from absence of the central portion of one or both of these arteries. Rarely, it is caused by atresia of at least the distal pulmonary trunk and origins of both pulmonary arteries. (Patients having TF with pulmonary stenosis rarely have discontinuity of the RPA and LPA.) Confluent RPA and LPA may be associated with either a patent or atretic pulmonary trunk.

Figure 38-66 Specimen of tetralogy of Fallot with congenital infundibular atresia. Infundibular septum is small and divisions of trabecula septomarginalis prominent. Ventricular septal defect is perimembranous but extends anteriorly and superiorly almost to anterior free wall of ventricle. The danger of inadvertently cutting into the aortic root when making the right ventriculotomy is evident. There is marked overriding of noncoronary aortic cusp. Key: FW, Anterior free wall; L, left coronary cusp of aortic valve; LA, left anterior division of trabecula septomarginalis; N, noncoronary cusp of aortic valve; R, right coronary cusp of aortic valve; RP, right posterior division of trabecula septomarginalis; TSM, trabecula septomarginalis; TV, tricuspid valve.
Stenoses of Origins of Pulmonary Arteries

Among patients with confluence of the RPA and LPA and normal distribution arborization of pulmonary arteries, about 10% have stenosis of the origin (central portion) of the RPA, and about 20% have stenosis of the LPA. The latter anomaly seems clearly related to extension onto the LPA of the process of ductal closure.

Distribution (Arborization) of Pulmonary Arteries

An important feature of the morphology of TF with pulmonary atresia is frequent failure of the pulmonary arteries to distribute to all 20 pulmonary vascular segments. In this regard, patients with relatively normal caliber confluent central portions of the RPA and LPA are very different from those with either hypoplastic confluent branches or non-confluent ones. Also, the presence or absence of a ductus arteriosus is an important factor determining arborization abnormalities. If a ductus arteriosus is present and the branch pulmonary arteries are confluent, arborization abnormalities and large AP collaterals are rarely if ever seen. If a ductus arteriosus is present and the branch pulmonary arteries are discontinuous, the branch pulmonary artery (usually the left) that receives flow from the ductus rarely if ever has arborization abnormalities, and that lung rarely if ever has large AP collaterals. In this setting, the opposite branch pulmonary artery (usually the right) is almost always hypoplastic and has arborization abnormalities or is completely absent, and the lung blood supply is solely from large AP collaterals.

In one series, distribution of the pulmonary arteries was complete to all 20 pulmonary arterial segments in slightly more than half (53%; CI 48%-58%) of the patients with confluent RPA and LPA, and normal distribution was associated with relatively normal caliber of the confluent LPA and RPA (Table 38-12). In contrast, more than 80% of those with nonconfluent RPA and LPA or confluent but hypoplastic pulmonary arteries had incomplete distribution of one or both arteries, and in slightly more than one third of this group less than 10 pulmonary vascular segments were in continuity with a central or proximal extrapericardial portion.
Stenoses of Pulmonary Arteries

Stenoses beyond the origins of the pulmonary arteries are identified in only a small percentage of cases. However, when these small pulmonary arteries are subjected to increased pressure and flow after a palliative or corrective operation, they may enlarge in some areas and not in others. Thus, localized areas of noncompliance in the pulmonary arterial walls may not present as stenoses until after a procedure that increases pulmonary blood flow.

Overall, stenoses are most common at the origin of the pulmonary artery on the side of the ductus arteriosus, when one is present. Such juxtaductal stenoses (pulmonary artery coarctations) were found in 65% of patients studied by Elzenga and colleagues.

Size of Pulmonary Arteries

The immediately prebranching portion of the RPA and LPA varies widely, from normal caliber in some patients to extremely small in others—as low as McGoon ratios of about 0.5, which corresponds to a Nakata index of about 20 and a z value of about −10. These dimensions are particularly small in the subset with nonconfluence (discontinuity) of the RPA and LPA. In a subset of patients, intrapericardial pulmonary arteries are completely absent. In the series of 462 cases of TF with pulmonary atresia and large AP collaterals reported by Malhotra and Hanley, among the 77% of patients who had centrally confluent native pulmonary arteries, mean diameter of the branches was 2 mm. In general, patients with TF with pulmonary atresia have considerably smaller RPA and LPA than those with TF with pulmonary stenosis; in the latter group, these dimensions are similar to those in normal individuals.

Abnormal Hilar Branching Patterns

Even when the pulmonary arteries distribute to all parts of the right and left lung, hilar branching patterns may be abnormal, particularly in patients with large AP collateral arteries.

Alternative Sources of Pulmonary Blood Flow

Large Aortopulmonary Collateral Arteries

The most dramatic route of collateral flow is through large AP collaterals of an ipsilateral pulmonary artery (see Table 38-12). Pulmonary arterial segments that are not connected to a central pulmonary artery usually receive large AP collateral arteries. As a general rule, there is an inverse correlation between the number of lung segments supplied by collaterals and those supplied by the native pulmonary arteries. Fig. 38-69 shows this relationship. In one large series of patients with pulmonary atresia and collateral-dependent pulmonary blood flow, 23% of all patients had no vascular distribution from native pulmonary arteries to the lungs, and 13% had complete vascular distribution from native pulmonary arteries to 18 lung segments (considered to be complete arborization in this study). The remaining 64% of patients had vascular distribution from both native pulmonary arteries and collaterals along the spectrum shown in Fig. 38-69. In contrast, most patients having TF with pulmonary stenosis have all 20 pulmonary arterial segments in continuity with a central or proximal extrapericardial portion of an ipsilateral pulmonary artery.

### Table 38-12

<table>
<thead>
<tr>
<th>No. of Pulmonary Artery Segments</th>
<th>Confluent (n = 132)</th>
<th>Nonconfluent* (n = 28)</th>
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<tbody>
<tr>
<td></td>
<td>No. of Patients</td>
<td>%</td>
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<tr>
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</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>132</td>
<td>100</td>
</tr>
</tbody>
</table>

*Absence of one or both central pulmonary arteries.

Data from Shimazaki and colleagues. 

Stenoses of Pulmonary Arteries

Stenoses of the pulmonary arteries beyond their origins are identified in only a small percentage of cases. However, when these small pulmonary arteries are subjected to increased pressure and flow after a palliative or corrective operation, they may enlarge in some areas and not in others. Thus, localized areas of noncompliance in the pulmonary arterial walls may not present as stenoses until after a procedure that increases pulmonary blood flow.

Overall, stenoses are most common at the origin of the pulmonary artery on the side of the ductus arteriosus, when one is present. Such juxtaductal stenoses (pulmonary artery coarctations) were found in 65% of patients studied by Elzenga and colleagues.

Size of Pulmonary Arteries

The immediately prebranching portion of the RPA and LPA varies widely, from normal caliber in some patients to extremely small in others—as low as McGoon ratios of about 0.5, which corresponds to a Nakata index of about 20 and a z value of about −10. These dimensions are particularly small in the subset with nonconfluence (discontinuity) of the RPA and LPA. In a subset of patients, intrapericardial pulmonary arteries are completely absent. In the series of 462 cases of TF with pulmonary atresia and large AP collaterals reported by Malhotra and Hanley, among the 77% of patients who had centrally confluent native pulmonary arteries, mean diameter of the branches was 2 mm. In general, patients with TF with pulmonary atresia have considerably smaller RPA and LPA than those with TF with pulmonary stenosis; in the latter group, these dimensions are similar to those in normal individuals.

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### Table 38-12

| Confluence or Nonconfluence of Central Pulmonary Arteries and Number of Pulmonary Artery Segments Centrally Connected in Patients with Tetralogy of Fallot with Pulmonary Atresia |
|---------------------------------|---------------------|------------------------|
| No. of Pulmonary Artery Segments | Confluent (n = 132) | Nonconfluent* (n = 28) |
|                                 | No. of Patients | %                     | No. of Patients | %                     |
| 20                              | 62       | 47                    | 5               | 18                    |
| 19                              | 8        | 6                     | 2               | 7                     |
| 18                              | 8        | 6                     | 2               | 7                     |
| 17                              | 13       | 10                    | 0               | 0                     |
| 16                              | 6        | 5                     | 0               | 0                     |
| 15                              | 8        | 6                     | 0               | 0                     |
| 14                              | 6        | 5                     | 1               | 4                     |
| 13                              | 6        | 5                     | 0               | 0                     |
| 12                              | 5        | 4                     | 0               | 0                     |
| 11                              | 4        | 3                     | 0               | 0                     |
| 10                              | 2        | 2                     | 8               | 29                    |
| 9                               | 2        | 4                     | 1               | 4                     |
| 8                               | 0        | 0                     | 0               | 0                     |
| 7                               | 0        | 0                     | 2               | 7                     |
| 6                               | 1        | 1                     | 0               | 0                     |
| 5                               | 0        | 0                     | 1               | 4                     |
| 4                               | 1        | 1                     | 0               | 0                     |
| 3                               | 0        | 0                     | 0               | 0                     |
| 2                               | 0        | 0                     | 0               | 0                     |
| 1                               | 0        | 0                     | 0               | 0                     |
| 0                               | 0        | 0                     | 6               | 21                    |
| **TOTAL**                       | 132       | 100                   | 28              | 100                   |

*Absence of one or both central pulmonary arteries.

Data from Shimazaki and colleagues.

**Figure 38-69** Spectrum of lung perfusion in pulmonary atresia with ventricular septal defect. This is a hypothetical relation between number of pulmonary segments perfused by native pulmonary arteries (PAs) and those perfused by major aortopulmonary collateral arteries (MAPCAs).
arteries, which are present in about 60% of patients having TF with pulmonary atresia (Fig. 38-70). In this context, “large” implies embryologic rather than acquired origin of the collaterals, the latter typically resulting in smaller, more numerous collateral vessels. Large collaterals occur rarely in TF with pulmonary stenosis. AP collateral arteries are large discrete arteries, typically from one to six in number but sometimes more, most commonly originating from the upper or mid-descending thoracic aorta. The most common origins after the mid-descending thoracic aorta are the aortic arch and the low thoracic aorta. Occasionally a collateral originates from the intraabdominal aorta. Regardless of origin, collaterals generally pursue a somewhat serpiginous course, occasionally passing through the esophageal wall, and most commonly terminate by joining an interlobar or intralobar pulmonary artery that arborizes normally within a pulmonary lobe or segment.

AP collateral arteries arise from the aorta (or other source) either as elastic vessels with a wide lumen or as muscular arteries with stenotic areas. In either event, beyond their origins they resemble muscular systemic arteries. Areas of intimal proliferation (intimal pads) are frequent and result in stenoses. Extensive areas of these are prominent at branching points and at the junction of AP collateral arteries with pulmonary arteries. This process eventually results in stenoses in about 60% of collateral arteries.

In most patients, stenoses are sufficient in number to prevent pulmonary overcirculation; when this is not the case, pulmonary overcirculation is present early in life, and pulmonary vascular disease develops in patients surviving past infancy. Even in the absence of clinical signs and symptoms of overcirculation, however, an unobstructed collateral may cause pulmonary vascular disease in the area of lung it supplies. Thus, both regional and localized overcirculation can occur.

Although stenoses in some cases are primarily related to structural abnormalities in the collateral vessel wall, in others they are acquired, the result of abnormal postnatal flow patterns. Severe stenoses have been documented angiographically in patients as young as age 3 to 4 months in vessels that showed normal caliber at neonatal angiography. Stenoses can evolve variably and unpredictably.

An AP collateral artery that joins end to end with an intrapulmonary artery changes in histologic appearance as it becomes a pulmonary artery and changes its positional relation to the bronchi. Thus, peripherally, its histologic appearance and position become typical for “true” pulmonary arteries. In this situation, the distal pulmonary arterial
branches may be abnormally small\textsuperscript{11} and fewer in number than in normal individuals.

In about 50% of patients with large AP collateral arteries, the collateral enters end to side into a complex manifold in the hilum of the lung. This manifold usually includes the hilar portion of the pulmonary artery, and from this manifold interlobar and intralobar pulmonary arteries distribute distally, and central pulmonary arteries may fill retrogradely.\textsuperscript{52} The lung segments in this situation are said to have dual supply from the collateral and the true pulmonary artery. In other cases, the collateral distribution distally into the lung does not communicate with the central pulmonary artery system. In this situation, the involved lung segments are said to have isolated supply from the collateral only.

Less commonly, an AP collateral artery may connect end to side to a central pulmonary artery. Rarely, a single AP collateral artery on each side connects end to end with the hilar portion of the ipsilateral pulmonary artery.\textsuperscript{11,14,30} It is this last form that gave origin to the erroneous appellation “truncus type IV.”

AP collateral arteries are usually associated with abnormal branching patterns and incomplete distribution of the hilar portion of the pulmonary arteries. There may be associated single or multiple, localized or segmental, pulmonary arterial stenoses or diffuse hypoplasia.\textsuperscript{11,14,30}

**Paramediastinal Collateral Arteries** These are no different from AP collaterals, with the exception that their systemic origin is from a vessel other than the aorta. A large right or left paramediastinal collateral artery occasionally arises from the right or left subclavian artery, most often on the side opposite that of the aortic arch. It may connect end to side to the right or left central or hilar pulmonary artery, or it may distribute end to end to the intrapulmonary arteries of the upper lobe. It may be difficult to distinguish such a collateral from an unusually positioned and tortuous patent ductus arteriosus if the collateral is the sole vascular supply to one lung.

**Bronchial Collateral Arteries** Systemic vessels that originate from the mid-descending thoracic aorta and follow the course of the trachea and major bronchi before communicating with the lung parenchyma are often designated as bronchial collateral arteries. These vessels are often adherent to the airways and give off numerous small branches that supply the walls of the airways. They tend to be thin walled and tortuous, but may be large and carry a large amount of collateral flow. Collaterals that fit this description can be found in some but not all patients with TF and pulmonary atresia. They may also occur in the same patients who have more typical AP collaterals.

Increased use of various collateral arteries in surgical reconstruction has stimulated their careful pathologic evaluation. The picture is complex. It is becoming increasingly clear that the distinction between bronchial collaterals and other AP collaterals, and between intraparenchymal and extraparenchymal vessels, is simplistic; rather, the course and structure of those vessels that carry these labels is highly variable and unpredictable. Thus, these distinct labels may not apply to many vessels.\textsuperscript{18} This observation corresponds with embryologic evidence that AP collateral artery formation occurs over extended periods during development.\textsuperscript{11,13}

**Other Collaterals** Small collateral channels may pass from coronary arteries to the bronchial arteries.\textsuperscript{11} Relatively large communications between the proximal right or left coronary artery and the central pulmonary artery confluence occur in up to 10% of cases.\textsuperscript{11} In rare cases a fistula between the RCA and pulmonary trunk may be the sole large collateral source of pulmonary blood flow.\textsuperscript{238} Even more rarely, an AP window may serve this function (see Chapter 44).\textsuperscript{110}

**Acquired Collaterals** These vessels are stimulated or promoted by several factors, primarily cyanosis and adhesions from previous surgery or procedures. They typically arise from intercostal, internal thoracic, and smaller mediastinal and diaphragmatic arteries and are almost always multiple (dozens or even hundreds), small, and tortuous. Thus, they are almost impossible to control or eliminate using either surgical techniques or interventional coil occlusion. This collateral circulation may be so well developed as to make even the most careful mobilization of the lung hazardous. Such situations are not encountered in infants who are not chronically cyanotic and who have not undergone previous surgical procedures.

**Ductus Arteriosus**

In the absence of AP collaterals, pulmonary circulation at birth is dependent on ductal flow to the site of pulmonary artery confluence. This represents about 40% of these patients. Ductus orientation and position are usually abnormal—a downwardly directed branch coming from beneath the left aortic arch.\textsuperscript{15} It is also longer and more tortuous than is otherwise the case (Fig. 38–71) and is often narrowed at its pulmonary end. In the setting of left aortic arch, a right-sided patent ductus arteriosus is rare. When present, it comes off the right subclavian or brachiocephalic artery, or if associated with an aberrant right subclavian artery, it may come from an aortic diverticulum and pass to the right behind the esophagus.

When the pulmonary arteries are confluent, presence of large (embryologic rather than acquired) AP collaterals almost always means that there will not be a ductus arteriosus. When the pulmonary arteries are not confluent, a ductus arteriosus may or may not be present (see “Distribution [Arborization] of Pulmonary Arteries” earlier in this section).

**Morphogenesis**

A feature that distinguishes patients having TF with pulmonary atresia from those with pulmonary stenosis is the association of pulmonary atresia with chromosome 22q11 deletion. This association is particularly high in those with pulmonary artery arborization abnormalities and large AP collaterals.\textsuperscript{11,17,117,119,116} This deletion is associated with clinical evidence of DiGeorge syndrome, or velocardiofacial syndrome, in approximately 90% of cases. In those cases, careful consideration must be given to the typical immunologic, calcium metabolism, and neurodevelopmental abnormalities that may be part of this syndrome.

**Tetralogy of Fallot with Acquired Pulmonary Atresia**

Pulmonary atresia may develop spontaneously after birth in patients born with TF with pulmonary stenosis, or may be stimulated by a palliative operation.\textsuperscript{11,114} Acquired atresia is usually valvar, but may develop in the immediately subvalvar region or in the os infundibulum. This type of TF has the morphologic characteristics of TF with pulmonary stenosis.
CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

When the patient has TF with congenital pulmonary atresia and no AP or other large collateral arteries, cyanosis is usually evident during the first few days of life, becoming extreme as the ductus narrows and closes. This rapid progression is modified when there are large collaterals supplying the pulmonary bed, when the ductus stays open, or when an operation is performed.

Infants with pulmonary atresia and large AP collateral arteries present at birth with varying degrees of cyanosis. In approximately 80%, cyanosis is mild to moderate and hemodynamics are stable. In about 10%, presentation is with heart failure, which usually peaks at age 4 to 6 weeks as neonatal Rp decreases and Qp becomes large; cyanosis is mild. In about 10%, cyanosis is severe at birth, occasionally to the degree that hemodynamic instability develops. Regardless of presentation at birth, without intervention there is a general trend for cyanosis to worsen as collateral stenosis and pulmonary vascular disease develop. Both processes may occur in the same patient within different collateral areas.

Primary and secondary airway problems have been recognized with increasing frequency. The reasons are many, including upper airway extrinsic compression from a large aorta or collateral vessel to small airway hyperresponsiveness. Children who first present at an older age are usually symptomatic, cyanotic, and polycythemic no matter what the source of collateral blood flow, because it has become inadequate by that time.

Physical examination discloses findings similar to those of patients who have TF with pulmonary stenosis. In pulmonary atresia, however, a systolic murmur is usually absent. There is frequently a continuous murmur from large AP collateral arteries, a patent ductus arteriosus, or a coronary–pulmonary artery fistula. The murmur is maximal over the site of the collateral at its point of stenosis and may therefore be heard to the left or right of the sternum or posteriorly.

Clinical presentation, examination, and special studies are similar to those described for TF with pulmonary stenosis, with some important distinctions.

Echocardiography

Echocardiography is diagnostic for all cases of TF with pulmonary atresia, but it is definitive only if confluent normal-caliber branch pulmonary arteries connected to a patent ductus arteriosus can be identified.
Catheterization and Angiography

Cardiac catheterization and angiography should be performed at birth in all patients with an echocardiographic diagnosis of TF with pulmonary atresia and non–duct-dependent pulmonary blood flow. The origin, course, and distribution of every collateral should be clearly identified. Characterization of the collateral blood supply to a given lung segment should be further assessed to determine whether the collateral vessel provides the sole blood supply or is part of dual or multiple sources of blood flow coming from other collaterals or from the central or “true” pulmonary arteries. Further assessment is performed to identify whether any of the sources of blood supply come from a ductus arteriosus or the coronary artery system. Central and peripheral stenoses are identified both external to and within the lung parenchyma. Finally, specific effort should be made to fully characterize the central true pulmonary arteries using collateral and pulmonary wedge injections. Only after this level of definition is achieved can an appropriate surgical management plan be formulated.

Although clinical status of the patient and specifics of the management plan may influence the need for repeat study at any time, in almost all cases, repeat cardiac catheterization and detailed angiography are required in a matter of months. The reason may be to reevaluate an infant at age 3 to 4 months immediately before a one-stage unifocalization and intracardiac repair, because collaterals can change dramatically in the first few months of life, or it may be to assess the results of a previous palliative procedure performed in the neonatal period. Clinical stability (i.e., a thriving infant with SaO2 of 80% ± 5%) is not an indication to postpone cardiac catheterization. Such infants are likely to have important maldistribution of pulmonary blood flow despite their clinical stability, putting some lung segments at risk of developing pulmonary vascular disease due to overcirculation, and other segments at risk of being lost due to collateral occlusion.

In patients with ductus-dependent pulmonary blood flow with normally developed confluent pulmonary arteries, early repeat catheterization is typically not necessary, whether the initial neonatal procedure was one-stage repair or shunt placement. Although cardiac catheterization and standard angiography are absolute necessities in the workup of TF with pulmonary atresia and complex pulmonary arteries, newer imaging modalities such as 3D CTA or MRI currently provide an adjunctive role and may eventually take on increasing diagnostic importance in defining the complex morphology of abnormal pulmonary arteries and AP collaterals. Echocardiography is important in defining the intracardiac morphology, but has a subordinate role in the arterial assessment.

Computed Tomographic Angiography

This modality is being used increasingly in the neonatal period for TF with pulmonary atresia and large AP collaterals (Fig. 38-72). CTA in the neonatal period may prevent need for invasive catheterization if the CT demonstrates that a particular patient does not fall within one of several specific morphologic subgroups requiring neonatal surgery. The examples shown in Fig. 38-72 represent two specific subgroups that require neonatal surgery, according to the Stanford Management Protocol for TF with pulmonary atresia and aortopulmonary collaterals (Fig. 38-73). Because neonatal surgery is required in these subgroups, preoperative catheterization with detailed angiography of the collaterals is indicated. Catheterization can be deferred until the preoperative evaluation, typically at 3 to 4 months of life, in the majority (75%) of patients who make up the other morphologic subgroups. Thus, CT can serve as the definitive neonatal study in patients who will not require a neonatal operation. It should be emphasized that catheterization with angiography is strictly indicated if immediate surgery is anticipated.

Natural History

The natural history of patients with TF and congenital pulmonary atresia cannot be described simply, in part because of the great variability of morphology. This is reflected in the more complex hazard function for death compared with that for TF and pulmonary stenosis (see Fig. 38-23, C). It consists of a short-lasting early hazard phase, considerably more acute than for TF with pulmonary stenosis, that merges with a constant hazard phase (exponentially decreasing survival) that lasts to about age 50, followed by an increasing late hazard (with wide confidence limits). Unfortunately, morphologic characteristics of the anomaly corresponding to early death were not available to Bertranou and colleagues for their study of natural history, nor is it certain that reported groups of patients were an unselected sample of all patients born with this condition. This is particularly unfortunate in this condition, because it is likely that morphologic and physiologic characteristics influence survival.

Nevertheless, knowledge of the pathophysiology of the anomaly suggests that the shape of the natural history hazard function (see Fig. 38-23, C) may result from a mixture of different morphologic and physiologic subgroups that have been conveniently formed because of their surgical significance.

- **Confluent and normally distributing RPA and LPA and patent ductus arteriosus.** In this group, the only source of pulmonary blood flow is a patent ductus arteriosus, and the RPA and LPA are confluent, usually minimally hypoplastic, and distribute to all 20 pulmonary arterial segments.
- **Confluent, nonconfluent, or absent RPA and LPA with AP collaterals.**

The branch pulmonary arteries vary from confluent and almost normal size to confluent and severely hypoplastic, to nonconfluent, to completely absent. If they are not confluent, a ductus will connect to a normally arborizing (usually left) branch pulmonary artery, and the opposite branch pulmonary artery will be absent, with the lung solely supplied by AP collaterals. To add to the complexity, the degree of hypoplasia of the branch pulmonary arteries (as judged by their luminal diameter) does not necessarily correlate with the degree of arborization. Arborization of the pulmonary arteries, if present and confluent, may be to the majority of the lung segments or to a minority of lung segments. Segments not supplied by the pulmonary arteries are supplied by AP collaterals. There is an inverse relationship between the distribution of the pulmonary arteries and the distribution of the AP collaterals.
Computed tomographic angiography (CTA) of patients with pulmonary atresia with ventricular septal defect and large collateral arteries, illustrating the Stanford University management protocol. **A1 and A2**, Two CTA images of a 1-week-old girl with very small centrally confluent native pulmonary arteries and large collaterals (MAPCAs). Images show a small right and left native right pulmonary arteries (RPA, LPA) and two major aortopulmonary collateral arteries (MAPCA2, MAPCA3) arising from the mid-thoracic descending aorta. Collaterals are connected peripherally to native pulmonary arteries. RML PA identifies right middle lobe branch of the RPA. LUL PA and LLL PA identify left upper and left lower branches of LPA. An additional very small collateral was present in this patient, but is not visualized in these images. According to the Stanford management protocol, this patient is identified as requiring neonatal surgery because of the normally arborizing and centrally confluent native pulmonary arteries, with all "dual-supply" collaterals. A neonatal preoperative cardiac catheterization with detailed angiography of the collaterals is required. **B**, Coronal cut of a volume-rendered image of airways and aorta in a 1-week old girl with large collaterals to right lung. There is a right-sided aortic arch. Peripheral LPA is connected to aorta through a patent ductus arteriosus originating from left brachiocephalic artery. According to the Stanford management protocol, this patient would require neonatal surgery because of the presence of the unilateral ductus. A preoperative neonatal catheterization would be required to define the details of the right lung collateral distribution. Key: *Ao*, Aortic arch; *LLL*, left lower lobe branch; *LPA*, left pulmonary artery; *LUL*, left upper lobe branch; *MAPCA*, major aortopulmonary collateral artery; *PA*, pulmonary artery; *PDA*, patent ductus arteriosus; *RML*, right middle lobe branch; *RPA*, right pulmonary artery.
Physiologically. Cyanosis is always present, and symptoms may develop, depending on the number, size, and behavior of collateral vessels, but not as quickly nor as severely as in the group described in the preceding paragraph. Symptoms early in life are related either to severe cyanosis or to severe pulmonary overcirculation. Over time, a gradual increase in cyanosis is typical because of collateral stenosis with reduced pulmonary blood flow, Eisenmenger-like physiology in unobstructed collaterals, or both. Without interventional therapy, 10% of this group may die within the first few years of life, half by age 3 to 5 years, and 90% by age 10.

Pulmonary Arterial Disease

Patients with pulmonary atresia and AP collateral arteries probably differ from other patients with TF with respect to pulmonary arterial disease. The phrase pulmonary arterial disease rather than “pulmonary vascular disease” is used because of uncertainty regarding how much the increased pulmonary vascular resistance is due to hypoplasia and

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**Figure 38-73** Treatment protocol for patients with tetralogy of Fallot and pulmonary atresia with major aortopulmonary collateral arteries. Key: AP, Aortopulmonary; MAPCAs, major aortopulmonary collateral arteries; PA, pulmonary artery; TF, tetralogy of Fallot.
stenoses of the distal pulmonary arteries themselves and of the distal portions of the AP collateral arteries, versus how much is due to microvascular hypertensive pulmonary vascular disease.\textsuperscript{58} Without question, both mechanisms occur.

Pulmonary arterial disease tends to develop in those pulmonary arterial segments that are centrally connected. It progresses at a considerably accelerated rate, and perhaps even in fetal life or in the first few months after birth, in segments whose only or major source of pulmonary blood flow is large AP collateral arteries.\textsuperscript{512} Patients who survive without correction into the second and third decades of life often develop massive and sometimes fatal hemoptysis related to these large AP collaterals.\textsuperscript{58}

\section*{TECHNIQUE OF OPERATION}

\subsection*{Repair of Tetralogy of Fallot with Acquired Pulmonary Atresia}

Occasionally, and particularly in patients with pulmonary atresia that has developed after a shunting procedure, atresia is at the level of the infundibulum. The operation described for TF with pulmonary stenosis can then be done (see Technique of Operation in Section I), often without a transanular patch. When acquired atresia is at the pulmonary “anulus” and the pulmonary trunk is present (which it usually is), a transanular patch repair can be used, as described next under “Repair of Tetralogy of Fallot with Pulmonary Atresia and Confluent and Normally Distributing Right and Left Pulmonary Arteries and Patent Ductus Arteriosus.” In about 90\% of patients with TF and acquired pulmonary atresia, these straightforward repairs are feasible.

\subsection*{Repair of Tetralogy of Fallot with Pulmonary Atresia and Confluent and Normally Distributing Right and Left Pulmonary Arteries and Patent Ductus Arteriosus}

This operation is generally performed in neonates and young infants in whom atresia is usually at the pulmonary “anulus” and the pulmonary trunk and confluence of the RPA and LPA are generally patent and of reasonable size. Occasionally, it is performed in older infants and in children who have been palliated by a shunting operation early in life. Operation proceeds much as described under Technique of Operation in Section I for TF with pulmonary stenosis with respect to CPB management, myocardial protection, and many technical details (see “Decision and Technique for Transanular Patching” and “Repair of Uncomplicated Tetralogy of Fallot with Pulmonary Stenosis via the Right Ventricle” under Technique of Operation for details of most aspects of the procedure except for those described in text that follows). There are, however, several important differences. The ductus arteriosus is always present and large and may be tortuous. There are, however, several important differences. The ductus arteriosus is always present and large and may be tortuous. It is dissected, and ligatures placed around it, prior to establishing CPB. It is then immediately ligated and divided as CPB is initiated (see “Closure of Associated Patent Ductus Arteriosus” under Technique of Operation in Section I of Chapter 35).

The VSD is always closed through a longitudinal incision in the RV infundibulum, never through the right atrial approach. The incision, RV muscle resection, and VSD closure are performed as described for TF with pulmonary stenosis under Technique of Operation in Section I.

There are several options for managing the RV-to-pulmonary trunk reconstruction. Preferably, a valved conduit is used to connect the RV to the pulmonary trunk. This is performed as described later in “Establishing Right Ventricle–to–Pulmonary Artery Continuity” under Repair of Tetrology of Fallot with Pulmonary Atresia and Large Aortopulmonary Collaterals. Alternatively, it may be possible in some cases to make a single vertical incision in the RV infundibulum and extend it through the atresia to an appropriate point distally on the pulmonary trunk. This is appropriate when the atretic area is very short. Sufficient tissue must be present posteriorly at the site of the atresia so that growth of the area can proceed satisfactorily. The transanular patch must be appropriately contoured at the atretic area to accomplish satisfactory widening. The patch is roughly diamond shaped, with the widest portion applied to the atretic area. Great care is taken to avoid damage to the left anterior descending coronary artery (LAD) and right coronary artery by the patch suture line. Severe pulmonary regurgitation will be present immediately when this technique is used.

Management of the atrial septum will vary. If a valved conduit is used to reconstruct the RV outflow tract, closure of the atrial septal defect or PFO, if present, is performed. If a transanular patch is used, especially in neonates and young infants, a PFO is left open using the same criteria as given in “Managing the Atrial Septum” under Technique of Operation in Section I.

\subsection*{Repair of Tetralogy of Fallot with Pulmonary Atresia and Confluent, Nonconfluent, or Absent Right and Left Pulmonary Arteries and Aortopulmonary Collaterals}

Vascular supply of blood to the lungs in this condition represents, arguably, the most variable and complex “lesion,” both morphologically and physiologically, in congenital heart disease. As such, no single operative approach is applicable to all patients. That said, recent techniques have been developed, supported by midterm follow-up data, demonstrating that a majority of patients with TF with pulmonary atresia and large AP collaterals can be managed with one-stage repair in early infancy, involving left and right lung unifocalization, VSD closure, and RV outflow tract reconstruction.\textsuperscript{1,2,9,16,31,33,38,39,48,67}

This approach can be applied to patients having relatively large confluent true pulmonary arteries, minor or moderate arborization abnormalities, severely hypoplastic confluent true pulmonary arteries with major arborization abnormalities and dominant collaterals, or completely absent intrapericardial true pulmonary arteries and collaterals only.

There are specific subpopulations, both morphologic and physiologic, in which the one-stage approach is contraindicated; these are discussed under “Alternatives to One-Stage Unifocalization and Intracardiac Repair” under Special Situations and Controversies later in this section. It should also be emphasized that individual surgeons selectively use one-stage repair based on morphologic details and their own experience.\textsuperscript{5,7,18,38,51,21,27,26,53,96}

\subsection*{One-Stage Unifocalization and Intracardiac Repair}

In the text that follows, various components of the operation are described, including preliminary procedures leading up to it. These components include:
Assessing intrapericardial true pulmonary artery system
Identifying and assessing collateral system
Managing sources of pulmonary blood flow on CPB
Completing unifocalization
Assessing adequacy of unifocalization
Performing intracardiac repair
Establishing RV-to–pulmonary arterial continuity
Assessing complete repair

This procedure is typically performed in infants at approximately 3 to 4 months of age. Occasionally it is performed in neonates or in younger infants whose condition is unstable because of either profound cyanosis or severe pulmonary overcirculation, or in whom there are nonconfluent central pulmonary arteries and a ductus arteriosus providing blood flow to one of the lungs, with collateral supply to the contralateral lung. Exposure is through median sternotomy. The skin incision is extended from the suprasternal notch to well below the xiphoid to provide adequate exposure for the extensive dissection that is necessary. If a thymus gland is present, it is subtotally removed, leaving a small remnant of thymic lobes above the brachiocephalic vein. The pericardium is opened anteriorly with a longitudinal incision; a piece of anterior pericardium may be removed and treated in glutaraldehyde for later use in the operation.

**Assessing True Pulmonary Artery System** The first task is to assess the intrapericardial true pulmonary artery system. Commonly there are confluent and very hypoplastic central pulmonary arteries with a small pulmonary trunk segment that ends blindly at the level of an atretic pulmonary valve (Fig. 38-74). The pulmonary trunk and branch pulmonary arteries are dissected over their entire course beginning centrally and moving to the periphery, clearly identifying major branches of the RPA and LPA as they enter the lung parenchyma.

**Identifying and Assessing Collateral System** The next task is to identify and assess the collateral system. This requires a clear mental image of it based on careful study of the preoperative angiograms. The technical maneuvers used in this part of the procedure are variable and depend on the number and positions of the large collaterals. This may take several hours to accomplish. Each large collateral artery is identified at its systemic source and dissected over its entire length to the point where it enters the lung parenchyma. The specific approach to each collateral depends on its point of origin. The most common site of origin is the upper descending aorta with the collaterals coursing anteriorly through the posterior mediastinum into the middle mediastinum and then into the lung hilum (see Fig. 38-74). It is best to approach these collaterals through direct mediastinal dissection rather than by entering the pleural space. With the ascending aorta retracted anteriorly and to the left and the superior vena cava retracted to the right (see Fig. 38-74), the posterior pericardial reflection is opened in the midline within the space bordered above by the tracheal bifurcation and below by the dome of the left atrium. If confluent central pulmonary arteries are present, it may be necessary to work around them as the posterior dissection proceeds. Once the posterior pericardium is opened and the soft tissue of the posterior mediastinum is entered, collateral vessels are easily identified. Further posterior dissection exposes the esophagus and descending aorta, allowing access to the origin of collaterals that arise from this aortic position (see Fig. 38-74).

Occasionally, large collateral arteries arise lower on the descending aorta or from the major head and neck vessels. Those arising from head and neck arteries can be accessed directly by dissecting the artery of origin and then exposing the collateral along its length until it enters lung parenchyma. Collaterals originating from the lower thoracic aorta and occasionally intraabdominally are best exposed by opening the appropriate pleural space anterior to the phrenic nerve and gently retracting the lung out of the pleural space to expose the descending aorta and collateral origin. These lower collaterals may enter the hilum of the lung directly or travel in the inferior pulmonary ligament before entering the lung parenchyma. It is not uncommon for collateral vessels to pass through the muscle of the esophagus before entering the lung tissue.

**Managing Sources of Pulmonary Blood Flow on Cardio pulmonary Bypass** Once the true pulmonary artery system and all collateral vessels have been identified and fully dissected, cannulation sutures are placed in preparation for CPB. Aortic and bivacal cannulation are standard (see Section III of Chapter 2). After full heparinization and aortic and bivacal venous cannulation, CPB is initiated. All collateral vessels (or remaining collaterals, if some are ligated prior to initiation of CPB) are rapidly ligated at their aortic or systemic vessel origin using appropriately sized permanent metal clips. Patients with TF generally have a large intracardiac return during repair because of acquired collateral flow to the pulmonary arteries; those with pulmonary atresia, and especially those with the large AP collateral arteries, may have a particularly large intracardiac return requiring special consideration. Thus, an important goal in patients who will be placed on CPB is to have control of as much pulmonary blood flow as possible. The surgeon should be aware of all sources of pulmonary flow. This is accomplished by detailed review of the preoperative cardiac catheterization and angiographic data. Possible sources include the ductus arteriosus, surgically created systemic–pulmonary arterial shunts, large AP collateral arteries, and acquired AP collaterals. Before commencing CPB, all sources should be surgically identified and dissected to the degree that instantaneous control can be achieved. This is most easily accomplished with the ductus or with surgically created shunts. Although more difficult, it is also necessary to dissect the origin of all large AP collaterals as described in the preceding text. Acquired collaterals, usually smaller in size but more numerous and diffuse, pose the greatest challenge. They usually arise from the internal thoracic artery, intercostal arteries, bronchial arteries, or other unnamed mediastinal vessels. If previous surgery has been performed, acquired collaterals may form at sites of pleural fusion. Some, and sometimes many, acquired collaterals can be coil occluded by an interventional cardiologist at preoperative catheterization. The surgeon should attempt to control remaining acquired collaterals during the operation before placing the patient on CPB (still, it is not unusual for intracardiac return to increase once CPB is established).

CPB is established with the perfusate at about 34°C and with ionized calcium at a normal level so that ventricular fibrillation does not occur before proper preparations are made for managing intracardiac return. After aortic and bicaval cannulation is accomplished, CPB is slowly established with the heart continuing to beat vigorously. A left
ventricular vent of appropriate size (10F for patients weighing 4.0 kg or less; 13F for patients weighing 4 to 10 kg; adult size for patients weighing more than 10 kg) is placed via a purse-string suture into the right upper pulmonary vein, and the vent tip is passed across the mitral valve into the LV. At this point, full CPB and vigorous venting are established, and immediately, all sources of pulmonary blood flow, previously identified and dissected at their systemic origin, are permanently closed using metal clips. If appropriate pre-CPB dissection has been accomplished, all major sources, including complex situations with up to eight large AP collaterals, can be controlled in 30 to 90 seconds. Commonly, especially in patients with baseline SaO2 greater than 80%, a substantial portion of the multiple sources can be closed before initiation of CPB, with this process limited only by decrease in SaO2. It is not unusual, particularly if the patient is in early infancy and has not undergone prior palliation, for these maneuvers to reduce intracardiac return to normal levels.

In older children who have been chronically cyanotic or palliated, acquired collateral vessels from the systemic to the pulmonary circulation have often developed. In these cases, control of the embryologic large AP collaterals may still leave substantial cardiac return through the acquired collaterals. Then, a larger LV vent and higher perfusion flow rates may...
be needed to account for the abnormally high runoff. Once CPB is established, perfusion temperature is gradually reduced, aiming for a core body temperature of 25°C.

In addition to these precautions against damage from large intracardiac return, cerebral perfusion can be further maintained at an adequate level by blood gas control despite rapid aortic runoff. Arterial PCO₂ is maintained at 45 mmHg or greater to maximize cerebral blood flow.

Completing Unifocalization The next task is to complete the unifocalization process. This again depends on number and positions of the collateral arteries and status of the central pulmonary artery system. Depending on number and complexity of collaterals, this aspect of the procedure may take several hours. It is performed without an aortic clamp so that the myocardium is well perfused in an empty beating state. Most collateral arteries can be connected directly to the central pulmonary artery system by working within the central mediastinal space previously dissected. Most commonly, long side-to-side anastomoses between the collaterals and true pulmonary arteries, extending from a midline position all the way to the periphery where the arteries enter the lung parenchyma, are performed using 7-0 absorbable monofilament suture (Fig. 38-75). Occasionally, collateral arteries arising from head and neck vessels or from much lower on the descending thoracic aorta can be connected in end-to-side fashion to the central system. Collateral arteries are usually connected to the superior-posterior, directly posterior, or inferior-posterior circumferential aspect of the central pulmonary artery system, leaving its anterior aspect untouched. Typically, collateral vessels that are candidates for unifocalization will not reach the true pulmonary artery easily if the collateral artery is rerouted over the hilum of the lung, and this technique is avoided.

Once all collateral vessels have been unifocalized, it is often beneficial to incise the remaining anterior aspect of the central true pulmonary arteries from left hilum to right hilum, and then patch them with a segment of cryopreserved allograft pulmonary artery. In this fashion, a completely unifocalized pulmonary artery system with newly reconstructed branch pulmonary arteries that are of normal or even supranormal diameter can be achieved, with no areas of circumferential pulmonary artery patch throughout the system.

With rare exceptions (i.e., small remote collaterals with single lung segment distribution or less), all isolated supply collaterals should be unifocalized because failure to do so will eliminate lung segments from the central pulmonary artery circulation after repair. In many cases, dual-supply collaterals (those that communicate with the true pulmonary arteries) should also be unifocalized. Even though a dual-supply collateral will distribute to the same distal vascular bed as that portion of the true pulmonary artery with which it communicates, the value of unifocalizing such a collateral is that it can be used to augment the diameter of the small true pulmonary artery. If the true pulmonary arteries are of adequate size, a dual-supply collateral need not be unifocalized and can be simply ligated at its origin.

If there is complete absence of true pulmonary arteries within the pericardium, collateral vessels from the right and left lungs can be easily connected to one another across the midline within the dissected central mediastinal space. Most frequently, on each side, all ipsilateral collateral vessels are first connected to one another with long side-to-side anastomoses, with the anastomoses beginning at the transected systemic end of the collaterals and extending to the lung parenchyma. Then the left side is connected to the right, achieving complete unifocalization and left-right confluence. Occasionally the older child or young adult will present as a good candidate for unifocalization. In this case more liberal use of circumferential synthetic material (no growth potential) is acceptable (Fig. 38-76). This should be avoided if possible in the growing infant and child.

Assessing Adequacy of Unifocalization Once unifocalization is complete, an assessment must be made regarding whether the pulmonary artery system will have adequately low resistance to allow intracardiac repair with subsequent low RV and pulmonary artery pressure. Following intracardiac repair, peak RV pressure should be less than 60% of peak systemic arterial pressure. Experienced surgeons can often predict this by size of the true pulmonary arteries and collateral arteries and adequacy of the unifocalization. In such cases, proceeding directly to intracardiac repair is indicated. In other circumstances, typically those in which neither the true pulmonary artery system nor the collateral system is sufficiently large to ensure low pulmonary arterial resistance, or in which unifocalization was difficult and a question remains regarding adequacy of anastomoses or positioning of the unifocalized vessels, it is most prudent to assess pulmonary arterial resistance objectively before deciding whether to move ahead with intracardiac repair.

Objective assessment can be made using an intraoperative blood flow study. The perfusionist primes a separate circuit, which draws blood from the venous reservoir and perfuses a cannula that is placed into the central portion of the newly unifocalized pulmonary artery system. Based on body surface area, controlled perfusion into the pulmonary artery circuit is then performed in incremental steps beginning at 20% of baseline indexed cardiac output and increasing in increments of 20% up to 100% indexed cardiac output. At each increment, after a steady state is achieved, pressure is measured using a small catheter placed into the pulmonary artery system and connected to a pressure transducer. During the assessment, careful attention is paid to the left atrial appendage. If the heart is not beating vigorously because of hypothermia or hypocalcemia, or if it is arrested with cardioplegia or is fibrillating, the left atrium and LV can be quickly overdistended by pulmonary venous return. To counter this, the LV vent is placed on vigorous suction and the vent pop-off valve is completely occluded. Even then, careful attention should be paid to the left atrial appendage to be sure that the vent system is not overwhelmed by pulmonary blood flow at higher incremental flows.

If mean PPA remains less than 25 mmHg at full indexed cardiac output in a 3- to 4-month-old infant, intracardiac repair can proceed. These values have been shown to predict accurately that P_{IV/LS} will be less than 0.5 following intracardiac repair in both controlled laboratory studies and in the clinical situation. In older children, a mean PPA of 25 to 30 mmHg at full indexed cardiac output usually indicates ability to move ahead with intracardiac repair. If pressures increase to more than these threshold values at any incremental step in the pulmonary blood flow study, then the test is terminated and intracardiac repair is not performed. In this case, a central aorta to pulmonary artery shunt is performed from the left side of the ascending aorta to the central portion of the unifocalized pulmonary artery system using standard
Figure 38-75  One-stage complete unifocalization and intracardiac repair via median sternotomy for tetralogy of Fallot with pulmonary atresia and large aortopulmonary collateral arteries. Median sternotomy preliminary dissection of true pulmonary arteries and collaterals, and cardiopulmonary bypass (CPB) details are described in the text, in Section III of Chapter 2, and in Fig. 38-74. Once CPB is established, previously dissected collateral vessels are immediately ligated at their systemic origin. This preserves entire length of each collateral so that this tissue can be used in the reconstruction that results in complete unifocalization. For clarity, heart, ascending aorta, and trachea have been eliminated in this figure. A, Hypoplastic centrally confluent true pulmonary arteries are present. Hypoplastic left pulmonary artery (LPA) distributes to left upper lobe and hypoplastic right pulmonary artery (RPA) distributes to lateral aspect of right lower lobe. Three large collateral arteries are present. One arises from right carotid artery and takes a tortuous course (dashed lines) to provide blood flow to medial aspect of right lower lobe (APC2). Two other collaterals arise from typical upper descending thoracic aortic position. One courses to right upper and middle lobes (APC3) and the second to left lower lobe (APC1). The surgeon should be acutely aware, based on careful preoperative evaluation of the angiograms, of all stenotic areas within each collateral artery. Stenotic areas must be eliminated (dashed lines on APC2) if they are proximal within the collateral, or addressed surgically with either patching or some other form of augmentation if they are more distal. B, All three collateral arteries have been ligated and divided at their systemic origins. Hypoplastic pulmonary trunk has been transected just distal to atretic pulmonary valve. Unifocalization sites (dashed lines) have been chosen on the true pulmonary arteries in accordance with positions and lengths of collateral arteries to be unifocalized. In this case the two short dashed lines on the true pulmonary artery represent sites of implantation of the left and right mid-thoracic collateral vessels (APC1 and APC3). These incisions on the true pulmonary arteries are placed directly posterior. APC1 has been incised over part of its length to allow a side-to-side anastomosis over left hilum. Dashed line on APC3 identifies intended incision that will allow a side-to-side anastomosis with the true RPA. Tortuous APC2 has been mobilized, and the dashed line along its length indicates proposed incision that will allow performing an extensive side-to-side anastomosis onto the true pulmonary arteries beginning in the left hilum and extending all the way to the right hilum. The long incision on the true pulmonary artery, represented by the dashed line, is positioned on the superior-posterior aspect of the true pulmonary arteries.
The three collateral vessels have been connected to the true pulmonary artery system as shown using running 7-0 absorbable monofilament sutures. Exquisite attention to detail and a three-dimensional vision of the result are required to avoid kinking, overstretching, and twisting of the delicate vessels. In this particular case, large tortuous collateral APC2 provides a large degree of “raw material” to augment the central pulmonary artery system adequately. In the absence of such abundant raw material, a less extensive anastomosis of the collateral to the true pulmonary artery would be performed, similar to the other two collateral anastomoses in this example, and the central pulmonary artery system would be augmented centrally from hilum to hilum with a patch of pulmonary arterial allograft tissue. At this point in the operation the decision is made whether to perform an intraoperative pulmonary blood flow study as an aid in designing the remainder of the operation. In this case operation is completed by ventricular septal defect (VSD) closure and right ventricular outflow tract conduit (see text for other options). The small opening at transected pulmonary trunk is enlarged to the left and right sides in order to perform distal anastomosis of valved allograft conduit into newly reconstructed central pulmonary artery system. This aspect of the procedure and remaining VSD closure and proximal conduit to right ventricular anastomosis is performed in standard fashion for tetralogy with pulmonary atresia without large aortopulmonary collateral arteries. Key: APC, Aortopulmonary collateral artery; Desc Ao, descending thoracic aorta; PT, pulmonary trunk.
Intracardiac Repair

If pulmonary arterial resistance is acceptable, intracardiac repair commences. The aorta is clamped and cardioplegic solution introduced into the aortic root in the usual manner (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). After adequate cardiac

Figure 38-76 Alternative unifocalization repair of tetralogy of Fallot (TF) with pulmonary atresia and large aortopulmonary collateral arteries with absent true pulmonary arteries. In most cases when true pulmonary arteries are completely absent, central confluence between left- and right-sided collaterals is provided by creating direct continuity between collateral arteries from each side, working within the dissected space in central mediastinum, as described in Fig. 38-75. This is especially important in infants and young children, who require growth potential of living tissue. Occasionally a patient will present at an older age with stenotic but open collaterals with well-developed distal vasculature, as shown in this case. Under these conditions, native tissue-to-tissue anastomoses are not critical because growth potential is not required. For clarity, the heart and ascending aorta are eliminated from this figure. A, Four collateral vessels are shown arising from the upper mid-thoracic aorta. They have been exposed according to the dissection process described in the text and in Fig. 38-75. There is one large collateral vessel supplying the entire left lung; it is stenotic at its origin. Three separate collateral vessels, all stenotic at their origins and in their proximal segments, supply the right lung—one each to the right upper, right middle, and right lower lobes. B, All collaterals have been ligated and divided at their aortic origins. A polytetrafluoroethylene (PTFE) conduit of appropriate diameter is used to connect left and right sides. The large left-sided collateral is connected end to end to the PTFE tube graft, and the three right-sided collaterals are unifocalized either directly or with a separate smaller PTFE tube, after resecting proximal stenotic segments. C, Conduit placement and ventricular septal defect closure are performed as for typical TF with pulmonary atresia without large aortopulmonary collateral arteries. Key: Desc Ao, Descending thoracic aorta.

techniques for creating systemic–pulmonary arterial shunts (see “Techniques of Shunting Operations” in Section 1). Size of the shunt is based on body size and on total pulmonary arterial resistance as assessed from the pulmonary blood flow study just completed. If resistance is particularly high, then a slightly larger shunt may be needed.
arrest is achieved, superior and inferior caval tapes are tightened around the venous cannulae to isolate systemic venous return. A longitudinal incision is made in the infundibulum of the RV and the ventricular cavity is entered. Hypertrophied muscle is removed from the septal and parietal bands and infundibular free wall. This adequately exposes the VSD, which is then closed with either a glutaraldehyde-treated autologous pericardial patch or a woven polyester patch. Depending on the surgeon’s preference, either a running nonabsorbable monofilament suture or interrupted pledgeted mattress sutures are used for attaching the patch to the borders of the VSD. All the same considerations are addressed in this situation as in VSD closure in more typical TF (see Technique of Operation in Section 1).

A small right atriotomy is made and status of the atrial septum examined. If a competent but patent foramen ovale is present, it is usually left as is. A secundum atrial septal defect is typically closed either primarily or, if needed, with a pericardial or polyester patch attached with running nonabsorbable monofilament suture. If the atrial septum is intact, it is left in this state. If appropriate decisions have been made with respect to Rp, presence of a competent RV to pulmonary artery valve conduit usually allows for adequate RV function early postoperatively, minimizing the potential benefits of an open atrial septum (as described in the text that follows). The right atrial incision is then closed in standard fashion and the aortic clamp removed, allowing reperfusion of the myocardium.

At this point, RV-to-pulmonary artery reconstruction is undertaken. With adequate unifocalization and central pulmonary artery augmentation as described earlier, the conduit procedure is the same as used in the more straightforward case with duct-dependent TF, pulmonary atresia, and normally arborizing confluent central pulmonary arteries.

Establishing Right Ventricle-to-Pulmonary Artery Continuity Valved polyester conduits were used in the early era of this type of surgery; today, allograft conduits, either aortic valve with ascending aorta, or pulmonary valve with pulmonary trunk, with or without the bifurcation, are preferred. The allograft pulmonary valved conduit with its bifurcation is often the optimal replacement device. When a bifurcated graft is not required, there is no secure evidence that the pulmonary or aortic valve allograft has an advantage over the other; however, the thinner wall of the pulmonary allograft may have more tendency to become aneurysmal if pulmonary artery pressure becomes importantly elevated.

During the early stages of the procedure, the allograft valved conduit is selected, thawed, and rinsed. In neonates and infants, depending on their size, a 10- to 18-mm-diameter valve can be used; in children older than age 5, a 22- to 25-mm-diameter valve can be used. These sizes should not be flow limiting.

Two somewhat different techniques of allograft insertion are used. In one (preferable), the proximal end of the allograft is sunk into the RV outflow tract and a piece of pericardium, allograft arterial wall, or polyester is used as a roof over the ventriculotomy (Fig. 38-77). The distal end of the allograft is attached to the newly reconstructed transverse central pulmonary artery system before making the proximal anastomosis of the allograft conduit directly onto the right ventriculotomy site. This method has the advantages of minimal use of foreign material on which a thick neointima may develop, and freedom from sternal compression. However, care must be taken that the allograft valve anulus retains its proper circular geometry and that the opening from RV into allograft is large.

In the second method, a woven polyester tube 2 to 5 mm larger than the diameter of the allograft valve anulus is sutured to the proximal end of the allograft. Before insertion, the proximal polyester end is cut in a severely beveled fashion so that it serves primarily as a roof on the ventriculotomy incision, with only a few millimeters of fully circular polyester conduit just proximal to the allograft. With care, the conduit can be kept completely away from the sternum. This technique has the advantage that the perfectly circular geometry of the allograft valve is well maintained and that with it all types of RV and pulmonary trunk morphology can be managed. It has the disadvantage of a very short 2- to 3-mm cylinder of polyester in the proximal end of the conduit.

There are situations in which one or the other method is mandated, depending on RV morphology and availability of the pulmonary trunk, but more often selection is one of preference.

Using either technique, the proximal end of the allograft is cut transversely about 5 mm below the nadir of the valve cusps, leaving the muscular remnant at least 4 mm thick (thicker than when the valve is used for aortic valve replacement). The conduit is not trimmed distally until the nature of the pulmonary artery confluence is established following completed unifocalization and central pulmonary artery augmentation and the distance between this and the right ventriculotomy is measured.

With the first method (see Fig. 38-77, A), a limited longitudinal incision is made in the superior RV wall where the pulmonary trunk would normally arise. Care is taken in extending the incision distally so that the anterior margin of the VSD and right coronary cusp of the aortic valve are not damaged. The RV opening is also enlarged proximally, and any thick trabeculations from the free wall, particularly inferiorly, are excised. The VSD is repaired in a fashion similar to that described for TF with pulmonary stenosis (see Fig. 38-27). The distal end of the allograft conduit is cut so that it is the correct shape and the conduit is the correct length. It must not be too long, or it may kink and possibly compress either branch of the pulmonary artery. The reconstructed or augmented pulmonary artery confluence is opened with an incision extending out along the RPA and LPA. The opening is made long enough to match exactly the diameter of the allograft. The distal anastomosis is made with continuous 5-0 or 6-0 polypropylene suture (Fig. 38-77, B). The proximal conduit anastomosis is made by commencing the suturing posteriorly where the allograft is apposed to the superior margin of the ventriculotomy and any remnant of infundibular septum. A 4-0 polypropylene suture is used, and often both the RV wall and superior edge of the VSD patch are picked up in the suture line to make it particularly secure posteriorly. The suture line is continued from the midline along both sides around about half the circumference of the conduit, and the sutures are held. A patch of pericardium, polyester, or allograft arterial wall is cut to an approximate semilunar shape and sutured into place to complete the anterior half of the anastomosis (Fig. 38-77, C). Its straight superior edge is anastomosed to the muscular portion of the graft as the first step, and its curved inferior edge is attached to the edges of the right ventriculotomy. Good bites of muscle are taken all around and care is used to avoid...
Figure 38-77  Right ventricular outflow tract conduit placement for tetralogy of Fallot (TF) with pulmonary atresia. Much of the surgical technique for repair of TF with pulmonary atresia is similar to that for TF with pulmonary stenosis (e.g., cardiopulmonary bypass [CPB], myocardial management, and intracardiac management of ventricular septal defect [VSD] and atrial septum). Management of these two malformations, however, deviates at several important points. Specific management of the pulmonary arteries depends on the form of pulmonary atresia. For duct-dependent atresia, ligation and division of ductus arteriosus is performed at commencement of CPB. For more complex forms of TF with pulmonary atresia and large aortopulmonary (AP) collateral arteries, complex reconstruction of the pulmonary vasculature is often required (see Figs. 38-74 to 38-76). Although in TF with pulmonary stenosis the VSD closure may be managed through a right atrial incision working through the tricuspid valve orifice, in TF with pulmonary atresia the VSD is always closed through an infundibular incision in the right ventricle (RV).

In the various parts of this figure (and in Fig. 38-78), pulmonary artery anatomy is that of normally arborizing, normal diameter, confluent branch pulmonary arteries with patent ductus arteriosus. However, RV outflow tract conduit placement is the same for more complex TF with pulmonary atresia in which the pulmonary artery system has been reconstructed through unifocalization. A, Ductus arteriosus has been ligated, taking care to avoid narrowing the left branch pulmonary artery. Dashed line on the distal pulmonary trunk shows site of transection in preparation for distal anastomosis of valved conduit to it. Opening in pulmonary trunk may need to be extended with incisions along left and right pulmonary arteries to accommodate circumference of the conduit. A longitudinal infundibular incision has been made and VSD closed with a patch and running suture technique. Note in this case that VSD has an inlet component. Hypertrophic muscle of the RV infundibulum and VSD closure are handled in a manner similar to that in TF with pulmonary stenosis. B, Ductus arteriosus has been divided. A pulmonary allograft valved conduit is shown with the distal anastomosis performed end to end, allograft to pulmonary trunk. A running suture technique using fine monofilament suture is used. Proximal aspect of conduit is then attached to RV. Conduit is placed into ventriculotomy with the suture line attaching its proximal end to the infundibular septum within the ventricular incision. Although not shown in this figure, commonly the proximal suture line incorporates the upper aspect of VSD patch, which is also attached to the anteriorly displaced edge of the infundibular septum. C, Posterior suture line of proximal conduit anastomosis is completed as it transitions onto free edge of infundibular incision. Proximal component of the reconstruction is completed using a roughly hemi-oval patch made of polyester, polytetrafluoroethylene, or glutaraldehyde-treated autologous pericardium. Straight edge of patch is sewn around remaining anterior aspect of proximal conduit, and curved edge is sewn around ventriculotomy site to complete the reconstruction. All sutures lines are running nonabsorbable monofilament suture.
damaging the valve cusps of the graft or the LAD. The conduit arises from the RV in nearly the same position as a normal pulmonary artery and passes superiorly and posteriorly directly to the pulmonary artery bifurcation. It is in little danger of being compressed by the sternum.

In the second method, a longitudinal incision is made in the downstream portion of the RV (Fig. 38-78, A). If a rudimentary infundibular septum and parietal extension are present, these are dissected away from the RV free wall. The VSD is repaired as described in “Ventricular Septal Defect Closure” under Technique of Operation for TF with pulmonary stenosis in Section I, and preparations are made for inserting the conduit. The conduit, once in position, should be directed toward the patient’s left shoulder as it comes off the right ventriculotomy (it need not be oriented parallel to the ventriculotomy) and then curve gently back to the right to approach the pulmonary trunk with just a little redundancy and in an undistorted fashion. This is accomplished by cutting the distal end of the allograft exactly transversely (not obliquely). The proximal end of the conduit is cut obliquely so that the tubular part of the proximal polyester extension is only a few millimeters long and the rest is merely a hood (Fig. 38-78, B). The distal and proximal anastomoses are made using a running polypropylene suture (Fig. 38-78, C).

Completing the Procedure After reconstruction is completed, rewarming and separation from CPB is the same as for TF with pulmonary stenosis, as described in Section I (see also “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Assessing Complete Repair Immediately after discontinuing CPB, postrepair (OR) $P_{RV/LV}$ is measured (see “Measuring Postrepair [OR] $P_{RV/LV}$” under Technique of Operation in Section I). A polyvinyl catheter is introduced into the right atrium and advanced into the RV. The level of postrepair (OR or ICU) $P_{RV/LV}$ that is acceptable in this situation is arguable. Thus, repair is left if the $P_{RV/LV}$ is less than about 0.7 and the patient is clinically stable. Although the probability of early death is low for a $P_{RV/LV}$ up to 0.9 (Fig. 38-79), important RV dysfunction occurs at midterm follow-up at these higher RV pressures. If the $P_{RV/LV}$ is greater than 0.7, or if cardiac output is compromised at levels between 0.5 and 0.7, the VSD patch is taken down and the conduit removed, and a central aortic-to–pulmonary artery shunt is placed. This situation, however, should be encountered rarely if the intraoperative blood flow study is used appropriately.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is similar to that described for TF with pulmonary stenosis (see Section I). When the patient has come from the operating room with a complete repair, including closure of the VSD, and postrepair (ICU) $P_{RV/LV}$ (or some surrogate for it) is consistently less than about 0.7 and the patient is hemodynamically stable, further intervention is seldom needed. However, if the ratio approaches that level, there is a considerable probability of death (see Fig. 38-79), and either the cause of the residual obstruction must be removed or ameliorated or the VSD patch perforated. If the patient’s original morphology was pulmonary atresia with confluent pulmonary arteries and a ductus arteriosus, the $P_{RV/LV}$ will rarely reach this value unless the RV-to-pulmonary trunk reconstruction (usually conduit) is technically inadequate, resulting in obstruction. Immediate revision of the conduit is indicated.

If the patient’s original morphology involved AP collaterals that were unifocalized, the situation is more complex. Use of the intraoperative flow study will minimize the number of cases that result in an elevated $P_{RV/LV}$. However, should the situation arise, and the elevated pressure is proven not to be due to obstruction in the conduit but rather to elevated resistance in the pulmonary vascular bed, surgical revision is indicated. Cardiac catheterization should be performed to identify the precise cause of the elevated pressure. If surgically reparable obstruction is found in the reconstructed pulmonary arteries, revision aimed at relieving the obstruction is indicated. If there is no surgically correctable obstruction, the cause of the elevated pressure is elevated resistance in the pulmonary microvascular bed. In this case, if the $P_{RV/LV}$ is above 1.0, VSD perforation is performed; if the $P_{RV/LV}$ is between 0.7 and 1.0, VSD patch removal, conduit takedown, and placement of a systemic-to–pulmonary artery shunt is performed.

Occasionally, pulmonary hypertension is caused by reactivity in the microvascular bed rather than by proximal or fixed distal obstruction. This is more likely if the PPA and PVR had been low earlier postoperatively. Increased ventilatory support, sedation, and a trial of inhaled nitric oxide are typical maneuvers that are both diagnostic and therapeutic.

Postoperative airway difficulties are more common in TF with pulmonary atresia than in TF with pulmonary stenosis, especially if complex unifocalization was performed. Large airway problems caused by external compression by the aorta, unifocalized collaterals, or conduits can occur. $M^{17}$ Unmasking of subclinical, or exacerbation of clinically important, preoperative tracheobronchial malacia can also occur. Phrenic nerve injury is an important concern when extensive dissection has been performed. Small airway reactivity also appears to be more common than in TF with pulmonary stenosis, possibly related to an intrinsic predisposition, but also almost certainly related to direct trauma, autonomic nerve disruption, or airway blood supply disruption. $^{R4}$ Careful and aggressive pulmonary toilet is an important component of treatment, both intraoperatively after CPB and in the ICU. Tracheobronchial suctioning and lavage, and even bronchoscopy, may be needed to keep airways free of both clear and bloody secretions.

A problem particular to certain unifocalization cases is lung reperfusion injury. This is most likely to occur in cases that preoperatively have severely underperfused segments of lung. The acute increase in flow and pressure into these vascular beds can result in important lung parenchymal edema, increased airway secretions, and pleural effusion. The process typically reaches a peak in severity 24 to 48 hours after surgery and resolves gradually over the following 3 to 5 days. The diagnosis is made by chest radiogram findings of pulmonary edema and consolidation, with evidence of intrapulmonary shunting (hypoxemia) in the appropriate clinical setting and with no evidence of infection. The treatment is largely expectant, with mechanical ventilator support until there is clinical evidence that the process has peaked and is resolving.

If the PLA is considerably higher than the PPA (see “Risk Factors for Low Cardiac Output” in Section I of Chapter 5), a left-to-right shunt may be present at some level. Unless
Figure 38-78  Alternative method for right ventricular (RV) outflow tract valved conduit placement in tetralogy of Fallot with pulmonary atresia. General operative management is similar to that described in Fig. 38-77. Using this method, a circumferential polyester conduit is attached to proximal end of allograft valved conduit to facilitate ventricle-to-conduit anastomosis. A, Dashed lines indicate incisions to be made on central pulmonary artery and on RV infundibulum. B, Inset shows polyester conduit being connected to proximal end of allograft valved conduit with a running monofilament suture. In main figure, distal anastomosis between allograft conduit and incision in pulmonary trunk is performed, leaving atretic pulmonary trunk intact. Proximal polyester extension of allograft is tailored with a sharp bevel to accommodate its connection to the RV. C, Beveled free edge of polyester conduit is connected to ventriculotomy to complete operation. As seen here, there may be only several millimeters of length to circumferential component of polyester extension of the conduit, which mostly serves as a proximal hood, similar to freestanding patch used for hood in technique shown in Fig. 38-77. Key: PTFE, Polytetrafluoroethylene.
the patient is convalescing well, an echocardiographic and cineangiographic search is made for sites of shunting that can be closed percutaneously or surgically.

RESULTS

After Repair

Early (Hospital) Death

Overall hospital mortality after repair in a heterogeneous population varies between less than 3% and up to 20%, depending on era, patient characteristics, and institution.

Most recent studies report hospital mortality of less than 5% for a heterogeneous population and less than 3% when patients undergoing extensive unifocalization procedures are excluded. When examining clinical series dealing only with complete repair involving unifocalization, hospital mortality historically has generally been less than 10% as experience with surgical management of this difficult group of patients has accumulated, the typical pattern of improved hospital mortality has emerged. Large series indicate that over the last 5 to 10 years, hospital mortality can be as low as 2% (as compared to 5% for a heterogeneous population) and less than 3% when patients undergoing extensive unifocalization procedures are excluded.

Incremental Risk Factors for Death

Variables relating to morphology of the pulmonary arterial circulation have traditionally been considered the strongest risk factors for death after repair, presumably accounting for most of the historical differences in outcome between these patients and those having TF with pulmonary stenosis. Available data for patients who do not require unifocalization, as well as for those who do, suggest that at least in the medium term, these variables can be and are being neutralized.

Pulmonary Artery Abnormalities

Size of central and proximal extracardiac right and left pulmonary arteries, congenitally nonconfluent right and left pulmonary arteries, and number of large AP collateral arteries have been identified as risk factors for death after repair, presumably accounting for most of the historical differences in outcome between these patients and those having TF with pulmonary stenosis. Available data for patients who do not require unifocalization, as well as for those who do, suggest that at least in the medium term, these variables can be and are being neutralized.

Modes of Death

Most early postoperative deaths are attributable to acute cardiac failure, although some are due to acute or subacute pulmonary failure and a few to hypoxia or hemorrhage. In the large series of patients undergoing one-stage unifocalization and repair by Hanley and colleagues, acute hepatic failure was an important cause of death in the early years of the experience, accounting for much of the early 10% mortality; however, in the most recent decade, this cause has been virtually eliminated, with overall early mortality improving to approximately 2%. Most late postoperative deaths are due to chronic heart failure, although an appreciable number are sudden. These latter may be arrhythmic deaths. Unifocalized patients may experience fatal hemothysis.

Incremental Risk Factors for Death

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the latter identified in early studies is probably a surrogate for that of increased Rp. Early and aggressive complete unifocalization of all collateral vessels and patch augmentation of centrally hypoplastic pulmonary arteries have eliminated the association between higher Rp and native pulmonary arterial arborization abnormalities.\textsuperscript{54,86,87}

**Age (Size)** Age older than about 5 to 8 years is a risk factor for death, primarily late after repair.\textsuperscript{5,17} The incremental risk of young age, once important, has largely been neutralized. This is evident in more recent experiences from institutions in which one-stage repair is typically performed in neonates and young infants.\textsuperscript{16,1,20,84,86,74}

**Postrepair \(\text{P}_{\text{RV/LV}}\)** Higher postrepair \(\text{P}_{\text{RV/LV}}\) is a risk factor for death after repair, probably an immutable one (see Fig. 38-79).\textsuperscript{5} This factor is the final common expression, which includes the influences of intrinsic Rp, degree of arborization of the pulmonary arteries (which includes completeness of unifocalization), size of the large pulmonary arteries, and precision with which any reconstruction or unifocalization has been accomplished.

**Duration of Cardiopulmonary Bypass** Duration of CPB was identified as a risk factor for death in early studies, particularly in the early period after repair.\textsuperscript{1,5,17,24} Duration of CPB may carry risks related to CPB’s intrinsic damaging effects, but it may also be a surrogate for technical complications during surgery. More recently, duration of CPB has not been associated with increased risk of early death in the large series of one-stage unifocalization and repair cases reported by Hanley and colleagues.\textsuperscript{36} Prolonged duration of CPB is a necessity in these patients in order to complete the unifocalization process, and thus does not represent difficulties or complications during surgery. Also, in more recent years, a reduction of the damaging effects of CPB has almost certainly been achieved.

**Heart Block**

Heart block is rare after repair, just as it is after repair of TF with pulmonary stenosis.

**Functional Status**

Most patients who survive repair have a good functional status (Table 38-13). Importantly, a tendency to declining functional status across time exists, but this may be attributable to chance alone (Fig. 38-81). Few objective studies of exercise performance have been reported.

### Table 38-13 New York Heart Association Functional Class after Repair of Tetralogy of Fallot with Pulmonary Atresia

<table>
<thead>
<tr>
<th>NYHA Class at Last Follow-up</th>
<th>(n)</th>
<th>% of 95</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>89</td>
<td>94</td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>III</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Subtotal</strong></td>
<td>95</td>
<td>100</td>
</tr>
<tr>
<td><strong>Dead</strong></td>
<td>39</td>
<td></td>
</tr>
<tr>
<td><strong>Alive, unknown class</strong></td>
<td>5</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>139</td>
<td></td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues.\textsuperscript{524}

**Pulmonary Artery Pressure and Resistance**

As with other postoperative outcome events, information about P\(\text{PA}\) and Rp is limited. RV pressure can in no way substitute for P\(\text{PA}\) and Rp, because almost all patients have a pressure gradient between the RV and pulmonary arteries after repair. Shimazaki and colleagues found that 75% of patients had a gradient of at least 20 mmHg late after repair, and 10% had one of 60 mmHg.\textsuperscript{512} When patients undergoing repair in infancy or the neonatal period are considered, gradients progress inevitably over time, and at midterm follow-up essentially all patients will have important gradients.

Early data suggested that about 50% of a heterogeneous group of patients will have elevated P\(\text{PA}\) and Rp late after repair, with elevated Rp correlating highly and inversely with extent of native pulmonary artery arborization.\textsuperscript{512} More recent data from patients undergoing surgical management plans that include early and complete correction of pulmonary artery arborization abnormalities demonstrate low P\(\text{PA}\) and Rp, both early and at midterm follow-up and regardless of degree of original arborization,\textsuperscript{84,86} indicating that this correlation is not immutable (Table 38-14). At midterm follow-up, \(\text{P}_{\text{RV/LV}}\) was similar to the perioperative value, indicating that the unifocalized vascular bed grows over time.\textsuperscript{36}

**Reintervention**

Reoperations other than those on valved conduits and on peripheral pulmonary arteries in patients undergoing unifocalization are rare. Reintervention is infrequently needed to repair a residual or recurrent VSD or to close an overlooked large AP collateral artery (both in 3% of patients).\textsuperscript{24} Progressing dilatation of the aortic root and development of aortic valve regurgitation has required aortic valve replacement in 1% of patients.\textsuperscript{24} For patients undergoing early aggressive unifocalization, reoperation on the peripheral pulmonary
arterial vasculature for persistent or recurrent obstruction is less than 15% at 5-year follow-up. The most common reoperation is replacement of an obstructed xenograft or allograft valved conduit. Among a heterogeneous group of patients receiving these conduits for a variety of conditions, but most commonly for TF with pulmonary atresia, freedom from reoperation for conduit obstruction was 99%, 95%, 59%, and 11% at 3.5, 5, 10, and 15 years, respectively. Among very young patients receiving 12-mm porcine valve xenografts in a polyester conduit, 3.5-, 5-, and 10-year freedom from replacement was 60%, 35%, and 9%, respectively, related in part to rapid growth of the patient. Time-related freedom from reoperation on allograft aortic and pulmonary valved conduits larger than about 21 mm is not yet known with a high degree of certainty. Currently, for properly preserved allograft aortic conduits, this appears to be about 95% at 5 years, falling to about 90% at 10 years and 60% at 20 years (Fig. 38-82, A). The hazard function for reoperation has a steadily rising single phase (Fig. 38-82, B), suggesting that all such conduits may ultimately require replacement. Small patients require small allograft valved conduits, and the very small conduits required in neonates and infants clearly have a shorter reoperation-free interval than do larger conduits that can be used in children (Fig. 38-83). Despite these general trends, individual patient reoperation-free intervals can be quite variable, with some neonates having intervals up to a decade.

Prevalence and rate of reoperation for conduit obstruction are considerably greater when an allograft valved conduit is extended with a polyester cylinder than when it is not. It is not known whether this applies to proximal or distal extensions, or to both. A proximal polyester gusset in the RV does not seem to have this effect. Use of the valved bovine jugular vein conduit for RV to pulmonary artery reconstruction has received mixed reports. One individual institution report showed a high degree of midterm obstruction, whereas an eight-institution multi-institutional study, as well as individual institutional studies, showed midterm results that compare favorably with those of valved allografts.

After Palliative Operations for Increasing Pulmonary Blood Flow

**Effect on Size of Pulmonary Arteries**

Important enlargement of at least some portions of the pulmonary arteries can be obtained by increasing pulmonary flow. The ratio improved when the periods between years 1992 through 1997 and 1999-2005 were compared. The ratio in patients younger than 1 year, the most common operation was repair of truncus arteriosus; in older patients, it was repair of tetralogy of Fallot with pulmonary atresia. Key: $P_{RV/LV}$ Ratio of right-to-left ventricular pressures.

### Table 38-14

<table>
<thead>
<tr>
<th>Era</th>
<th>$P_{RV/LV}$ (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total experience</td>
<td>0.41 ± 0.12</td>
</tr>
<tr>
<td>1992-1998</td>
<td>0.46 ± 0.14</td>
</tr>
<tr>
<td>1999-2005</td>
<td>0.37 ± 0.11</td>
</tr>
</tbody>
</table>

*The ratio improved when the periods between years 1992 through 1997 and 1998 through 2005 were compared.

Key: $P_{RV/LV}$ Ratio of right-to-left ventricular pressures.
blood flow and pressure. This observation has influenced a number of institutions to follow management plans in patients with small pulmonary arteries that include staging procedures to achieve increased flow and pressure into both the pulmonary arteries and collateral vessels. Various ways of achieving this have been described, including placing PTFE systemic–pulmonary arterial shunts, directly connecting central pulmonary arteries to the ascending aorta, placing RV–pulmonary trunk conduits or patches, and constructing shunts into individual or partially unifocalized collateral vessels. Although vessel growth clearly results from these procedures, it is difficult to document how frequently they lead to intracardiac repair with acceptable PRV and PPA. Reports suggest that approximately 20% of anastomoses performed in the palliative setting will occlude, and about half the patients undergoing staged palliative procedures will eventually undergo intracardiac repair. A substantial portion of these patients will have unacceptably high PPA.

Also well established is the fact that enlargement is not always diffuse, and there may remain areas of stenosis, presumably because pulmonary arterial walls are not uniformly compliant. Reasons for the noncompliance are not completely clear. Intrinsic abnormalities within the vessel wall and persistently abnormal blood flow patterns related to the palliative procedure may both play a role. These areas can be approached by percutaneous balloon dilatation or stenting, or by reoperation. An immediate favorable response can be achieved in more than 80% of cases; however, later stenosis and occlusion are common.

Likewise, the degree of enlargement that can be obtained in individual patients cannot be accurately predicted. However, it is correlated with the magnitude of increase in the Qp and PPA that can be brought about by the palliative procedure. When the central pulmonary arteries are small, palliative RV–pulmonary trunk and systemic–pulmonary arterial shunts can provide maximal stimulus for pulmonary arterial enlargement. There is no reason to believe that this growth is any greater than that occurring in the pulmonary arteries and unifocalized collaterals following reparative surgery. Although there are no definitive data, there is a suggestion that focal areas of stenosis may be reduced in the setting of the normal pulmonary blood flow patterns that attend reparative, as opposed to palliative, operations.

**Survival**

Early mortality (1-month) for palliative operations, as reported in the mid-1980s, was 17%, with most of the deaths occurring in very small (young) infants with severe hypoplasia of the pulmonary arteries or other kinds of pulmonary arterial anomalies (Fig. 38-84). It is likely that mortality would be lower in a more contemporary series, considering recent improvements in perioperative care. Recent reports from institutions that emphasize palliative procedures for TF support this. Survival for at least 12 years has been good (75%) in patients receiving a systemic–pulmonary arterial shunt and no further procedures (see Fig. 38-84). These patients were deemed unsuitable for repair in the era of 1967 to 1983. There is no way, it seems, to compare in a risk-adjusted manner this survival with that had these same patients undergone one-stage repair or received no treatment. Most of the deaths occurred within the first 3 postoperative months.

**Figure 38-84** Time-related survival in patients having tetralogy of Fallot (TF) with pulmonary atresia who underwent no interventional therapy (n = 22) and who underwent only a systemic–pulmonary arterial shunt with no further intervention (n = 49). (Analysis is based on cross-sectional follow-up of 244 patients having TF with pulmonary atresia seen at UAB between 1967 and July 1983; follow-up was in mid-1986.) A, Survival. Depiction is as in Fig. 38-47. B, Hazard function for death.

**Modes of Death**

Death early after operation is usually due to acute cardiac failure, whereas late postoperatively it is usually from hypoxia.

**Functional Status**

There is little information on functional status; however, because all palliated patients have a completely mixed circulation, function is reduced in this population.

**Results of No Interventional Therapy**

**Historical Perspective**

Because there has been increasing recognition over the past 20 years that surgical or other interventional therapy is beneficial to patients with all forms of TF with pulmonary atresia, unselected patient cohorts receiving no intervention no longer exist.

**Survival**

Survival for at least 12 years in 22 patients receiving no interventional treatment was 75%, with most of the deaths occurring within a year of presentation (see Fig. 38-84). These were patients considered unsuitable for complete repair and

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**PART VII Congenital Heart Disease**

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**Survival**

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too well oxygenated to require a systemic–pulmonary arterial shunt when they presented between 1967 and 1983. Most were older children who had fewer than 10 pulmonary arterial segments in continuity with central or hilar RPA or LPA. Again, there is no way to make a risk-adjusted comparison of their survival with that of patients who received interventional therapy. It is, however, almost a certainty that this patient group is highly selected and does not represent the newborn population with this malformation.

**Modes of Death**
Among the four patients who died within the follow-up period, one died of hypoxia and one of massive pulmonary hemorrhage. Mode of death was unknown in the other two.

**Functional Status**
Functional status of living patients was unknown, except in four. Two of these considered themselves to be fully active (NYHA class I), whereas one each was in NYHA classes II and III.

**After Staged Palliative Operations for Unifocalization**
Results of unifocalization operations, performed as a preliminary step before complete repair in patients who have TF with pulmonary atresia and considerably incomplete distribution of the RPA and LPA, are not yet clear (see Special Situations and Controversies later in this section). Some reports refer only to a few patients; others contain information that is insufficient for assessing results. The best estimate based on available reports is that as many as half, but often less, actually undergo repair. Of those who do, a substantial percentage, even a majority, will have $P_{RV/LV} > 0.67$.18,M23,P21,S3,W6,Y1

One exemplary report from the Hospital for Sick Children at Great Ormond Street, London,530 states that among 26 infants and children undergoing staged unifocalization operations of various types through a lateral thoracotomy, most commonly with interposition of prosthetic tubes, 4 (15%; CL 8%-26%) died in hospital postoperatively. Eleven of 20 patients restudied had 10 or fewer pulmonary artery segments connected to central pulmonary arteries before the unifocalization procedure, whereas at restudy 9 were in this state (Fig. 38-85). Patency of the unifocalizing anastomoses varied between 5% and 100%, depending on the type of procedure. Seven (27%; CL 17%-39%) of the original group of 26 patients either underwent complete repair or were suitable for it.

A large experience has also been reported from the Mayo Clinic.521 Among 38 patients undergoing unifocalization, hospital mortality was 5% (CL 2%-12%), similar to that at Great Ormond Street. Sixty-one percent (CL 51%-70%) underwent complete repair, a higher prevalence than at Great Ormond Street; however, there is insufficient information to determine whether patient groups were comparable. Among the 23 patients undergoing complete repair, 21 (91%; CL 81%-97%) survived; these represent 55% (CL 46%-65%) of the original group, a higher prevalence than at Great Ormond Street. Of the 23 patients undergoing repair, 13% had postrepair (OR) $P_{RV/LV} > 0.85$, and the mean value was 0.63.

Fifty-eight patients with TF and pulmonary atresia were reported from the Royal Children’s Hospital in Melbourne, Australia, 34 of whom had unifocalization procedures. It is difficult to determine the outcome in these 34 separately from that of the entire group. However, among the 58 patients, 27 (47%; CL 39%-54%) either died after preliminary procedures or were ultimately considered unsuitable for repair. Results were good among the 30 patients who underwent repair, with one early death and three late deaths. In 2 of the 30 patients, late VSD patch fenestration was required because of $P_{RV/LV} > 1$. Among 27 survivors who had undergone postoperative hemodynamic study, 5 (29%; CL 17%-45%) had postrepair $P_{RV/LV} < 0.7$ to 0.9.18

Thirty-four similar patients were reported from the Heart Institute of Japan at the Tokyo Women’s Medical Colleges.53 Twenty-two had incomplete distribution of one or both pulmonary arteries. Among 16 of the 34 patients who underwent final repair, postrepair $P_{RV/LV}$ ranged between 0.86 and 1.00, with a mean of 0.71. In four other patients, a perforated VSD patch was used because severe elevation of postrepair $P_{RV/LV}$ was predicted if complete repair was done. Clearly, some patients are correctable after a staged unifocalization operation and successfully undergo complete repair. For those whose repair is not successful, many factors may come into play, including natural attrition of healthy lung segments that occurs over time due to either vessel occlusion or pulmonary vascular obstructive disease, iatrogenic loss of lung segments directly related to palliative surgery, inability to create vascular continuity between lung segments due to scarring from prior palliative operations, and general cardiovascular complications related to chronic mixed circulation. Risk-adjusted, time-related probabilities of death and of importantly elevated postrepair $P_{RV/LV}$ are not yet available. As a general observation, however, the number of patients who achieve complete repair, and in particular who achieve complete repair with a $P_{RV/LV} < 0.5$, when the routine approach is initial palliation, appears to be substantially less than when the routine approach is early one-stage unifocalization and intracardiac repair.

![Figure 38-85](image)

Figure 38-85 Number of pulmonary arterial segments connected centrally before and after unifocalization in 20 patients. $P < .01$ for difference in means (vertical bar represents one standard deviation).
Key: CPA, Central pulmonary arteries; Preop, preoperative. (From Sullivan and colleagues.139)
INDICATIONS FOR OPERATION

Proper indications for operation, and their sequencing in the various subsets of patients who have TF with congenital pulmonary atresia, cannot be identified with certainty. This is not surprising, because the necessary patient-specific (risk-adjusted) comparisons of outcomes after no interventional treatment vs. the various types and combinations of procedures are not yet available. Therefore, indications can only be discussed in general terms for the major groups.

Confluent and Normally Distributing Right and Left Pulmonary Arteries and Patent Ductus Arteriosus

The highly unfavorable natural history of newborns in this subset, coupled with the fact that up to 95% survive complete repair in early life and 75% of those undergoing repair are alive and in good health for at least 10 years, indicates that complete repair as early in life as possible should be undertaken, almost always meaning neonatal repair. It must be emphasized, however, that equal outcomes appear to be achievable with neonatal shunting followed by later repair.

In those patients first seen after the neonatal period and usually living because of an AP anastomosis of some type, repair as soon as possible is likewise advisable.

Confluent, Nonconfluent, or Absent Pulmonary Arteries and Aortopulmonary Collaterals

Although the natural history is much more variable in this morphologic group, rarely do patients reach adult life in a healthy state if left untreated. Based on early surgical outcomes before 1990, it has been argued by some that surgical intervention is not indicated unless the individual is very symptomatic. More recent surgical results following both staged unifocalization and one-stage unifocalization and intracardiac repair demonstrate that repair with low PRV and PPA can be achieved in a high percentage of patients whether symptomatic or not. Although long-term outcome using these newer techniques is not yet known, the combination of low operative mortality and resultant low PRV suggests that outcomes over the long term are likely, in many cases, to be comparable with those achieved in the more favorable morphologic subset of patients with TF with pulmonary atresia and ductus-dependent, confluent, normally distributing pulmonary arteries. The most important principles in achieving results comparable with this more favorable group are incorporating blood supply from all lung segments into the central pulmonary artery system and achieving this in a timely manner such that the microvasculature in each lung segment remains undamaged.

SPECIAL SITUATIONS AND CONTROVERSIES

Alternatives to One-Stage Unifocalization and Intracardiac Repair

Situations may arise in the setting of large AP collaterals and true pulmonary artery arteriography abnormalities in which one-stage unifocalization and intracardiac repair is not indicated. One of these is described earlier in which one-stage unifocalization through a midline sternotomy is accomplished, but Rp is proven to be elevated, intracardiac repair is aborted, and unifocalized pulmonary arteries are connected to the systemic circulation by a shunt. It has been demonstrated that approximately 80% to 90% of patients with large AP collaterals can achieve complete bilateral unifocalization through a midline sternotomy in one procedure in early infancy, and of these, approximately two thirds can undergo intracardiac repair at the same time. Of the one third of patients who undergo complete unifocalization, but in whom Rp is too high to permit immediate intracardiac repair, most achieve repair within 2 years.

There are various reasons why midline complete unifocalization is contraindicated in approximately 10% to 20% of patients with major AP collaterals. The most important is a lack of pulmonary vascular “raw materials.” *Raw materials* are defined as the combination of true pulmonary arteries and major AP collaterals taken together. If both the true pulmonary artery system and AP collateral system are severely underdeveloped, an alternative approach should be considered. In the setting of poorly developed collaterals and absent true pulmonary arteries, a lateral thoracotomy with single lung unifocalization connected to an AP shunt may be the procedure of choice. This would be followed by a similar procedure on the contralateral lung at a future time. At a third procedure, a median sternotomy approach would be used to achieve vascular confluence between the left and right lungs, with later intracardiac repair and takedown of the previously placed shunts. Many techniques, using native tissue as well as prosthetic material, have been described to accomplish this type of reconstruction. In other situations the true central pulmonary arteries are present, confluent, but extremely hypoplastic in the mediastinum; however, they arborize to all or almost all of the lung segments, and communicate to the collateral system extensively within the lung parenchyma. In this situation, there are few if any isolated segments of lung that are supplied by only collateral flow. In this setting, creation in the neonatal or early infancy period of a central native tissue anastomosis between the ascending aorta and blind end of the pulmonary trunk can be performed to promote growth of the central system with communication to most lung segments. Following an interim period of central pulmonary artery growth, a second procedure with ligation of the dual-supply collateral sources at their systemic origin, and subsequent intracardiac repair and placement of an RV-to-pulmonary trunk conduit, can be accomplished. It should be emphasized that there is wide variability among experienced surgeons in the approach to TF with pulmonary atresia and large AP collaterals. Experienced surgical teams may prefer one of the alternative surgical approaches described earlier as their procedure of choice.

One common approach is to perform an initial procedure that provides increased blood flow and pressure into the confluent hypoplastic central artery system whenever there exists confluent central pulmonary arteries. This can be accomplished through many techniques—for example, by creating the central systemic–pulmonary tissue-to-tissue connection described earlier. Another approach is to create an RV-to-pulmonary trunk conduit using various tissue or synthetic prostheses, leaving the VSD open. A third approach is to create a prosthetic systemic–pulmonary arterial shunt to the pulmonary trunk or one of its branches.

There are several major concerns about all of these approaches when they are used unselectively as first-line
management, especially when the central pulmonary arteries have limited arborization. First, they leave collateral flow untouched, allowing for time for detrimental changes to occur in the lung vasculature supplied by collaterals, either in the form of overcirculation with development of pulmonary vascular obstructive changes or in the form of stenosis and occlusion leading to loss of lung segments. These negative effects inevitably lead to reduction in healthy lung cross-sectional area, increasing Rp. Another concern is that any surgical procedure is followed by scarring and adhesions, markedly reducing the surgeon’s ability to manipulate, reroute, and unifocalize collaterals at subsequent operations. A final concern is that following any shunt or conduit procedure, no matter how small the shunt or conduit is, the flow and pressure transmitted into the distal vasculature of the true pulmonary arteries are likely to be pathologically elevated when there is a very limited distal bed in association with reduced arborization.

Regardless of the specific surgical approach, most programs with substantial experience with this lesion believe that unifocalization of large collaterals is an important component of overall management; however, this view is not universally acknowledged.

**Percutaneous Balloon Dilatation of Stenoses of Right and Left Pulmonary Arteries**

Lock and colleagues first demonstrated the feasibility of this procedure. Intimal disruption with tearing of the media is one mechanism of dilatation, with the tears being subsequently filled in by scar tissue. In a multi-institutional study of a heterogeneous group of 156 patients, the largest subset of which had some form of pulmonary atresia, systolic pressure gradient across the stenosis was reduced only 10 to 14 mmHg, on average. A single-institution analysis of results in 135 patients indicated that about 60% of the procedures were satisfactory, defining this as a decrease of 20% or more of the peak pressure ratio between RV and aorta. Risk of death or other major complication was 1% to 3%. Patient age had no correlation with outcome. Effectiveness may be increased in the future by use of expandable stents.

Effectiveness of balloon dilatation can also be assessed by its effect on normalizing the flow distribution in the lungs as measured by nuclear lung perfusion scan, even if Ptv is not reduced. Following complete repair, normalization of homogenous flow to the lungs can be promoted by balloon dilatation of lobar and segmental stenoses within the unifocalized pulmonary artery system.

**Percutaneous Closure of Large Aortopulmonary Collateral Arteries**

Yamamoto first demonstrated the feasibility of this procedure in 1979 and Szarnicki and colleagues accomplished it by embolizing a Gianturco wire coil device in 1981. Subsequently, a number of studies have demonstrated the effectiveness and safety of percutaneous closure of large AP collateral arteries as long as proper precautions are taken. When wire coil uniformly coated with thrombogenic polyester strands is used, occlusion by thrombosis usually occurs within about 10 minutes. Other devices for promoting thrombosis have been used, including bucrylate adhesive and detachable silicone balloons. With wire coil and proper techniques, complete occlusion is achieved in about 70% of instances and subtotal occlusion in another 25%.

A large AP collateral artery should never be closed surgically or percutaneously when it connects end to end to distal pulmonary arteries, and thus is the sole or major source of blood flow to one or more pulmonary segments. Even when blood supply to a pulmonary segment occurs from dual sources, occlusion of the collateral source may not be indicated. For example, if upon review of detailed angiograms, it is determined that the collateral tissue can be used productively in surgical unifocalization, it should not be occluded prematurely. In this case, the collateral should be left open at catheterization and then ligated and divided during surgery, with its tissue used in the unifocalization and pulmonary artery augmentation process. When it is determined that tissue from a dual-supply collateral is not needed in surgical reconstruction and coil occlusion is being considered, it is prudent to occlude the vessel temporarily to be certain that its presence is not necessary for maintaining reasonable SaO2.

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**Section III  Tetralogy of Fallot with Absent Pulmonary Valve**

**DEFINITION**

Tetralogy of Fallot with absent pulmonary valve is a subset of TF in which the pathologic and clinical states are determined largely by the vestigial, severely hypoplastic, nonfunctioning pulmonary valve cusps at the RV–pulmonary trunk junction.

**HISTORICAL NOTE**

The first apparent description was by Royer and Wilson in 1908. A second example was not reported until Kurtz and colleagues described their case in 1927.

**MORPHOLOGY**

The pulmonary valve cusps are myxomatous nubbins of valvar tissue at the RV–pulmonary trunk junction. They are so severely hypoplastic that they are both nonfunctioning and only minimally stenotic. The pulmonary “anulus” is markedly narrow.

The VSD is large and similar to that in TF with pulmonary stenosis. The typical associated malalignment of the outlet septum contributes to infundibular narrowing. In addition, and perhaps related to the large flow, the RV outflow tract is often dilated and elongated. The sinus portion of the RV is hypertrophied and its volume large.

The pulmonary trunk and central portions of the right pulmonary artery and left pulmonary artery are often aneuysmally dilated at birth. This dilatation may extend into the hilar portions of these arteries, particularly the right, which then produces tracheobronchial compression. This often results in either hyperexpansion from air trapping or collapse of lobes or even an entire lung.
Beyond their hilar portions, pulmonary arteries are usually of normal size. Rarely are distal branches hypoplastic or hilar branching pattern abnormal.\textsuperscript{23} However, segmental distribution of the RPA and LPA is abnormal. Instead of single segmental arteries, tufts of arteries entwine and compress the interpulmonary bronchi in some patients. This pathology, when present, may in part account for symptoms of severe pulmonary dysfunction seen in some neonates and young infants.\textsuperscript{1,4}

There is controversy regarding the histopathology of the dilated pulmonary arteries in this syndrome. Arensman and colleagues report a normal pulmonary arterial wall in five of six children, with one child having a reduction in the amount of elastic tissue.\textsuperscript{5,19} Osman and colleagues have reported similar findings,\textsuperscript{8,10} but histopathologic abnormalities have been reported by others.\textsuperscript{11,25,9,9,11,19} Whatever the histology, physiologic studies indicate a marked decrease in RPA compliance in sick small babies.\textsuperscript{11,19}

Cause of massive dilatation of the pulmonary arteries in utero is unclear, but when there is severe pulmonary regurgitation and a large VSD, absence of ductal flow between the pulmonary trunk and aorta seems to be essential to intrauterine survival.\textsuperscript{26} Thus, a ductus arteriosus (or ligamentum) is almost always absent at autopsy\textsuperscript{22,25} unless the ductus connects to a pulmonary artery isolated from the pulmonary trunk. Thus, a likely cause of intrauterine dilatation of the pulmonary arteries is hemodynamic. The combination of a severely regurgitant valve in association with limited distal runoff from the pulmonary arteries from a combination of absence of a ductus and normally elevated intrauterine pulmonary vascular resistance (Rp) results in an exaggerated pulse pressure in the central pulmonary arteries.

There may be origin of the RPA or LPA from the ascending aorta,\textsuperscript{3} or a pulmonary artery (usually the left) may originate from a patent ductus arteriosus.\textsuperscript{26} When a pulmonary artery arises from a ductus, it is not aneurysmatically dilated, consistent with the hemodynamic explanation mentioned earlier.

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

TF with absent pulmonary valve generally results in both severe pulmonary regurgitation and a somewhat increased pulmonary blood flow (Qp). Narrowing at the pulmonary “anulus” in combination with the large VSD results in low PPA and similar peak pressures in both ventricles.\textsuperscript{11} Part of the pressure gradient between the RV and pulmonary trunk is related to large Qp (the \(Qp/Qs\) [ratio of Qp to systemic blood flow, \(Qs\)] is generally 1.5 to 2.0); part is related to mild “anular” and infundibular narrowing.

When pulmonary regurgitation is severe, \(Qp\) increased, and pulmonary arteries dilated and compressing the tracheobronchial tree, presentation may be in early infancy, often in the first weeks of life, with heart failure and severe intractable tracheobronchitis and respiratory distress responding poorly to routine medical measures. In the most severe cases, presentation may be immediate at birth, with the neonate \textit{in extremis} from an inability to breathe due to bronchial compression. Cyanosis is absent unless hypoxia develops from pulmonary complications. There is marked failure to thrive, and there may be low cardiac output, acidemia, and death.

In other cases, especially, but not always, when pulmonary regurgitation is less severe (in association with slightly more pulmonary stenosis, a near-normal \(Qp\), and less marked aneurysmal dilatation of the pulmonary arteries), presentation is later in life and less severe, usually confined to recurrent respiratory infections or mild heart failure. Notably, however, severity of the major morphologic and physiologic changes (size of the aneurysmal central pulmonary arteries and degree of pulmonary regurgitation) does not always predict severity of presentation. The important variable in critical neonatal presentation seems to be the inability of the airways to resist compression.

### Physical Examination

Severely affected infants are in considerable respiratory distress, with tachypnea, substernal retraction, and wheeze with rales and rhonchi audible throughout both lung fields. The heart is overactive and its rate rapid, pulse is of low volume, and there is obvious cardiomegaly, hepatomegaly, and raised venous pressure. There may be a precordial bulge. The infant is frail, cachectic, and febrile. On auscultation a to-and-fro murmur is audible along the left sternal edge, with the diastolic component often the more prominent. The second heart sound is single, and there may be an apical gallop.

### Chest Radiography

Chest radiography is distinctive, showing from birth marked supracardiac mediastinal widening caused by aneurysmal dilatation of central and hilar pulmonary arteries, usually equal on both sides although sometimes asymmetric, with relatively oligemic lung fields. Segmental or lobar atelectasis is common, and sometimes an entire lung is collapsed. Atelectatic portions of the lung may be overinflated (Fig. 38-86). Atelectasis is

\begin{figure}
\centering
\includegraphics[width=\textwidth]{image38-86.png}
\caption{Chest radiograph of a newborn having tetralogy of Fallot with absent pulmonary valve. Heart is markedly enlarged. Hyperlucency is seen at the right lower lung (R) and left upper lung (L), corresponding to areas of air trapping due to airway compressions by enlarged pulmonary arteries.}
\end{figure}
Volume rendering from a computed tomographic
angiography image of a 5-year-old boy born with tetralogy of Fallot with absent pulmonary valve. The pulmonary trunk (PT), right pulmo-

nary artery (R), and left pulmonary artery (L) are markedly enlarged compared with the aorta (Ao).

Figure 38-87

associated with mediastinal shift, and in cases with partial or complete lung collapse, with acquired dextrocardia. \(^{228}\) In severe cases, there is considerable cardiomegaly. The left atrium may be pushed downward \(^{62}\) and the carina splayed with compression of lower trachea and both main bronchi.

Other Studies

The ECG is typical for patients with TF. In patients who are asymptomatic or mildly symptomatic and do not require neonatal surgery, 2D echocardiography is diagnostic and definitive. In unstable neonates and infants, further studies are indicated once the patient is resuscitated and stabilized. Currently, CTA provides the most information, characterizing the pulmonary artery and airway abnormalities and their interrelationships (Fig. 38-87). In some institutions cardiac catheterization is also performed, or is performed as an alternative to CT.

NATURAL HISTORY

TF with absent pulmonary valve is present in about 5% of patients born with a large VSD and pulmonary stenosis. A high percentage (perhaps 50%) die in the first year of life if untreated, and most in the first few months of life, from respiratory distress caused by the massively dilated RPA and LPA compressing the tracheobronchial tree. \(^{219,3,34,91}\) Such critically ill infants also have heart failure associated with a left-to-right shunt, and the RV is markedly enlarged and systolic function reduced. \(^{191}\)

Patients who survive infancy, however, generally do well for 5 to 20 years, because RV outflow obstruction is only moderate and cyanosis mild or absent. \(^{59}\) They tend to become symptomatic ultimately and die of intractable RV failure as a result of its chronic pressure and volume overload.

TECHNIQUE OF OPERATION

When operation is delayed to age 3 to 5 years or older, the usual procedure is repair of the VSD and orthotopic insertion of an allograft aortic or pulmonary valve conduit (see “Establishing Right Ventricle–to–Pulmonary Artery Continuity” under Technique of Operation in Section II; see also Fig. 38-77). An end-to-end anastomosis is usually made between the distal end of the conduit and the divided pulmonary trunk. Usually no “roofing” of the right ventriculotomy is required, because the large infundibulum permits direct approximation.

In critically ill neonates and infants, a number of palliative operations have been used, but the corrective repair just described is preferred. In addition, however, elliptical strips of arterial wall are removed from the anterior and posterior aspects of the RPA, LPA, and pulmonary trunk bifurcation; the resultant defects are closed with a continuous suture before inserting the allograft valve cylinder. \(^{221,30,31,85}\) This takes pressure off the underlying tracheobronchial tree. Waterston \(^{65}\) and Godart and colleagues \(^{221}\) report good results in infants using extensive pulmonary arterioplasty, closure of the VSD, infundibular resection, and placement of a transanular patch; a valved conduit is not used. Often the large pulmonary trunk can be transected, shortened, and moved ventrally and caudally to roof the infundibulum and relieve pressure from the tracheal bifurcation. Nevertheless, in unstable neonates and infants, it can be anticipated that residual airway problems will almost certainly persist following repair, even when aggressive reduction pulmonary arterioplasty is performed; therefore, normalizing the hemodynamics as much as possible by using a valved conduit is strongly recommended.

An alternative surgical approach for patients with airway compression involves translocating the pulmonary arteries anterior to the aorta \(^{310}\) in addition to VSD closure, conduit placement, and reduction pulmonary arterioplasty.

SPECIAL FEATURES OF POSTOPERATIVE CARE

When operation is performed electively in a patient age 3 to 5 years or older, care is the same as that usually given to patients after intracardiac surgery.

When operation has been performed urgently in neonates, infants, or young children, severe respiratory distress has usually been present and the patient receiving intensive treatment. This treatment (see Indications for Operation later in this section) is intensified in the postoperative period and then slowly withdrawn as the patient’s condition improves.

RESULTS

Survival

Early (Hospital) Death

Historically, absent pulmonary valve syndrome has been associated with a high probability of hospital death after repair in young infants. \(^{219,55,214,216}\) In the current era emphasizing pul-
monary arterioplasty, Waterston and colleagues \(^{65}\) report 16%
mortality (CL 7%-29%) in infants, and Godart and colleagues\textsuperscript{\textcircled{52}} 20% mortality (CL 6%-41%) in infants and 3.7% (CL 0.5%-12%) in children older than 1 year. Mortality in infants is related in part to their poor preoperative condition and severe respiratory problems. When operation is undertaken beyond the first year of life, respiratory problems have usually resolved or not been present, and hospital mortality is low.

\textit{Time-Related Survival}

This, and the incremental risk factors for premature death, as well as other outcome events, are similar to those in other patients with TF whose repair includes insertion of an allograft valved conduit.

**INDICATIONS FOR OPERATION**

Help is urgently needed for small babies with this morphologic variant who present with severe respiratory distress. Some have unrelated congenital hypertrophic lobar emphysema, and a few have severe hypoplasia of the RPA and LPA; in either event, salvage may be impossible. In others an intense medical program is begun as soon as the condition is recognized. It includes managing the baby while continuously in a prone position on a hinged board placed in head-up position with maximal ventilator support.\textsuperscript{\textcircled{549}} This allows the pulmonary arteries to fall forward and away from the bronchi, particularly the RPA.\textsuperscript{\textcircled{549}} In the most severe cases, even this maneuver may be ineffective, and emergency sternotomy in the ICU may be required.\textsuperscript{\textcircled{5117}}

Most often, critically ill babies with this condition remain seriously ill even if ventilation is stabilized, and operation is required.

In patients with this morphology who require no special care in early life, repair is advised electively at 3 to 5 years of age.

Although various procedures have been recommended from time to time, that described under Technique of Operation is considered indicated. This is because alternative palliative procedures\textsuperscript{\textcircled{537,517,699}} have not resulted in improved long-term outcomes.

**Section IV  Tetralogy of Fallot with Flap Valve Ventricular Septal Defect**

**DEFINITION**

Tetralogy of Fallot with flap valve VSD is a subset of TF characterized by a thick fibrous flap hinged on the right side of a large VSD that narrows the interventricular communication and thereby limits right-to-left shunting.

**MORPHOLOGY**

The VSD is typical for TF. Its inferior margin either reaches the tricuspid anulus or is separated from it by a ridge of muscle (see “Ventricular Septal Defect” under Morphology in Section I). A fibrous flap is attached posteriorly to the aortic margin of the VSD, and its inferior margin may or may not be fused with the base and superior margin of the anterior tricuspid leaflet. Elsewhere, the flap is unattached, and it rarely plays any part in tricuspid valve function (Fig. 38-88). It can hinge freely toward the right, but its thickness and bulk prevent movement through the VSD into the LV. Therefore, in the presence of severe pulmonary stenosis and raised RV pressure, it virtually occludes the defect.\textsuperscript{\textcircled{N7}}

Pulmonary stenosis is typical of TF, but the infundibular component is made more evident by the severe degree of RV hypertrophy that involves chiefly the sinus portion of the ventricle because of high ventricular pressure. Thus, there may be a localized high-, intermediate-, or low-level infundibular stenosis, or the narrowing may be diffuse, and the valve may or may not be stenotic. Congenital pulmonary atresia is occasionally present and pulmonary artery branch origin stenosis may occur.

This subset of TF is one of a group of conditions in which there is an accessory fibrous flap or pouch or excrescence arising in the region of the atrioventricular valve apparatus and sometimes from the leaflets themselves.\textsuperscript{\textcircled{C14,88,31}} They have sometimes been called, usually erroneously, “aneurysms of the membranous septum.”\textsuperscript{\textcircled{N99}} Such anomalies associated with the tricuspid valve may prolapse into the RV outflow tract and pulmonary valve and cause severe pulmonary stenosis\textsuperscript{\textcircled{226,99,97}} a phenomenon that may occur in the absence of a VSD.\textsuperscript{\textcircled{356}} A mobile mass of fibrous tissue related to the tricuspid valve may prolapse through a VSD and produce LV outflow tract obstruction.\textsuperscript{\textcircled{M4,95,96}} This type of subaortic stenosis is easily corrected by operation.\textsuperscript{\textcircled{M38}} When transposition of the great arteries and VSD coexist, prolapse of accessory tricuspid valve tissue through the VSD results again in LV outflow tract obstruction, which is then subpulmonary (see Chapter 52).\textsuperscript{\textcircled{H32,R18}} In cases with congenitally corrected transposition of the great arteries (see Chapter 55), accessory valvar tissues of the right-sided, morphologically left atrioventricular valve may coexist; in this situation, the tendency is for the accessory tissue to prolapse in ball-valve fashion into the morphologically LV outflow tract, producing subpulmonary stenosis.\textsuperscript{\textcircled{L12}}

This may occur with or without an associated VSD. Such prolapsing accessory tissue is uncommon, but appears to be more often associated with the systemic venous rather than the pulmonary venous (systemic) atrioventricular valve. Maclean and colleagues\textsuperscript{\textcircled{M5}} and Levy and colleagues\textsuperscript{\textcircled{L12}} each report such a case in which subaortic obstruction resulted. Such a phenomenon may rarely coexist with TF.\textsuperscript{\textcircled{Y3}}

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Right-to-left shunting through the restricted VSD may be large enough to produce important cyanosis; usually it is not, so when the atrial septum is also intact, the patient is acyanotic or only mildly cyanotic despite severe pulmonary stenosis. When pulmonary stenosis is severe, the virtually intact ventricular septum results in severe RV hypertrophy on ECG (in contrast to the moderate RV hypertrophy typical of TF), near-normal splitting of the second heart sound (because Qp and PPA are maintained at a near-normal level), and a prominent a wave in the jugular venous pulse. Presentation is similar to that of pulmonary stenosis with intact ventricular septum (see Chapter 37). These features and the larger cardiac silhouette on chest radiograph than in classic TF make the diagnosis likely. Echocardiography defines the
intracardiac morphologic details and provides important information for estimating the degree of obstruction in the RV outflow tract and across the VSD. Cardiac catheterization is indicated only if there is a need to define pulmonary hemodynamics or morphology of the distal pulmonary arteries.

TECHNIQUE OF OPERATION

Intracardiac repair is similar to that for TF with pulmonary stenosis. However, severe RV hypertrophy makes relief of pulmonary stenosis more difficult and may also limit exposure of the VSD. Usually, wide excision of muscle is required. The fibrous flap is identified and excised unless it is atypical and part of the AV valve mechanism, which is rare. Then, its herniation into the VSD is simply reduced and the VSD repaired in the usual way. It may be necessary to attach the herniated portion to the tricuspid valve to prevent it from obstructing the RV outflow tract.

RESULTS

Hospital mortality after repair has, in the past, been relatively high. Four (24%; CL 12%-39%) of 17 patients in the GLH and UAB experiences died in hospital after repair (Table 38-15). One UAB death occurred in association with anomalous origin of the left main coronary artery from the pulmonary trunk and one GLH death in association with pulmonary atresia and a large fistulous communication between the left coronary artery and RV. Severe RV hypertrophy appears to be the primary incremental risk factor, and improved myocardial management may neutralize it. Late results in hospital survivors have been good.

INDICATIONS FOR OPERATION

Palliative shunting operations are inappropriate because they do not relieve the progressive RV pressure overload. Similarly, blind (or open) pulmonary valvotomy could result in excessive shunting from left to right through the VSD. One-stage repair is the proper treatment and is advisable when diagnosis is made.

Section V  Double-Chamber Right Ventricle (Low-Lying Infundibular Pulmonary Stenosis with or without Ventricular Septal Defect)

DEFINITION

Low-lying infundibular pulmonary stenosis, so-called double-chamber RV, is a type of intraventricular stenosis that clearly separates the sinus (inflow) portion of the RV...
from a typically, but not always, large and thin-walled infundibulum. It is usually but not always associated with a small or moderate-sized and occasionally large VSD, which is usually juxtatricuspid in position, but it may have a narrow bar of muscle between it and the valve anulus. Also included in this section are similar cases with an intact ventricular septum, because they may be considered part of this overall spectrum. In many cases with intact ventricular septum, a VSD was present earlier in life, with spontaneous closure occurring because of the same process of hypertrophy and fibrosis that contributes to the RV obstruction.

Low-lying infundibular pulmonary stenosis may coexist with otherwise typical TF (see Section I). Low-lying infundibular pulmonary stenosis may also coexist with double outlet RV (see Chapter 53).

HISTORICAL NOTE

Like many cardiac anomalies, low-lying infundibular pulmonary stenosis was encountered by cardiac surgeons during the mid- and late 1950s, before the malformation was well recognized by morphologists as a discrete entity. However, case 1 in the 1933 report by Eakin and Abbott and cases 1 and 3 in the 1959 report by Blount and colleagues were examples of the entity, and Grant and colleagues clearly discussed this malformation in their 1961 publication. However, credit for the first description of the entity is generally given to Tsifutis and colleagues, who published their paper in the same year.

MORPHOLOGY

The important morphologic characteristics relate to the infundibulum, the ventricular septum, and the LV outflow tract. There can be substantial variation in all three areas.

The classic morphologic finding is the large thin-walled infundibular chamber, which gives rise to the appellation “two-chambered RV.” The pulmonary valve and “anulus” are normal sized or large, as is the pulmonary trunk, and the right and left pulmonary arteries are virtually always large and free of stenoses or distributional anomalies. In some variations the infundibular chamber is not large. There is infundibular hypoplasia, and the anomalous muscle bundles arise from the infundibular septum a little more distally (downstream).

The stenosis is formed by accessory bulky muscle bundles concentrated at the junction of the sinus portion of the RV and infundibulum. In the most florid form, there is a bulky trabeculated muscular shelf lying almost in a coronal plane that separates a large, thin-walled infundibular chamber from a hypertrophied, thick-walled sinus portion containing the tricuspid valve apparatus and VSD. The shelf is often formed by medial and lateral anomalous muscle bundles that join the anterior free wall about halfway between ventricular apex and base. However, the shelf may be, in part, hypertrophied septoparietal bands. The stenotic ostium is usually centrally located, and in older patients it is surrounded by a bulky fibrous collar that further increases stenosis. There may be more than one ostium. This obstructing muscular diaphragm inserts so far inferiorly on the free wall that it lies nearly in a coronal plane, which predisposes the ventricular incision to be in the infundibular chamber. The muscular band on the right side usually seems to be the parietal extension of the infundibular septum.

The VSD is usually small or moderate in size, although it may be large or it may have closed, identified only by a fibrous dimple. It is usually perimembranous and juxtatricuspid and is overhung by thick tricuspid chordae, but it may have a bar of muscle at its posterior margin rather than abutting the tricuspid anulus. Importantly, the VSD, regardless of its size, does not demonstrate the characteristics of the VSD in the various forms of TF. Specifically, the infundibular septum is not anteriorly malaligned.

In about 5% of cases, important and otherwise typical subaortic stenosis (see Section II of Chapter 47) coexists with low-lying infundibular pulmonary stenosis. Why this relatively large proportion exists is unknown. A unifying theory, yet to be fully characterized, is the tendency for many of these
patients to produce exuberant endocardial fibrosis that importantly contributes to the RV obstruction, closes or narrows the VSD, and extends across the VSD into the LV outflow tract, causing the subaortic stenosis (personal observation, Frank Hanley).

Other morphologic variations rarely exist. These include combined infundibular and valvar pulmonary stenosis with membranous or muscular VSD, or isolated valvar pulmonary stenosis with membranous or muscular VSD. It is likely that these cases represent coincidental occurrence of unrelated defects.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Patients usually present with mild cyanosis in the midpoint of the first decade of life, but they may present in the second decade or even in adult life. Increasingly, patients are diagnosed earlier in life, usually between 1 and 3 years of age, with clear evidence of mid-cavity RV obstruction. On examination the most striking feature is the loud systolic murmur, often grade 6 (heard with the stethoscope off the chest wall). Chest radiography is not specific, but the pulmonary trunk shadow along the upper left cardiac border is usually prominent.

Diagnosis is made by 2D echocardiography, which defines the typical mid-cavity RV obstruction, the VSD, if present, and the subaortic obstruction, if present (Figs. 38-89 and 38-90).

**NATURAL HISTORY**

Natural history can only be surmised. Because in some cases only a dimple remains in the perimembranous area at operation, the VSD presumably has a tendency to close spontaneously. Because few patients with this entity present in infancy, it is not surprising that the stenosis has been demonstrated to increase gradually in severity as the child grows.\(^\text{C25,D5,F11,H8,H9}\)

The progression can lead to complete infundibular atresia.\(^\text{P10}\)

Cyanosis is also presumed to be an acquired event. If a VSD is present, it will shunt left to right early in life before the RV obstruction progresses; no cyanosis will be present. If the VSD remains open and the RV obstruction progresses such that the VSD shunts right to left, cyanosis will develop.

**TECHNIQUE OF OPERATION**

Preparations for CPB, median sternotomy, and placement of stay sutures and purse-string sutures are as usual (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Examination of the heart may confirm presence of a characteristically large, thin-walled infundibular chamber, but this is not always evident externally. Usually a marginal branch of the right coronary artery courses over the underlying infundibular stenosis and should be preserved if the ventriculotomy approach to repair is used.

CPB is established, employing direct caval cannulation or caval cannulation via the right atrium (see Fig. 2-22 in Chapter 2). The left side is vented using a catheter placed through the right upper pulmonary vein. Mild hypothermia is typically used. The aortic root infusion catheter is inserted, the aorta clamped, and cold cardioplegia given (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).

When the infundibulum is large and thin walled, repair can be through a transverse low infundibular incision or a right atrial incision.\(^\text{P10,P9}\)

With the infundibular incision the view is interesting and unique, because the interior of the smooth thin-walled infundibulum is exposed, and in its depth inferiorly is seen the ostium of the low-lying infundibular stenosis. A moment of carelessness could lead to misidentifying it as the VSD,\(^\text{C23,L21}\) but further examination confirms it as the infundibulum because the tricuspid valve apparatus, lying entirely in the sinus portion of the RV, cannot be visualized.

Incision is made in the obstructing muscle mass anteriorly and to the left, which allows visualization of the interior of the sinus portion (proximal chamber) of the RV, tricuspid apparatus, and VSD. The part of the obstructing muscle mass that arches up and to the right from the infundibular septum (probably the parietal extension of the infundibular septum)
is dissected and largely resected. Before resecting the left side of the obstructive muscular collar, which is usually in part moderator band, location of the tricuspid papillary muscles is visualized, and they are protected as the left-sided heavy muscular band is dissected and largely amputated. There is then a wide exposure of the sinus portion of the RV and VSD. Although the VSD is typically small, it is repaired with a patch, just as for other VSDs in this area. If the VSD is small and overhung by thick chordae, a completely interrupted suture technique is preferable. The ventriculotomy is closed either primarily or with a narrow patch. The remainder of the procedure is completed as usual.

From the right atrial approach (Fig. 38-91, A), the obstructing muscle is located at its insertion anteriorly at the region of the moderator band. The anterior papillary muscle of the tricuspid valve is retracted. Relief of the muscular narrowing is accomplished much as for the atrial approach to classic TF, but exposure is easier because the obstruction is less anteriorly placed and more proximal in the RV. After muscle resection, the VSD, if present, is closed with a patch in a fashion similar to patch closure for isolated VSD by way of the right atrium (Fig. 38-91, B) (see Technique of Operation in Section I of Chapter 35). The right atriotomy is closed directly, and remainder of the procedure is completed as usual.

When the infundibular chamber is more hypoplastic, a vertical ventriculotomy and infundibular patching should probably be used routinely.

When associated subaortic obstruction is present, it should be addressed. If the patient has a large VSD, the fibrous tissue causing the obstruction in the LV outflow tract can often be visualized through the VSD and resected before closing the VSD. When the VSD is small or absent, the subaortic obstruction is addressed by way of an aortotomy, in a similar fashion to isolated subaortic membrane (see Chapter 47).

The morphology is so well suited to repair that usually no gradient is present after repair, nor are murmurs present postoperatively.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Postoperative care is as usual (see Chapter 5).

**RESULTS**

**Early (Hospital) Death**

Hospital mortality after repair should approach zero.\textsuperscript{1,5}

**Time-Related Survival**

Long-term results are excellent, with no late deaths and all patients asymptomatic.\textsuperscript{1,16,75} In the University of Michigan experience, among 20 patients followed for at least 20 years, 85% were in NYHA functional class I and only one (5%) had hemodynamically important impairment of cardiac function.\textsuperscript{63} Similarly, in the study by Telagh and colleagues,\textsuperscript{75} there was no functional or hemodynamic impairment at follow-up extending to 11 years.

**INDICATIONS FOR OPERATION**

Diagnosis of the malformation is an indication for elective repair.
Chapter 38 Ventricular Septal Defect with Pulmonary Stenosis or Atresia

A few patients with infundibular pulmonary stenosis, with or without a VSD, do not meet the criteria for diagnosis of TF or low-lying infundibular stenosis. These are included in this section.

Some of these malformations may be similar in origin to low-lying infundibular pulmonary stenosis, except that there is infundibular hypoplasia and the anomalous muscle bundles arise from the infundibular septum a little more distally (downstream). Other examples in this subset probably represent instances in which the only discernible malformation at birth is a large VSD. With time, however, the parietal extension of the infundibular septum hypertrophies out of proportion to the rest of the right ventricle, and in some cases the VSD narrows or closes.\textsuperscript{525} Finally, occasionally valvar and infundibular stenosis may both coexist along with a VSD, in the absence of the typical morphology of TF.

Diagnosis, natural history, and techniques of repair are similar to those for low-lying infundibular pulmonary stenosis, except that a vertical ventriculotomy and infundibular patching should probably be used routinely. It is important to recognize the infundibular stenosis at time of repair of the VSD, because otherwise it can persist or worsen and reoperation may be required for relief.\textsuperscript{D19,M11}

Figure 38-91 Low-lying infundibular pulmonary stenosis. A, Inset Usual high right atriotomy is made as for right atrial approach to repair tetralogy of Fallot (TF). Anomalous muscle band arises from moderator band and is downstream from ventricular septal defect (VSD). Proposed incisions for resecting obstructing anomalous bands are shown (dashed lines). B, After relief of the obstruction, VSD is closed in same manner as for TF. Key: RAA, Right atrial appendage; SVC, superior vena cava.
Indications for operation are the same as for low-lying infundibular pulmonary stenosis.

Surprisingly, isolated valvar pulmonary stenosis with VSD is only rarely reported in the literature. It does exist but is not common (and may well be underreported), and may merely represent chance coexistence of these two malformations. The combination is an indication for elective operation by the techniques described earlier.

### Values of Variables Used in Nomograms

#### Values in Fig. 38-49

Specific values entered into the multivariable equation were hematocrit 50%, no more than one previous palliative operation, no Potts anastomosis, no previous direct approach to RV outlet obstruction, no multiple VSDs, no dextrocardia, no absence of unbranched hilar portion of one pulmonary artery, average prevalence of transanular patch placement (31%), and postrepair (OR) $P_{RV/LV}$ of 0.55. For age 6 months, 12 months, 24 months, and 48 months, body surface area was entered as $0.345 \, m^2$, $0.4125 \, m^2$, $0.5025 \, m^2$, and $0.630 \, m^2$, respectively.

#### Values in Fig. 38-51

Specific values entered into the multivariable equation were hematocrit 50%, no more than one previous palliative operation, no Potts anastomosis, no previous direct approach to RV outlet obstruction, no multiple VSDs, no dextrocardia, no absence of unbranched hilar portion of one pulmonary artery, date of operation 1988, and postrepair (OR) $P_{RV/LV}$ of 0.6.

#### Values in Fig. 38-53

Specific values entered into the multivariable equation were age 6 months at repair and postrepair (ICU) $P_{RV/LV}$ of 0.45.

### Relation of Body Surface Area to Age

#### Figure 38B-1

Nomogram of equation relating body surface area to age in patients with tetralogy of Fallot. Equation is based on data from 1533 patients with tetralogy of Fallot and pulmonary stenosis or atresia (UAB experience). They ranged in age from 1 day to 57 years, and in body surface area from 0.12 to 2.3 $m^2$. The equation is as follows:

$$
\ln(BSA) = 4.504 + 27.82 \cdot a^3 - 45.51 \cdot a^4 + 26.39 \cdot a^5 - 5.238 \cdot a^6
$$

where $a = \ln[\ln(age+9)]$, age is in months, $\ln$ is the natural logarithm (double logarithmic transformation), and $\ln[BSA(m^2)]$ is the natural logarithm of body surface area.
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A


B


Chapter 38 Ventricular Septal Defect with Pulmonary Stenosis or Atresia


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H


PART VII Congenital Heart Disease


I


J


K


L


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PART VII Congenital Heart Disease

Q


Y


# Pulmonary Stenosis and Intact Ventricular Septum

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DEFINITION

Pulmonary stenosis and intact ventricular septum is a form of right ventricular outflow tract obstruction in which the stenosis can be valvar, infundibular, or both. Isolated infundibular stenosis is unusual. This chapter concerns primarily valvar pulmonary stenosis, with or without infundibular stenosis. When neonates present with the most severe form of this defect, the term neonatal critical pulmonary stenosis is used. When patients present beyond the neonatal period or in early infancy, the term pulmonary stenosis is used.

HISTORICAL NOTE

In 1913, as described by Dumont, Doyen first attempted to surgically relieve pulmonary stenosis in a 20-year-old woman who, in retrospect, is thought to have had infundibular obstruction. Thirty-five years later, in December 1948, Sellors performed a successful closed transventricular instrumental pulmonary valvotomy, closely following Doyen’s technique. Brock performed three successful closed valvotomies in early 1948. These patients probably all had tetralogy of Fallot. Blalock and Kieffer applied this procedure to patients with pulmonary stenosis and intact ventricular septum soon thereafter, reporting 19 patients and two hospital deaths. Swan and colleagues surgically corrected pulmonary stenosis and intact ventricular septum by an open technique in about 1953, approaching the valve through a pulmonary arteriotomy during circulatory arrest, with the patient rendered moderately hypothermic by surface cooling. Other techniques evolved.

Kirklin’s experiences with closed valvotomy at Mayo Clinic led to an appreciation of the importance of acquired infundibular obstruction caused by hypertrophy, and the need for a pump-oxygenator system that would allow relief by open operation. When cardiopulmonary bypass (CPB) became available in 1955, most surgeons began to use it to support patients during open valvotomy.

Surgical treatment of pulmonary stenosis was challenged in 1982 when Kan and colleagues reported successful percutaneous balloon valvuloplasty. This method of therapy is now applied to patients of all ages, and is, with the important exception of the morphologic variant called pulmonary valvar dysplasia, the initial procedure of choice.

AGE CONSIDERATIONS

Symptoms, signs, and treatment of valvar pulmonary stenosis in the neonate presenting in severe distress during the first few days of life have long been recognized as different from those of patients presenting later in life. Interrelationships exist between neonatal valvar pulmonary stenosis and intact ventricular septum and pulmonary atresia and intact ventricular septum. Now that percutaneous techniques are used for therapy, different groups of physicians, as a rule, care for valvar pulmonary stenosis in patients presenting for treatment for the first time as adults and those presenting in early childhood. For all these reasons, this subject seems best approached according to age categories.

Section I Critical Valvar Pulmonary Stenosis in Neonates

MORPHOLOGY

Pulmonary Valve

The pulmonary valve is commonly a uniform fibrous cone with a circular, central, and stenotic orifice and two or three ridges on its pulmonary arterial side. These ridges radiate from the central orifice to the periphery and outline two or three cusps that correspond to pulmonary sinuses of Valsalva, which are usually well formed. The valvar diaphragm is considerably thinner than normal cusp tissue, particularly around the ostium, but it is mobile. Thickening is produced by an increase in myxomatous tissue. Obstruction may be due to thickened, shortened, and rigid cusp tissue with little or no commissural fusion, known as pulmonary valvar dysplasia. This was described in 1969 by Koretzky, Edwards, and colleagues and further characterized by Stamm, Anderson, and colleagues. The right ventricular–pulmonary trunk junction (anulus) may be narrowed and the pulmonary trunk wall pulled inward or tethered at the site of commissural cusp attachment. The valve is often bicuspid. Although this condition may cause critical pulmonary stenosis in neonates, stenosis is typically moderate, a finding that is characteristic of Noonan syndrome.

Pulmonary Arteries

Although it has been reported that in about 50% of neonates with critical pulmonary stenosis, right and left pulmonary arteries appear to be moderately or severely hypoplastic.

Figure 39-1 Specimen from a neonate with congenital valvar pulmonary stenosis and intact ventricular septum viewed through open, dilated pulmonary trunk. Fibrous cone with its central, very stenotic orifice; well-formed sinuses of Valsalva; and potential three-cusp valve structure are typical. Moderate right ventricular hypoplasia coexists (see Fig. 39-3).
Rarely, the right ventricular (RV) cavity is severely reduced in size. More commonly, mild or moderate reduction is present (Fig. 39-2). Reduction in cavity size relates in part to the amount of concentric RV hypertrophy produced by the RV outflow tract (RVOT) obstruction (Fig. 39-3).

Histologic appearance of the RV varies. Concentric RV hypertrophy is characterized by increased muscle cell size and diffuse fibrosis. When imaged, this has not been confirmed by other studies (Table 39-1). As a rule, the appearance of pulmonary arterial hypoplasia is probably secondary to low pulmonary blood flow, because the pulmonary arteries are usually normal in size within a few years in those who survive interventional treatment.2

### Right Ventricle

The right atrium is usually large. There is generally at least a patent foramen ovale, and right-to-left shunting across it is a major contributor to arterial desaturation exhibited by many of these neonates.

### Right Ventricular Coronary Artery Fistulae

About 10% of neonates with critical pulmonary stenosis have RV sinusoids, but only 2% have RV coronary arterial fistulae. RV-dependent coronary circulation in such hearts is rare.

### Morphologic Correlates

RV cavity size and tricuspid valve dimension are not highly correlated in this condition, but mild to moderate hypoplasia is the rule in both locations.12 This is in contrast to pulmonary atresia and intact ventricular septum (see Morphology in Chapter 40), suggesting that reduction in RV cavity size in critical pulmonary stenosis is secondary to RV hypertrophy and thickening from outflow obstruction, rather than from genetic or developmentally induced hypoplasia. This is in harmony with the hypothesis that critical pulmonary stenosis develops relatively late in fetal life, in contrast to some types of pulmonary atresia.13

#### Table 39-1  Critical Pulmonary Stenosis in Neonates: Relationship of Moderate or Severe Hypoplasia of Right and Left Pulmonary Arteries to Right Ventricular Cavity Size

<table>
<thead>
<tr>
<th>RV Cavity Sizea</th>
<th>n</th>
<th>Moderate or Severe RPA and LPA Hypoplasiaa</th>
<th>% of n</th>
</tr>
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<tbody>
<tr>
<td>Enlarged (1-5)</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Normal (0)</td>
<td>37</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Mildly reduced</td>
<td>30</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Moderately reduced</td>
<td>11</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Severely reduced</td>
<td>3</td>
<td>1</td>
<td>33</td>
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</table>

Subtotal 84 4 4
Unknown 17 0
TOTAL 101 3

Data from Hanley and colleagues.15

1Numbers in parentheses refer to grading of RV cavity size.
2Degree of hypoplasia of the pulmonary arteries was graded as 0 to −5. Hypoplasia was considered moderate or severe when graded as −3, −4, or −5.
3Grading scheme was validated by comparison with actual measurements transformed to z values in patients for whom they were available.
4Key: LPA, Left pulmonary artery; RPA, right pulmonary artery; RV, right ventricle.

#### Figure 39-2  Cumulative frequency distribution of right ventricular (RV) cavity size in neonates with congenital pulmonary stenosis or atresia and intact ventricular septum (see Chapter 6 for details of construction). Zero represents normal RV cavity size, −5 represents severe RV hypoplasia, and +5 represents massive RV enlargement. The figure is based on data for 247 neonates. Only data for 82 patients with pulmonary stenosis and 136 with pulmonary atresia permitted an estimate of RV cavity size. Key: PA, Pulmonary atresia; PS, pulmonary stenosis; RV, right ventricular. (From Hanley and colleagues.)

#### Table 39-2  Total Pulmonary Artery and Right Ventricular Cavity Size in Neonates With Critical Pulmonary Stenosis or Atresia

<table>
<thead>
<tr>
<th>PA/PS</th>
<th>RV Cavity Size</th>
<th>Percent ≤ Size</th>
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<tbody>
<tr>
<td>10</td>
<td>−3</td>
<td>−5</td>
</tr>
<tr>
<td>25</td>
<td>−2</td>
<td>−4</td>
</tr>
<tr>
<td>50</td>
<td>−1</td>
<td>−4</td>
</tr>
<tr>
<td>75</td>
<td>0</td>
<td>−2</td>
</tr>
<tr>
<td>90</td>
<td>0</td>
<td>−1</td>
</tr>
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Figure 39-9-3  Ratios of RV sinusoids to RV cavity size in neonates with congenital pulmonary stenosis or atresia and intact ventricular septum (see Chapter 6 for details of construction).
Coexisting Cardiac Conditions

Coexisting cardiac conditions are uncommon. Ebstein malformation, which occurs in about 5% of patients with pulmonary atresia and intact ventricular septum, occurs in about 1% of those with critical pulmonary stenosis.112

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Neonates presenting with critical pulmonary stenosis and intact ventricular septum are usually critically ill, irritable, tachypneic, and severely hypoxic from right-to-left shunting at the atrial level. They usually present for treatment within a few days after birth and are generally of normal birth weight.112 When the atrial septum is intact, which is uncommon, cyanosis is absent.

Tachycardia and severity of heart failure often make auscultatory findings nondiagnostic. Physical findings of tricuspid regurgitation may be present. Chest radiograph usually shows a normal or somewhat enlarged heart. Pulmonary stenosis with hypoplastic RV is associated with less electrocardiographic (ECG) evidence of RV hypertrophy than expected.126 Diminished RV potentials are due to smallness of the RV cavity rather than to diminished muscle mass.

In a critically ill neonate with clear lung fields and a large cardiac silhouette, two-dimensional echocardiography provides near-certain diagnosis. The thick stenotic pulmonary valve is visualized, the RV cavity is seen, and size and cusp thickness of the tricuspid valve can be determined. Additionally, the pulmonary artery branch diameter can be accurately estimated, and color Doppler imaging can suggest presence of coronary artery anomalies such as RV-to-coronary artery fistulae.

Cardiac catheterization is indicated in essentially all cases for both diagnostic reasons (e.g., to define coronary artery anomalies) and therapy, because balloon pulmonary valvotomy is currently the treatment of choice. Cardiac catheterization usually shows peak RV pressure higher than that in the left ventricle (LV) or systemic arteries. Rarely, and in the presence of severe heart failure, peak RV pressure is less than that in the systemic circulation, despite severe valvar stenosis.

Cineangiography provides precise information regarding site of stenosis, size of RV cavity and infundibulum, presence
or absence of tricuspid regurgitation, morphology of the pulmonary trunk and right and left pulmonary arteries, and presence or absence of RV-to-coronary artery fistulae (Fig. 39-5). The tricuspid valve is competent in about 10% of patients, and in the other 90% it is moderately or severely regurgitant (Hanley and colleagues and the Congenital Heart Surgeons Society; personal communication; 1992). Regurgitation, which is not well correlated with degree of RV hypertension (Fig. 39-6), is probably a manifestation of RV failure.

Currently, magnetic resonance and computed tomographic imaging are not routinely used in neonatal critical pulmonary stenosis, simply because these studies provide little added value to echocardiography and the mandatory cardiac catheterization. Recently, fetal echocardiography has been used to predict the postnatal fate of patients with critical pulmonary stenosis.

**Figure 39-4** Cumulative frequency distribution of diameter of tricuspid valve, expressed as z value, in neonates with congenital pulmonary stenosis or atresia and intact ventricular septum. The z value of zero represents mean normal value, −2 represents 2 standard deviations (SD) below mean normal size, and +2 represents 2 SD above mean normal size. Figure is based on data for 247 neonates. Only data for 44 patients with pulmonary stenosis and 77 with pulmonary atresia permitted an estimate of tricuspid valve size. Key: PA, Pulmonary atresia; PS, pulmonary stenosis. (From Hanley and colleagues.)

<table>
<thead>
<tr>
<th>Percent at or below stated z value</th>
<th>PS (n=44)</th>
<th>PA (n=77)</th>
</tr>
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<tr>
<td>10</td>
<td>−2.6</td>
<td>−4.9</td>
</tr>
<tr>
<td>25</td>
<td>−1.9</td>
<td>−4.0</td>
</tr>
<tr>
<td>50</td>
<td>−1.0</td>
<td>−2.2</td>
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<tr>
<td>75</td>
<td>0.4</td>
<td>−0.4</td>
</tr>
<tr>
<td>90</td>
<td>1.3</td>
<td>1.2</td>
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**Figure 39-5** Cineangiogram of a neonate with extreme (pinhole) pulmonary stenosis and moderately severe right ventricular (RV) hypoplasia. **A**, Right anterior oblique view in diastole to show maximal degree of filling of apical half of sinus portion that is mainly occupied by thick muscular trabeculations. RV infundibulum, pulmonary trunk, and pulmonary artery branches are of good size. Left anterior descending coronary artery (arrow) is filling retrogradely from RV. There is no tricuspid regurgitation. **B**, Left anterior oblique view in systole demonstrates thickened domed pulmonary valve. A tiny central jet (arrow) is barely visible, but flow is sufficient to fill the pulmonary arteries well after several cardiac cycles.

**Figure 39-6** Scattergram illustrating lack of relationship between severity of tricuspid valve regurgitation and right ventricular peak pressure in neonates with critical pulmonary stenosis. (From Hanley and colleagues.)

![Graph showing cumulative frequency distribution of tricuspid valve diameter.](image1)

![Graph showing relationship between tricuspid valve regurgitation and right ventricular peak pressure.](image2)
Chapter 39  Pulmonary Stenosis and Intact Ventricular Septum

pulmonary stenosis. The aim is to predict whether a two- or single-ventricle circulation will result following postnatal therapy. These techniques are more applicable to pulmonary atresia and intact ventricular septum but also have a role, albeit a lesser one, in pulmonary stenosis. Morphologic and physiologic characteristics identified at fetal echocardiographic interrogation can accurately predict the fate of the circulation following birth. These data can be used for planning postnatal therapy, parental counseling, and possibly prenatal intervention.

**NATURAL HISTORY**

Presentation is usually within the first 2 weeks, and mean age at operation in the series at Toronto Hospital for Sick Children was 3.9 days. Most neonates in whom severe hypoxia develops, with or without heart failure, die without treatment, although some may live for a few months.

**TECHNIQUE OF OPERATION**

**Percutaneous Balloon Valvotomy**

The technique of percutaneous balloon valvotomy has been described in detail. Briefly, a guidewire is introduced via the femoral vein across the pulmonary valve and maneuvered through the ductus arteriosus into the descending aorta. A wire-guided balloon 1.2 to 1.3 times the measured size of the anulus is placed across the pulmonary anulus. The balloon is inflated rapidly two or three times. Several case reports of fetal intervention for critical pulmonary stenosis using percutaneous balloon valvotomy have been reported, documenting technical success. Efficacy of the procedure has not yet been documented.

**Open Pulmonary Valvotomy Using Cardiopulmonary Bypass**

When percutaneous balloon valvotomy has not been used or is unsuccessful, open pulmonary valvotomy using CPB is recommended. The surgical procedures of closed pulmonary valvotomy and open valvotomy with simple inflow stasis have also given good results; however, they are not currently recommended in most circumstances. Operation may be performed using one or two venous cannulae and CPB with mild (32°C-34°C) or moderate (25°C-28°C) hypothermia as described in Chapter 2. A single venous cannula and mild hypothermia are chosen when a simple patent foramen ovale is present that will not be closed; two venous cannulae and moderate hypothermia are chosen when an atrial septal defect (ASD) will be closed.

Before establishing CPB, the ductus arteriosus is dissected and ligated immediately after initiating CPB. After establishing CPB and hypothermia, the aorta is clamped and cold cardioplegia administered (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Alternatively, operation may be done on the beating heart, without aortic clamping.

If two venous cannulae are used and an ASD is to be repaired, a small-caliber vent can be placed into the left side of the heart through a purse-string suture in the right pulmonary vein. Alternatively, the right atrium is opened through a small oblique incision, and a pump sump-sucker is placed across the foramen ovale and into the left atrium.

The pulmonary trunk is opened through a vertical incision, and fine stay sutures are placed on the edge of the incision for exposure. Two or three fused commissures can usually be seen, and these are opened with a knife, extending the incisions to the pulmonary valve annulus. Because regurgitation is of less concern than residual narrowing, the incisions may be tailored to some extent to ensure that the valve has a wide opening. Portions of the valve are excised only when other methods fail to achieve a wide opening. Less commonly, the valve is dysplastic with three fully formed commissures and markedly thickened, even bulky, cusps. In this case, cusp debulking by partial resection of tissue is necessary to relieve obstruction. Rarely in neonates is there need to resect RV infundibular musculature. The pulmonary trunk is closed with one row of continuous 7-0 polypropylene suture. Usually, operation requires less than 15 minutes, and the aortic clamp, if used, is simply removed and de-airing accomplished. Remainder of the operation is completed in the usual manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

A patent foramen ovale, if present, is usually left open because the RV is very hypertrophied. The patient will benefit from allowing right-to-left atrial shunting until the RV remodels. If an ASD coexists, the decision is more complex because it is likely the patient will eventually develop significant left-to-right shunting through it once RV remodeling is complete. Judgment must be used in this setting. If there is concern that RV size and hypertrophy will result in perioperative RV failure, the ASD should be left open; it can be addressed at a later time once the RV has remodeled. If the RV is judged to be adequate, the ASD should be closed. Regardless of the initial decision, the physiology should be assessed carefully in the operating room following separation from CPB, and surgical readjustments (either opening or closing the ASD) made as necessary. Remainder of the operation is completed in the usual manner.

A concomitant systemic–pulmonary artery shunt may be added if $P_{a_{o}}$ is severely reduced (<30 mmHg) after discontinuing CPB. The neonate usually comes to the operating room well resuscitated by prostaglandin $E_1$ ($PGE_1$). However, in the rare circumstance in which this is not the case, methods employed for seriously ill adult patients will probably improve results (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).

Consideration should be given to placing a fine polyvinyl catheter into the RV, inserted through the right atrium across the tricuspid valve. It is used perioperatively to monitor RV pressure and typically is removed 48 hours later in the intensive care unit (see Special Features of Postoperative Care later). Measurements in the operating room after repair are not as informative and cannot serve as a guide to concomitant infundibular resection (see Results).

Transesophageal echocardiography should be used routinely to assess the outflow tract after separation from CPB, paying particular attention to gradients at the valvar and infundibular level, degree of pulmonary and tricuspid valve regurgitation, RV function, and presence and degree of intraatrial shunting.
Transanular Patch

Although the likelihood of needing a transanular patch is greater when the RV cavity is small, the decision to place one at the initial surgical procedure is generally best made during operation.\textsuperscript{12} When surgery is performed as a secondary procedure, the decision is usually made preoperatively. Operation proceeds as described earlier for open pulmonary valvotomy. The interior of the RV infundibulum is inspected by looking through the pulmonary valve orifice. If it appears to be narrowed and if the diameter of the opened pulmonary valve (and thus presumably the “anulus”) has a z value of \( -3 \) or less (see discussion of z value in “Standardization of Dimensions” under Dimensions of Normal Cardiac and Great Artery Pathways in Chapter 1), and particularly when the RV cavity is very small, a transanular patch is probably indicated.

Incision in the pulmonary trunk is carried across the anulus and down to the junction of the sinus and infundibular portions of the RV. The pulmonary valve cusps are excised. Conservative resection of hypertrophied muscular trabeculae in the infundibulum may be accomplished, but this is often impractical in neonates (see Fig. 38-11 in Chapter 38). An enlarging patch is fashioned from glutaraldehyde-treated or untreated autologous pericardium and sewn into place with continuous 6-0 or 7-0 polypropylene sutures (see “Decision and Technique for Transanular Patching” in Section I of Chapter 38). Remainder of the procedure, including placing the polyvinyl catheter, is as described in the preceding text. A systemic–pulmonary artery shunt is added only if \( \text{PaO}_2 \) is severely reduced after discontinuing CPB.

Systemic–Pulmonary Artery Shunt

If a systemic–pulmonary artery shunt is required as an isolated procedure (see Special Features of Postoperative Care later), a polytetrafluoroethylene (PTFE) interposition aorto-pulmonary shunt is made using a 3.5- or 4-mm tube via a median sternotomy. Whether shunting is an isolated procedure or concomitant to valvotomy or transanular patching, the PTFE tube is placed between the brachiocephalic trunk–right subclavian artery junction and the right pulmonary artery (see Technique of Operation in Section I of Chapter 38).

SPECIAL FEATURES OF POSTOPERATIVE CARE

Proper perioperative management of neonates is essential for success. Generally these deeply cyanotic and critically ill infants are started on PGE\(_1\) intravenously in doses of 0.05 to 0.4 \( \mu \)g · kg\(^{-1} \) · min\(^{-1} \) even before any studies are done; the resulting enlargement of the ductus arteriosus increases pulmonary blood flow and \( \text{PaO}_2 \) by the time of operation.\textsuperscript{16,11,03} PGE\(_1\) is continued during percutaneous valvotomy and early thereafter until the RV has a chance to remodel.

Caution must be used lest pulmonary overcirculation develop in a neonate whose pulmonary valve has been widely opened. The infant is left intubated and ventilated. As PGE\(_1\) is discontinued in the hours after the procedure, \( \text{SaO}_2 \) is monitored by pulse oximeter, or \( \text{PaO}_2 \) is measured frequently. If after 24 hours, \( \text{PaO}_2 \) remains well above 30 mmHg and the hemodynamic state is good, the neonate is gradually weaned from the ventilator and extubated. Even though some arterial desaturation persists, so long as \( \text{PaO}_2 \) stays above about 30 mmHg and the clinical condition remains good, the neonate is patiently followed in anticipation of continued improvement as the RV remodels and the pulmonary vascular resistance decreases. If \( \text{PaO}_2 \) falls to 30 mmHg or less, and if residual stenosis is mild or absent, a PTFE systemic–pulmonary artery shunt is performed. If important RVOT obstruction is present along with important hypoxia, a transanular patch as well as a systemic–pulmonary artery shunt is probably necessary.

If a primary surgical procedure is performed on the RVOT, the ductus has typically been ligated, and an appropriately sized systemic–pulmonary artery shunt may also have been placed. When a systemic–pulmonary artery shunt has been performed, the infant should be restudied at about age 6 to 12 months; plans should then be made for shunt closure by percutaneous or surgical means. In some surgical patients who do not receive a shunt at the time of the initial RVOT procedure, persistent cyanosis will occur, requiring return to surgery for placement of a shunt. Patients should be followed after hospital discharge until there is assurance that the RV–pulmonary artery peak pressure gradient is within acceptable limits. If it is not but can be remedied by further valvotomy, percutaneous techniques are generally recommended. In about 10% of patients, follow-up evaluation indicates important residual RV hypertension from “anular” or persistent infundibular narrowing; placing a transanular patch is then required to achieve the desired result.

RESULTS

Survival

Early (Hospital) Death

About 10% of heterogeneous groups of neonates die during initial hospitalization (Fig. 39-7). Risk-adjusted analysis indicates that early death occurs in only 6% of neonates treated by the surgical methods described in this chapter (Fig. 39-8). This very good result in critically ill patients is directly traceable to introduction of PGE\(_1\), general improvement in neonatal cardiac surgery, and advent of percutaneous balloon valvotomy.\textsuperscript{12} Results of balloon valvotomy in neonates compare favorably with those of surgical valvotomy. Tabata- baei and colleagues were able to accomplish balloon dilatation in 35 of 37 neonates with critical valvar pulmonary stenosis (generally with suprasystemic RV pressure),\textsuperscript{11} with only 3 deaths (8%; CL 0%-16%). Others have reported similarly good survival.\textsuperscript{14,15,72,71}

Time-Related Survival

Survival for at least 4 years after birth in heterogeneous groups of treated neonates is about 80% (see Fig. 39-7). The rapidly declining appreciable early rate of death (hazard function) begins to flatten out considerably about 3 months after intervention. Risk-adjusted survival for at least 4 years can be presumed to be 94% (see Fig. 39-8), because death rarely occurred between 6 months and 4 years postoperatively in a large study.\textsuperscript{12} Gudausky and Beekman have reviewed mid- and long-term outcomes following balloon valvotomy in neonates, citing 6 studies since 1995 in addition to their own experience, totaling 221 patients.\textsuperscript{112} There were a total of 249 patients, with successful dilatation in 224 (90%). Follow-up ranged from 1 to 116 months. Twelve serious
complications resulted from the procedure, and 13 total deaths; 5 of the deaths were early and 8 were late.

**Modes of Death**

The mode of virtually all deaths is either hypoxia or acute cardiac failure.

**Incremental Risk Factors for Premature Death**

Although uncommon, RV enlargement of an appreciable degree is a highly lethal coexisting cardiac anomaly. This is probably a special situation in which there is a coexisting cardiomyopathy or tricuspid valve lesion (e.g., Ebstein malformation) already present in fetal life because of genetic or developmental factors. Aside from these rare cases, no general patient-specific risk factors for death are identifiable in neonates. This is unusual in patients with congenital heart disease.

For open pulmonary valvotomy without inflow stasis or CPB and for certain morphologic variants (see text that follows), transanular patching without a shunt is a risk factor, and these procedures should not be used\(^2\) (Table 39-2).

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**Figure 39-7** Death after first intervention in a heterogeneous group of 98 neonates with critical pulmonary stenosis. A, Survival. Each circle represents a death, and vertical bars represent 70% confidence limits of nonparametric estimates. Numbers in parentheses are number of patients traced after these estimates. Solid line represents a parametric estimate of survival enclosed within dashed 70% confidence bands. B, Hazard function (solid line) enclosed within 70% confidence bands (dashed lines). (From Hanley and colleagues.)\(^3\)

**Table 39-2** Incremental Risk Factors for Death at Any Time after Initial Accomplished Procedure\(^4\)

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Single Hazard Phase P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedural</strong></td>
<td></td>
</tr>
<tr>
<td>Open pulmonary valvotomy without inflow stasis</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Transanular patching without a shunt</td>
<td></td>
</tr>
<tr>
<td>(Smaller) + Dimension (z value) of RV-PT junction</td>
<td>.01</td>
</tr>
<tr>
<td>(Greater) + Degree of tricuspid regurgitation</td>
<td>.0002</td>
</tr>
<tr>
<td>(Earlier) + Date of procedure</td>
<td>.04</td>
</tr>
</tbody>
</table>

Data from Hanley and colleagues.\(^2\)

\(^1\) Database consists of 101 neonates with critical pulmonary stenosis entered into a multiinstitutional study between January 1987 and 1991.\(^2\) Median age of entry was 3 days. Analysis was of 93 patients, excluding five with Ebstein anomaly, a large right ventricle, or both, and three (two are deceased) in which no procedure was performed.

\(^2\) The three factors listed under transanular patching without a shunt are interaction terms; that is, they pertain only to patients in whom transanular patching without a shunt was performed, not to patients undergoing other types of procedure. Transanular patching without a shunt, when examined without interaction terms, had a low P value of .9.

Key: PT, Pulmonary trunk; RV, right ventricle.

Other procedures give good results, with few differences between them (Fig. 39-9). In neonates and young infants, transanular patching unaccompanied by a systemic–pulmonary artery shunt is an incremental risk factor when the pulmonary “anulus” is severely hypoplastic or when there is important tricuspid regurgitation. Patients in this situation usually have severe RV hypertrophy and reduced cavity size; without a shunt, they tend to have marked hypoxia from right-to-left shunting across a patent foramen ovale secondary to acute RV failure.
Residual Right Ventricular Outflow Tract Obstruction

Limited information is available concerning residual gradients. In about 90%, any important residual gradient has disappeared or been overcome by repeat percutaneous valvotomy within 6 to 12 months of the initial procedure. Ultimately, the RV–pulmonary trunk gradient is usually less than 6 mmHg. About 75% of neonates successfully undergoing pulmonary valvotomy require no further procedure for at least 4 years. About 10% remain hypoxic and require a systemic–pulmonary artery shunt. About 10% remain hypoxic and require a systemic–pulmonary artery shunt. In a few, repeat balloon valvotomy is needed. About 10% of those not initially receiving a transanular patch will need one at some point. Rarely (<2%), a two-ventricle system cannot be attained, and a superior cavopulmonary anastomosis or Fontan-type operation is ultimately required. Similarly, Rao reports occurrence of reintervention was 25% following initial balloon valvotomy.

Occasionally, closure of an ASD is required as the RV remodels and important left-to-right shunting develops in patients in whom the ASD was purposefully left open at the time of the neonatal procedure. The long-term implications of severe pulmonary regurgitation, primarily in those patients who received a transanular patch, remain unclear. In patients who fail to develop adequate SaO₂ (>85% at rest) and right atrial pressure (<12-15 mmHg at rest) with the atrial septum and any systemic–pulmonary artery shunt temporarily closed, a superior cavopulmonary anastomosis can be considered to reduce the workload of the RV, allowing closure of the ASD and systemic–pulmonary shunt. Occasionally, a Fontan-type operation is ultimately indicated.

Morphologic and Functional Changes

Although some neonates initially have at least moderate reduction in RV cavity size, late after pulmonary valvotomy the RV cavity is normal or only mildly reduced in size in 90%. In only about 10% does an important degree of infundibular obstruction, cavity narrowing, or both persist. Following balloon valvotomy, pulmonary anulus and RV chamber size increase, cusp mobility improves, and cusp thickening resolves in the majority of cases studied by echocardiography 6 months to 8 years after intervention.

Whereas most patients have tricuspid regurgitation initially (in some cases, severe), more than 80% have no regurgitation late after valvotomy. However, in a few patients, moderate or severe regurgitation persists, and it is likely that the tricuspid valve is somewhat dysplastic in these patients. Pulmonary regurgitation following balloon valvotomy occurs with increasing frequency and severity over time in 41% to 88% of patients. Need for surgical placement of a competent pulmonary valve prosthesis is unusual but reported.

INDICATIONS FOR OPERATION

Interventional treatment is indicated for all neonates. It may be accomplished by percutaneous balloon valvotomy or by open surgical valvotomy with CPB. Balloon valvotomy is the procedure of choice in most circumstances. An exception is when the patient has severe hypoplasia (z value of −4 or less) of the pulmonary “anulus” and severe reduction of RV cavity size; inserting a transanular patch and concomitantly constructing a systemic–pulmonary artery shunt are indicated as the initial procedure. When only a valvotomy has been performed, a subsequent systemic–pulmonary artery shunt, transanular patch, or both will be indicated in 10% to 20% of patients (see Special Features of Postoperative Care earlier). Surgical valvotomy is also the procedure of choice if expertise in percutaneous balloon valvotomy is lacking.

Section II Pulmonary Stenosis in Infants, Children, and Adults

MORPHOLOGY

Valvar pulmonary stenosis and intact ventricular septum in patients presenting after the neonatal period is a spectrum ranging from critical (pinhole) pulmonary stenosis, through severe pulmonary stenosis with a normal-sized or dilated RV, to moderate or mild valvar pulmonary stenosis that remains relatively stable throughout life.

Figure 39-9 Risk-adjusted predicted percent survival for at least 6 months after first intervention in neonates with critical pulmonary stenosis. Depiction is similar to that in Figure 39-8. It indicates that in 1991 (value entered for date of operation), all procedures other than open pulmonary valvotomy without inflow stasis or cardiopulmonary bypass were followed by a 94% probability of survival for at least 6 months when the z value of right ventricle (RV)–pulmonary trunk (PT) junction (“anulus”) was −4 or larger. When the anulus was severely hypoplastic, survival was not as good as after a transanular patch (TAP) without a shunt (see text). (Data from Hanley and colleagues.)
Table 39-3  Morphologic Features of Pulmonary Stenosis with Intact Ventricular Septum in Infants, Children, and Adults$^a$

<table>
<thead>
<tr>
<th>Valve stenosis alone</th>
<th>82</th>
<th>59</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infundibular stenosis alone$^b$</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Valve + infundibular stenosis$^c$</td>
<td>45</td>
<td>32</td>
</tr>
<tr>
<td>TOTAL</td>
<td>140</td>
<td>100</td>
</tr>
<tr>
<td>PT and/or branch PA origin stenosis</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Hypoplastic right ventricle</td>
<td>19</td>
<td>14</td>
</tr>
</tbody>
</table>

$^a$Based on 140 patients with pulmonary stenosis and intact ventricular septum undergoing repair at GLH, 1960 to 1979.
$^b$Includes only patients receiving combined valvotomy and infundibular resection.
Key: PA, Pulmonary artery; PT, pulmonary trunk.

Pulmonary Valve

The pulmonary valve is usually better developed in infants and children with severe pulmonary stenosis than it is in neonates. Although the cusp tissue may have a myxomatous appearance and may be irregularly deformed and thickened, the two, three, or even four pulmonary valve cusps are relatively well formed with only partial commissural fusion.$^{510,53}$ In adults, the valve may become calcified, particularly when there has been preexistent infective endocarditis.$^{18}$ In older patients, a variable amount of infundibular hypertrophy results in secondary infundibular stenosis. Occasionally, infundibular stenosis alone accounts for RV outflow tract obstruction (Table 39-3).

Pulmonary Arteries

Post-stenotic dilatation of the pulmonary trunk (see Fig. 39-5) is characteristic of this malformation and is present in about 70% of infants and children with this lesion.$^{1,66}$ The left pulmonary artery may be involved as well.

Right Ventricle

In older patients, in contrast to neonates, important hypertrophy of the RV is uncommon, although marked thickening of the ventricular wall is often seen. When this thickening involves the infundibular septum and free wall of the RV, severe subvalvar obstruction gradually develops.$^{85}$ This has been anecdotally referred to as the “suicidal tendency” of the RV of patients with important pulmonary stenosis. In occasional cases, a low-lying and large moderator band or so-called anomalous muscle bands contribute to infundibular obstruction. In about 10% to 20% of patients, these are the only sites of obstruction, the valve being either normal or (rarely) bicuspid, but not stenotic (see Section V of Chapter 38).

Tricuspid Valve

In infants and children, the tricuspid valve is usually morphologically normal. However, mild regurgitation or, in the face of RV failure, moderate or severe regurgitation may develop.

Right Atrium

The right atrial wall is hypertrophied secondary to increased right atrial pressure. In about one fourth of infants and adults, the atrial septum is intact. However, in most the foramen ovale is patent, or there is a small ostium secundum ASD; right-to-left shunting results in cyanosis.$^{12,13}$ When a left-to-right shunt is present, there is usually a large ASD and only mild or moderate pulmonary stenosis.$^{87}$

Left Ventricle

Alterations in the LV (e.g., myocardial infarction, myocardial dysplasia, obstructive changes in the coronary arteries, abnormal media of the ascending aorta) have been shown occasionally to coexist with pulmonary stenosis and intact ventricular septum.$^{82,86}$ Muscular subaortic stenosis of the variety seen in hypertrophic obstructive cardiomyopathy may coexist. A combination of muscular subaortic and subpulmonary obstruction may be associated with abnormal facies and is a possible variant of Noonan syndrome.$^{N2}$ Important valvar pulmonary stenosis in infants and children can adversely affect LV function.$^{13}$ This is largely the result of RV hypertension that displaces the septum toward the left and alters LV geometry.$^{14}$ Cardiac output and LV function are adversely affected, but the abnormalities revert to normal after correction of the RV outflow obstruction.

Associated Anomalies

Pulmonary stenosis and intact ventricular septum occurs frequently in Noonan syndrome, which is characterized by small stature, hypertelorism, mild mental retardation, cardiac malformations (most commonly pulmonary stenosis), and at times ptosis, undescended testes, and skeletal malformations.$^{1,2}$ It is also associated with intrauterine rubella.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Symptoms

Infants may be symptomatic but usually have less severe symptoms than neonates. After the first year, patients often present because of a murmur only, produced by mild or moderate stenosis. In the second, third, and fourth decades, presentation may be with chronic RV failure. In all, 30% to 40% of patients are asymptomatic when first examined.$^{1,13}$ When symptoms occur, the earliest is often effort dysnea, which results from inability to increase pulmonary (and thus systemic) blood flow with exercise because of the relatively fixed resistance of the pulmonary valve.$^{1,13,14}$

Cyanosis appears when, in the presence of an interatrial communication, the RV becomes less compliant than the LV or its pressure becomes severely elevated. With a normally developed RV, this occurs only when its pressure is suprasystolic, and is associated with ECG evidence of considerable RV hypertrophy. When cyanosis is marked in older patients, polycythemia becomes severe, and all the complications associated with this condition can develop (see “Clinical Presentation” under Clinical Features and Diagnostic Criteria in Section I of Chapter 38).$^{113}$ However, these patients rarely squat for symptomatic relief as do those with tetralogy of Fallot.$^{1,13,14}$
Effort-related precordial pain is not uncommon and is presumably due to RV angina. Sudden death can occur in cyanotic and acyanotic children and in young adults.\textsuperscript{11,83}

Patients in the second and third decades of life with severe and long-neglected pulmonary stenosis and intact ventricular septum show development of right heart failure with elevated jugular venous pressure, hepatomegaly, and ascites, which eventually leads to death.

**Signs**

Except in young infants with severe heart failure, a systolic murmur (best heard in the second left interspace) is present, often with a thrill. Peak intensity of the murmur occurs later in systole in those with severe rather than mild stenosis.\textsuperscript{62} The pulmonary component of the second sound may be normal, decreased, or inaudible, whereas the aortic component is usually obscured by the murmur. The tighter the pulmonary stenosis, the longer the RV ejection time and the greater the delay in pulmonary valve closure.\textsuperscript{62,71}

In severe stenosis, an ejection click is absent because the dome of the pulmonary valve is pushed upward into the pulmonary trunk by the vigorous right atrial contraction before ventricular systole occurs. In some patients with mild stenosis, the abnormality of cusp movement may be insufficient to produce a click, although in other patients it may be prominent, the sound being magnified by a dilated pulmonary trunk.

The hypertrophied RV can often be appreciated as an RV heave palpable to the left of the sternum. The jugular venous “a” wave increases in amplitude as pulmonary stenosis increases in severity and is made more obvious by a noncompliant RV.\textsuperscript{73} In older children, diagnosis of associated RV hypoplasia is suspected when signs of pulmonary stenosis are combined with heart failure and cyanosis in the absence of severe RV hypertrophy on the ECG. Thus, in contrast to pulmonary stenosis with a normally developed RV, cyanosis may occur when its pressure is less than systemic and the ECG is unremarkable.\textsuperscript{51,82}

**Electrocardiography**

Right atrial enlargement from moderate or severe pulmonary stenosis is reflected in prominent P waves in the ECG.\textsuperscript{56} When pulmonary stenosis is mild or moderate, the R-wave height in V\textsubscript{1} is less than 10 mm, or there is a pattern of incomplete right bundle branch block. When it is severe, the R or R’ in V\textsubscript{1} becomes greater than 10 mm and corresponding in its height to degree of RV hypertension.\textsuperscript{63}

**Echocardiography**

In children and adults, as well as neonates, two-dimensional echocardiography can provide near-certain diagnosis. The thickened, immobile, or domed pulmonary valve can be imaged, along with post-stenotic enlargement of the pulmonary trunk and RV thickening. Severity of stenosis can be estimated by Doppler evaluation of the flow across the pulmonary valve in systole, and this can be confirmed by similar evaluation of the velocity of flow in the tricuspid valve regurgitant jet, if present. Echocardiography can also be used to diagnose restrictive RV physiology by demonstrating forward flow across the pulmonary valve in late diastole. This physiology can be present in up to 42% of adults with moderate or severe stenosis and correlates with increased symptoms.\textsuperscript{12}

**Cardiac Catheterization and Cineangiography**

Techniques and findings are the same as those described in Section I.

**NATURAL HISTORY**

Pulmonary stenosis with intact ventricular septum accounts for about 10% of congenital heart disease and is thus a common malformation. Most surgical series show a predominance of females.

Patients Presenting in Infancy

Patients who survive the neonatal period to present later in infancy have a wide variation in degree of pulmonary valve narrowing. About 40% (CL 32%-47%) have mild obstruction, 47% (CL 39%-54%) moderate, and only 14% (CL 9%-20%) severe. However, these percentages probably underestimate the proportion of patients in this age group with severe obstruction. Nugent and colleagues found that 58% (CL 51%-64%) of an unselected group of infants presenting in the first 2 years (n = 81) with this entity had severe RV outflow obstruction.\textsuperscript{73} Even in early life, and probably more so as time passes, infundibular (muscular) narrowing adds to RV output resistance.

When RV outflow obstruction is severe in infants and young children, heart failure, cyanosis, or both are common (more so than in older patients who have developed the same degree of obstruction).\textsuperscript{14,73} Prognosis of this group is poor. Levine and Blumenthal found that 56% of patients with heart failure died during follow-up.\textsuperscript{14}

Even when obstruction is moderate in this young age group, an important proportion have heart failure, with its same poor prognostic implication. It is probable that a degree of RV hypoplasia is often implicated in heart failure under these circumstances. According to Mody’s study of 17 patients with moderate RV outflow tract obstruction in the first year, 53% (CL 38%-68%) experienced progression to a severe lesion in the next several years (average 4.5 years).\textsuperscript{38} Similar conclusions can be drawn from the data of Wennevold and Jacobsen and Danilowicz and colleagues.\textsuperscript{2,81}

Even in asymptomatic infants with mild stenosis, Anand and Mehta reported rapid progression requiring intervention within 6 months in 15%.\textsuperscript{12} Experience of others, however, contradicts this, indicating that progression of mild pulmonary stenosis (gradient of ≤40 mmHg) in infants is rare and is similar to the natural history of mild pulmonary stenosis diagnosed in older children.\textsuperscript{44,66}

Patients Presenting after Infancy

Patients with isolated pulmonary stenosis that produces mild RV outflow obstruction (peak pressure gradient between RV and pulmonary trunk ≤ 25 mmHg or RV peak pressure ≤ 50 mmHg) have a predicted probability of survival equal to that of an age-gender-ethnicity–matched general population.\textsuperscript{44} These patients rarely experience progression of pulmonary stenosis and therefore rarely require interventional
therapy. Recent studies by Rowland and colleagues and Gielen and colleagues corroborate earlier findings.

Patients with moderately severe obstruction (peak pressure gradient between RV and pulmonary trunk > 25 mmHg but < 50 mmHg, or RV peak pressure > 50 mmHg but < 80 mmHg) sometimes experience progression in severity of their RV outflow obstruction. Without progression, as best as can be gleaned from currently available information, predicted probability of survival for at least 25 years is excellent. 

Patients with severe pulmonary stenosis are susceptible to eventual development of chronic heart failure (and thus premature death), the tendency being greater the older the patient. Secondary changes in the severely stenotic valve probably make it more obstructive as time passes, with the outflow tract becoming more hypertrophied and stenotic and the RV becoming thicker, more fibrotic, less contractile, and less compliant. 

In women with severe pulmonary stenosis who are in New York Heart Association functional class I or II, pregnancy is not associated with an increase in fetal or maternal complications, in contrast to similar disease of the mitral or aortic valve.

Effect of Right Ventricular Hypoplasia

RV hypoplasia seems to affect natural history unfavorably. However, some patients with hypoplasia do not die in infancy but present later in life, usually with progressive cyanosis from a right-to-left shunt at atrial level. Left untreated, progressive right heart failure develops and causes death.

TECHNIQUE OF OPERATION

Comment

In infants, children, and adults, as in neonates, percutaneous balloon valvotomy is the treatment of choice for valvar pulmonary stenosis. If this is not successful, or is not indicated, open surgical valvotomy using CPB is performed. Balloon valvotomy is ineffective in most cases of dysplastic pulmonary valve, and when the valve anulus is hypoplastic (\( z \) value < -3). The surgical technique is that described in Section I. When transanular patching is necessary, the technique is also that described in Section I.

Open Operation during Cardiopulmonary Bypass

The general aspects of operation described in Section I are applicable to pulmonary valvotomy in infants and adults. After the pulmonary trunk is opened through a vertical incision, valvotomy is performed (Fig. 39-10). When edges of the cusps are bulky and obstructive, and particularly when the valve is bicuspid, partial or complete valvectomy may be necessary, because a taut bicuspid valve cannot open properly even after incision of the two fused commissures. RV, LV, and pulmonary artery pressures are measured at this point, but they are of little value in decision making (see Special Features of Postoperative Care later). A polyvinyl catheter is placed to measure RV pressure. It can be brought from the pulmonary artery out the low RV or alternatively, can be advanced forward from the right atrium through the tricuspid valve. Pressure measurements made the following morning may indicate the need for return to the operating room for relief of infundibular or anular stenosis.

When an infundibular resection is indicated (Fig. 39-11), a vertical infundibular incision is preferred. After resection, the incision is closed using an oval-shaped patch of PTFE or pericardium. In a few patients, a transanular patch is required because of a small pulmonary valve anulus. Patients requiring this often have dysplastic pulmonary valves. Cineangiogram or echocardiogram may suggest need for the transanular patch, but the final decision is usually made in the operating room. At the time of valvotomy through the pulmonary arteriotomy, the anulus is sized with Hegar dilators. If it is small (\( z \) value of -3 or less), the arteriotomy is carried across the anulus and down the infundibular free wall. If there is doubt about need for transanular patching, the pulmonary arteriotomy is left open and a vertical incision made in the infundibulum.

After muscle resection has been accomplished, the anulus is again sized by Hegar dilators passed through the valve from below. If it is too small, the two incisions are joined by cutting across the anulus, and a transanular patch is inserted (see “Decision and Technique for Transanular Patching” under Technique of Operation in Section I of Chapter 38). Deleon and colleagues have described a reconstructive operation for patients with dysplastic pulmonary valve with hypoplastic anulus that preserves valve function. However, the experience involves only two patients, and follow-up is limited.

In the occasional patient with stenosis of the pulmonary trunk or branches in whom these have not, or cannot, be treated adequately by balloon dilatation and stenting, the narrowed pulmonary branch is dissected to a point beyond the stenosis and an enlarging repair made (see Technique of Operation in Section I of Chapter 38). Preliminary dissection of these branches is best made during CPB cooling. These stenoses must be identified in detail at preoperative cardiac catheterization.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is accomplished as described in Chapter 5. One special feature is that RV pressure should be assessed on the first postoperative day. This is accomplished by monitoring the RV pressure or withdrawal of the pulmonary artery pressure catheter that was placed at operation into the RV. These pressures are more reliable in predicting late results from operation than those taken in the operating room. However, if the patient’s hemodynamic state is good, reoperation within a few days of the initial procedure is rarely necessary, even when RV pressure is high, because of the known tendency for infundibular hypertrophy to regress with time.

RESULTS

Survival

Early (Hospital) Death

Hospital mortality is essentially zero after percutaneous balloon valvotomy. It is very low after surgical valvotomy as well and has been for many years. It approaches zero when patients with severe RV hypoplasia or advanced chronic heart failure are excluded.

Young age (down to 1 month) is not a risk factor. The few deaths that occur are associated either with severe
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Jarrar and colleagues report no late deaths in 62 patients during follow-up. Hemodynamic Outcomes and Reintervention

Immediate relief of the gradient usually is obtained, and it is rare for adequate initial relief of obstruction to be temporary. On average, a peak RV pressure of 128 mmHg before valvotomy is reduced to 51 mmHg shortly after valvotomy. Completeness of relief of pulmonary stenosis can be determined only by late postoperative studies because of the usual, but not invariable, tendency for RV peak pressure to decrease over time after valvotomy. This decline is believed to be due primarily to regression of RV hypertrophy and lessening of infundibular narrowing. It is known, however, that adequate isolated pulmonary valvotomy does not invariably provide excellent relief of pulmonary stenosis, even in infants. Roos-Hesselink and colleagues report a low but definable incidence of restenosis. In 64 patients with follow-up ranging from 22 to 33 years, the reintervention rate was 15%. Two patients required reoperation for recurrent RVOT obstruction at 2 and 3 years after initial surgery, and Jarrar and colleagues report no late deaths in 62 patients during follow-up.

Time-Related Survival

Long-term survival is the rule after surgical treatment. In the early Mayo Clinic experience, survival out to 25 years after hospital discharge was 91% in the overall group, but this was importantly affected by age at operation. Survival for at least 25 years after hospital discharge was 93% for those aged 0 to 4 years at operation, 100% for those aged 4 to 10 years at operation, 92% for those aged 11 to 20 years, and 71% for those older than 21 at operation. Although neonates were not represented in this experience, infants were, and this probably accounts for the effect of age in that era.

In a more recent longitudinal study of 51 patients, with follow-up ranging from 22 to 33 years (mean 25 years), late survival was 96%. Long-term survival is now available following balloon valvotomy. Fawzy and colleagues report 2- to 17-year follow-up (mean 10 years) in 90 patients, with no late deaths. All patients were older at the time of balloon intervention in this study, ranging from 15 to 54 years. Gupta and colleagues reported a single death in 166 patients and RV hypoplasia or, particularly in adults, advanced chronic heart failure.

In Figure 39-10, Pulmonary valvotomy through pulmonary trunk during cardiopulmonary bypass. A, Overview showing vertical incisions in pulmonary trunk and high right ventricle (RV). B, View of funnel-like stenosis of pulmonary valve. C, Commissures are incised sharply with a knife. As this is done, the surgeon and an assistant must carefully stabilize the cusp on either side to avoid inaccuracy in making the incision. If necessary, thickened valve tissue around the orifice may be resected, or a cusp may be partially detached. However, this is done only if the opening is otherwise unacceptable, because some degree of regurgitation results. When infundibular dissection and resection are also required, RV is opened through a vertical incision in the infundibulum. After performing the dissection and resection, vertical ventriculotomy is closed with a small oval patch of polytetrafluoroethylene or pericardium inserted with continuous polypropylene suture.
Figure 39-11 Infundibular resection for pulmonary stenosis with intact ventricular septum. In contrast to the situation in tetralogy of Fallot, this is a resection of muscle from the entire circumference of the severely hypertrophied outflow tract. A, Approach is through a vertical incision that will be closed with a polytetrafluoroethylene (PTFE), polyester, or pericardial patch as in tetralogy of Fallot. B, Working from below upward, muscle is cored out with a knife up to valve level. More muscle can be excised from recesses in front of either end of the infundibular septum than elsewhere. Excision is often also necessary from the walls (anterior, medial, and lateral) for a short distance below ventriculotomy.

Continued
two required subsequent balloon dilatation at 16 and 18 years postoperatively. Additionally, six other patients required surgical reintervention, ranging from 16 to 24 years postoperatively, for severe pulmonary regurgitation. Five of these six had a transanular patch placed at initial operation. Moderate to severe pulmonary regurgitation was present at late follow-up in 37% of patients.

Earing and colleagues, on the other hand, reported more concerning long-term reintervention. In 53 patients with a mean follow-up of 33 years, reintervention for recurrent pulmonary stenosis was similarly low, but 21 patients (40%) required pulmonary valve replacement for severe regurgitation. This may reflect the extremely long follow-up, because other authors have recognized the progressive increase in symptomatic pulmonary regurgitation the longer the follow-up; however, equally important is that this cohort of patients underwent their original surgery in a different era. To this point, in this study, closed pulmonary valvotomy was importantly associated with need for late reoperation.

Hemodynamic results after percutaneous balloon valvotomy are similar to those just described (see Results in Section I). Fawzy and colleagues report a reduction in pulmonary valve gradient from 105 mmHg to 34 mmHg in their series of 90 patients (mean age 24 years). The infundibular gradient was large immediately following the procedure in 43 patients, all of whom underwent later recatheterization. The gradient decreased from 42 mmHg following the initial procedure to 13 mmHg at repeat study. Other reports document similar results.

Gudausky and Beekman summarize results from five large studies reported between 1994 and 2003. A total of 866 non-neonatal cases were included. Restenosis occurred in 20%, with 7% requiring repeat balloon valvotomy and 7% requiring surgery. Severe pulmonary insufficiency was present in 1%. Freedom from either surgical or balloon reintervention at 5 and 10 years after intervention, reported by Rao and colleagues, was 88% and 84%, respectively (Fig. 39-12).

**Comparison of Surgery and Balloon Valvotomy**

Peterson and colleagues studied comparative outcomes between surgical and balloon valvotomy. Between 1969 and 2000, 62 patients underwent surgery, and 108 balloon valvotomy. Both techniques were effective, but there were differences at 10-year follow-up. Surgery reduced the gradient across the pulmonary valve more effectively than balloon valvotomy and had lower rates of restenosis and overall reintervention. Balloon valvotomy had a lower rate of moderate pulmonary regurgitation, which did not appear to influence reintervention rates in the two groups. Nevertheless, balloon valvotomy is today the procedure of choice because of its lower cost, shorter hospital stay, lower degree of invasiveness,
and effectiveness. Based on the study of Earing and colleagues, it can be inferred that the reintervention rate in the surgery group studied by Peterson and colleagues will continue to rise with longer follow-up as symptoms from pulmonary regurgitation develop.

Cyanosis

Cyanosis may persist late postoperatively when the foramen ovale or ASD is not closed, even when stenosis has been relieved, as a result of impaired RV compliance. This can occur occasionally with a normally developed, severely hypertrophied RV, presumably secondary to diffuse fibrosis, but it is the rule in the hypoplastic RV. Data from Freed and colleagues suggest that the reversed atrial shunt may lessen as an infant or young child grows and as the RV increases in size, and later closure of the ASD thus may not be required. This favorable sequence cannot be expected in patients with hypoplastic RV, and it is well known that important hypoxia can occur from a right-to-left shunt through a small atrial communication.

Morphologic Changes

The sinus portion of the RV enlarges and becomes normal in size in most patients. The infundibulum enlarges in many patients, but as in tetralogy of Fallot (see Chapter 38), a narrow pulmonary anulus may fail to enlarge as the child grows. The apparent size of the pulmonary arteries increases, and in most patients they become normal sized. Tricuspid regurgitation, even when severe preoperatively, is usually absent or mild late postoperatively.

Functional Capacity

Most patients have an excellent late functional result. Stone and colleagues have shown that during exercise, children who have undergone pulmonary valvotomy have a normal relationship between cardiac output and oxygen consumption, no increase in RV end-diastolic pressure (preoperatively it increased), and less increase than preoperatively in RV peak systolic pressure. The late result in patients with a hypoplastic RV is inferior to that in patients with a normally developed ventricle. Late mortality is higher, there may be a reversed shunt through an unclosed atrial communication, and there may be residual infundibular obstruction. There may also be persistent or recurrent right heart failure despite complete relief of stenosis. Although there are no techniques proven to be beneficial in managing the hypoplastic RV, a number of options are available in selected cases. Late heart failure may be prevented in this group, particularly in those who are young, by a complete valvotomy combined with enlargement of the RV cavity by excision of trabeculations. This may be particularly helpful if extensive endocardial fibrosis is present. In patients with persistent RV failure, volume unloading by creating a bidirectional superior cavopulmonary anastomosis may be beneficial.

INDICATIONS FOR OPERATION

When patients first show signs and symptoms at age 1 month or more, they are usually less critically ill than those presenting as neonates. Nonetheless, when diagnosis of severe stenosis is made, pulmonary valvotomy is advisable. As in critical pulmonary stenosis in neonates, percutaneous balloon valvotomy is usually the intervention indicated. Only in special circumstances is surgical intervention indicated. These include dysplastic valves, severely hypoplastic valves, severe infundibular stenosis, and associated intracardiac lesions requiring surgery.

Intervention is similarly advised in asymptomatic infants with severe stenosis. In those with moderate stenosis, intervention in infancy is debatable; it is not recommended when stenosis is mild. In older patients, management differs only in the group with moderate stenosis. In this subset, the older the age at diagnosis, the less likely there will be important progression and therefore less need for intervention.

In all patient groups beyond the neonatal period, a gradient across the pulmonary valve of 50 mmHg or greater is considered an indication for intervention. Presence and degree of RV hypoplasia are taken into account when deciding on intervention. Because of its effect in increasing cyanosis and heart failure, severe RV hypoplasia makes intervention more urgent in infants. In older children and adults presenting with this lesion, indications for intervention do not differ unless there is severe heart failure unresponsive to medical measures. Under these circumstances, risk of intervention is increased.

SPECIAL SITUATIONS AND CONTROVERSIES

Right Ventricular Hypoplasia in Children and Adults

When the RV is severely hypoplastic, symptoms and signs are substantially altered. Important symptoms are not necessarily present in infancy, but when they appear they tend to progress rapidly. Classically, there is a markedly prominent a wave and reversed (expiratory) splitting of the second heart sound. Pulmonary stenosis with hypoplastic RV is associated with less than the expected degree of RV hypertrophy, and in severe hypoplasia, LV forces are dominant despite severe stenosis. Diminished RV potentials are due to smallness of its cavity rather than to diminution in muscle mass. Balloon valvotomy may not be as effective in this group because of (1) frequent presence of organic infundibular obstruction, (2) necessity of closing the atrial communication to abolish the otherwise persistent right-to-left shunt, and (3) probable benefits of enlarging the RV cavity by excising muscle from its sinus portion. Taking all these factors into consideration, a surgical approach may be required. However, when severe heart failure is present, prognosis is still poor with any approach. In this setting, reducing volume load on the RV by performing a superior cavopulmonary anastomosis may be of benefit (see Special Situations and Controversies in Section III of Chapter 41).

Supravalvar Pulmonary Stenosis

The rarest form of pulmonary stenosis and intact ventricular septum is supravalvar pulmonary stenosis. It has been called bowstring pulmonary stenosis and is characterized by narrowing of the sinutubular junction, similar to that seen in supravalvar aortic stenosis. This lesion, like pulmonary valve dysplasia, does not respond to balloon dilatation; surgery is required. Various technical approaches have been described, all similar to those described for supravalvar aortic stenosis.
(see Section III of Chapter 47). The technique of repair can involve patching from the main pulmonary artery across the sinusuticular junction into the sinus of Valsalva. Alternatively, repair using only native pulmonary artery tissue has been described. 11

REFERENCES

A

B

C

D

E
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7. Roberts WC, Shemin RJ, Kent KM. Frequency and direction of interatrial shunting in valvular pulmonary stenosis with intact ventricular septum and without left ventricular inflow or outflow obstruction. Am Heart J 1980;99:142.

S
**Definition**

Pulmonary atresia and intact ventricular septum is a congenital malformation in which the pulmonary valve is atretic and no ventricular septal defect exists. It coexists with variable degrees of right ventricular (RV) and tricuspid valve hypoplasia, and variable degrees of coronary artery abnormalities. This chapter discusses this malformation in the setting of atroventricular and ventriculoarterial concordant connections.

**Historical Note**

In 1839, Peacock collected records of seven patients with pulmonary atresia and intact ventricular septum and gave credit to John Hunter for reporting the first case in 1783. Hunter described a premature male who died 13 days after birth. The RV had “scarcely any cavity,” and the tricuspid valve was “especially small.” Coronary sinusoids and RV–coronary artery fistulae were recognized by Grant in 1926 and later by others. RV-dependent coronary
circulation began to be recognized at least in 1975 by Essed and colleagues and more recently by others.\textsuperscript{87,126,267}

In 1955, Greenwold and colleagues at Mayo Clinic described two types of RV in this malformation: (1) small and (2) normal-sized or large.\textsuperscript{411,412} Subsequently, the idea evolved that values for RV cavity size and tricuspid valve dimensions, as well as morphologic details, comprised a spectrum embracing virtually all values between the extremes.\textsuperscript{414,222} Greenwold and colleagues also suggested that pulmonary valvotomy was appropriate treatment when the RV was near normal in size.\textsuperscript{411,412} In 1961, Davignon and colleagues at Mayo Clinic suggested that a systemic–pulmonary artery shunt be performed when the RV was small.\textsuperscript{143} Reports of successful surgery from the University of Minnesota, Mayo Clinic, and Henry Ford Hospital appeared in 1961.\textsuperscript{88,122}

The combination of a systemic–pulmonary artery shunt with an RV outflow operation was described by Bowman and colleagues in 1971 and by Trusler and colleagues in 1976.\textsuperscript{88,122}

In 1993, Hanley and colleagues introduced the concept that optimal outcomes are best achieved when neonatal and subsequent surgical management are specifically tailored to the variable morphology of this malformation.\textsuperscript{111}

**MORPHOLOGY**

Hearts with pulmonary atresia and intact ventricular septum include a spectrum extending from mild concomitant abnormalities of the RV and tricuspid valve to the most severe. Whether the entity of pulmonary stenosis and intact ventricular septum, particularly critical pulmonary stenosis in neonates, is part of this spectrum can be debated (see Section I of Chapter 39). Evidence supporting the continuum of these two entities is that at least some hearts at adjoining ends of the spectra have similar RV and tricuspid valvar abnormalities.

It has been hypothesized that the later the narrowing of the pulmonary valve develops in fetal life, including progression to atresia, the more fully and normally developed are the tricuspid valve, RV cavity, and RV myocardium. Conversely, the earlier these developments occur in fetal life, the more likely that these structures will be hypoplastic and abnormal.\textsuperscript{412,421,71} This hypothesis is also consistent with the concept that there is a continuity of the spectra of pulmonary atresia with intact ventricular septum and pulmonary stenosis with intact ventricular septum.

**Pulmonary Valve**

The nature of the structure at the junction of the RV and pulmonary trunk is arguable. Van Praagh and colleagues imply that fibrous components are pulmonary valve remnants.\textsuperscript{82} Others point out that in many cases, there is only poorly structured imperforate fibrous tissue overlying muscular atresia.\textsuperscript{\textsuperscript{415,412,222}} In any event, commissural ridges may be prominent and converge to meet in the center of the “valve,” an appearance similar to that in pulmonary valve stenosis.\textsuperscript{222} In some patients, commissural ridges are present only in the periphery, the center being a smooth fibrous membrane.\textsuperscript{39} In the combined U.K.-Ireland multicenter study of 183 patients, 75% had membranous atresia and 25% muscular atresia.\textsuperscript{121} Of greater importance is the nature of the structures immediately below the RV–pulmonary trunk junction (see “Right Ventricle” and “Tricuspid Valve” in text that follows).

**Table 40-1** Right Ventricular Cavity Size in Pulmonary Atresia and Intact Ventricular Septum\textsuperscript{a}

<table>
<thead>
<tr>
<th>RV Cavity Size\textsuperscript{b}</th>
<th>n</th>
<th>% of 136</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (0)</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Mildly reduced (−1, −2)</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Moderately reduced (−3)</td>
<td>25</td>
<td>18</td>
</tr>
<tr>
<td>Severely reduced (−4, −5)</td>
<td>78</td>
<td>57</td>
</tr>
<tr>
<td>Subtotal</td>
<td>136</td>
<td>100</td>
</tr>
<tr>
<td>Unknown</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>163</td>
<td></td>
</tr>
</tbody>
</table>

Data from Hanley and colleagues.\textsuperscript{87}

\textsuperscript{a}Based on data from 171 neonates with pulmonary atresia and intact ventricular septum in the Congenital Heart Surgeons Society study. Size of pulmonary arteries was known in 84.

\textsuperscript{b}Cavity size was graded (0, normal to −5, severe hypoplasia) based on echocardiographic and cineangiographic findings.

\textsuperscript{c}Five of six patients with moderate or severe hypoplasia of right and left pulmonary arteries on cineangiography had severely reduced ventricular cavity size (information available for 84 of 136 patients).

\textsuperscript{d}In addition, eight patients had enlarged right ventricular cavities, and one (12%) of these had moderately hypoplastic pulmonary arteries.

Key: RV, Right ventricle.

**Pulmonary Arteries**

The pulmonary trunk is usually nearly normal in size, but uncommonly is severely hypoplastic.\textsuperscript{413,439,411,32,222} Rarely, the pulmonary trunk is represented only by a fibrous cord.\textsuperscript{71}

Right and left pulmonary arteries are usually normal in diameter or slightly hypoplastic.\textsuperscript{42,413,71} Uncommonly, they are moderately or severely hypoplastic, usually in patients with severely reduced RV cavity size (Table 40-1). Rarely, there are major arborization abnormalities of the native pulmonary arteries in association with large aortopulmonary collaterals. Four such patients have been encountered by F.L. Hanley and colleagues (personal communication, February 2012).

**Right Ventricle**

Size of the RV cavity is variable. In about 5% of patients, it is enlarged (see Chapter 38, Fig. 38-2 and Chapter 39, Table 39-1). Ebstein malformation and severe tricuspid regurgitation may coexist with the latter.\textsuperscript{57,128,84,10,78,43,41,93,422} Many individuals with this combination die in fetal life.\textsuperscript{45} Rarely, the RV wall may be very thin (\textit{thin anomaly or parchment right ventricle}\textsuperscript{103}) and the cavity nontrabeculated adjacent to the tricuspid valve and heavily trabeculated in its apical half.

Much more frequently, cavity size is reduced, severely so in about 60% of patients. This appears to be the result of massive wall hypertrophy extending into the ventricular cavity. Often, this completely obliterates the infundibular cavity, and the atresia can be termed \textit{muscular} in such cases.\textsuperscript{514} At times, the apical-trabecular cavity is completely obliterated; in the most extreme cases, both portions are obliterated. Although these cavities are obliterated, the respective portions of the RV are not absent. Cavity obliteration can be localized by echocardiography as well as by anatomic studies.\textsuperscript{85} Cavity obliteration has been further characterized in the U.K.-Ireland multicenter study.\textsuperscript{121} All three components of the RV (inlet, trabecular, and infundibular) were present in all cases, but with different degrees of cavity obliteration from muscular ingrowth. A “unipartite” ventricle due
to muscular obliteration of the infundibular and trabecular components was present in 8%. A “bipartite” ventricle due to muscular obliteration of the trabecular component alone was present in 34%. There were no cases of muscular obliteration of the infundibulum alone. A “tripartite” ventricle was present in the remaining 58%.

There is associated diffuse fibrosis of the hypertrophied muscle and, especially when the RV cavity is small, a modest degree of RV endocardial fibroelastosis. Bulkley and colleagues found typical myocardial fiber disarray in 69% of the RV free wall and in 73% of the ventricular septum in this condition. The potential for impaired left ventricular (LV) as well as RV dysfunction is evident.

Right Ventricular–Coronary Artery Fistulae

Coronary sinusoids, or dilated portions of the coronary microcirculation, can be detected by cineangiography in about half of patients (Table 40-2). In some cases, fistulous connections between the RV cavity and these sinusoids form multiple small communications into branches of left or right coronary arteries. Occasionally they converge into a single large vessel that empties into the left anterior descending or right coronary artery. In many cases, the fistulae are minor. In the multicenter U.K.–Ireland study, 58% of patients had completely normal coronary circulation, 15% had minor filling of the coronary arteries with RV injection at catheterization, and about 25% had major fistulae, with about one third of these having no coronary connection to the aorta.

Prevalence of RV–coronary arterial fistulae is inversely related to dimensions of the tricuspid valve (and hence of the RV cavity) (Fig. 40-1) and amount of tricuspid regurgitation. It is also directly related to RV systolic pressure. However, the milieu for development of fistulae may be a consequence of genetically or developmentally induced myocardial abnormalities. Immunohistochemical studies demonstrate abnormal density and orientation of capillaries and myocyte disarray in the presence of fistulae. Desaturated RV blood, although vital in the presence of proximal coronary obstructions, compromises myocardial oxygen supply in regions to which it is distributed by these fistulae. This may account in part for the myocardial abnormalities described later in this chapter. Complexity of oxygen delivery to the myocardium is evidenced by the fact that the left anterior descending artery (or any coronary artery) may fill through these fistulae from the RV in systole, and from the aorta in the normal manner during diastole. There results a spectrum of percentages of LV myocardium dependent on the RV for coronary perfusion, albeit desaturated; the percentage depends on location and severity of proximal coronary artery stenoses as well as on the fistulae. At some critical point, sufficient myocardium is in jeopardy of developing such severe ischemia when RV hypertension is relieved that RV decompression becomes contraindicated as a surgical option. In an analysis by Giglia and colleagues of 16 patients with coronary angiography and subsequent RV surgical decompression, 7 of 7 (100%; CL 77%-100%) with no coronary stenosis survived, 4 of 6 (67%; CL 39%-88%) with stenosis in one major coronary survived, and 0 of 3 (0%; CL 0%-46%) with stenosis in two major coronaries survived.

When less severe coronary abnormalities are present in association with fistulae, regional LV wall motion abnormalities are commonly identifiable before RV decompression, and they increase after decompression; however, severe global LV dysfunction is unusual. In about 10% of patients (20% of those with RV–coronary fistulae), coronary circulation or some critical part of it is derived entirely or nearly so from the RV in the manner described, defining RV-dependent coronary circulation. This may occur because of development of arterial obstructions in the left main or right coronary arteries, or both, or in the proximal portion of the left anterior descending artery. RV cavity or RV wall thickness may be increased in RV–coronary fistulae. Proximal coronary arterial occlusions etiologic to the dependence may develop in fetal life; some develop or progress after birth.
RV-dependent coronary circulation is a major consideration in planning therapy (see Indications for Operation later in this chapter). The difficulty is in deciding how much myocardium at risk is considered too much, triggering the management decision to avoid decompressing the hypertensive RV. To address this difficulty, Calder and colleagues identified coronary abnormalities in 116 patients. They determined that presence of coronary fistulae alone did not correlate with mortality. The presence and extent of coronary interruptions, and the amount of LV myocardium that was RV dependent (determined with a 15-point scoring system), did correlate with mortality.

The problem, however, is even more complex than solely determining the amount of myocardium at risk, because even a small amount of extremely ischemic myocardium may be the source of a life-threatening dysrhythmia. Recently, LV coronary abnormalities unrelated to the presence of fistulae, sinusoids, or coronary interruptions have been discovered. Hwang and colleagues showed that patients with pulmonary atresia with intact ventricular septum, regardless of the presence of fistulae, have decreased density of intramyocardial arterioles relative to normal and hypertrophied hearts.

Tricuspid Valve

The tricuspid valve is usually abnormal in this malformation. Occasionally the abnormality is simply small size, but usually the leaflets are thickened and the chordae are abnormal in number and attachment. Local agenesis and incomplete leaflet separation occur. The importance of these abnormalities has been emphasized by Davignon and colleagues and by Paul and Lev.

In about 10% of neonates, the value of the tricuspid valve is less than 2.2, and in 50% it is less than 2.2 or less (Fig. 40-2). (See Appendix Fig. 40A-1 for a nomogram for estimating the value of the tricuspid valve.) Dimensions of the tricuspid valve are well correlated with those of the RV cavity, in contrast to dimensions in neonates with critical pulmonary stenosis, in whom they are not correlated.

In uncommon cases in which dimensions of the tricuspid valve are large, its leaflets usually show features of Ebstein malformation, with enlargement of the anterior leaflet and downward displacement onto the ventricle of the origin of a dysplastic septal leaflet. The posterior leaflet may or may not be abnormal. These valves are usually severely regurgitant. Another pathologic lesion of the tricuspid valve has been recognized in patients with dilated RV and severe tricuspid regurgitation—that of unguarded tricuspid orifice, in which the inferior (mural) leaflet is absent rather than displaced.

Right Atrium

The right atrium is enlarged, and it is more enlarged when there is severe tricuspid regurgitation. An interatrial communication is present in all cases, usually a patent foramen ovale of adequate size. However, shortly after birth the foramen becomes restrictive in some patients. The eustachian valve is frequently prominent.

Left-Sided Chambers

The left atrium is usually hypertrophied and somewhat enlarged, and the mitral orifice is usually larger than normal. The LV shows some hypertrophy and endocardial fibroelastosis. Occasionally the interventricular septum into the LV cavity has been noted, with some speculate that this might produce subaortic obstruction. Clinical and postmortem studies have demonstrated evidence of LV myocardial ischemia in virtually all patients, perhaps related to this, LV compliance is depressed in many.

Aorta

The aorta usually has adult morphology without ischemic narrowing and is usually left sided.

Ductus Arteriosus

The ductus arteriosus is patent at birth but has the usual tendency to close. Orientation of the ductus is typical for pulmonary atresia of all forms, with an obtuse proximal and acute distal angle at its aortic attachment. Usually the bronchial arteries are normal, and important aortopulmonary collateral arteries absent.

Coexisting Cardiac Anomalies

Other than Ebstein malformation, coexisting cardiac anomalies are uncommon.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Symptoms and Signs

Fetal distress is usually not evident except in those with a large RV. Delivery is typically uncomplicated and at term. The babies are generally well developed (Fig. 40-3) and are likely initially to appear healthy except for cyanosis. Cyanosis is usually obvious on the first day and becomes rapidly more severe as the ductus closes and there is respiratory distress and progressing metabolic acidosis. In the New England series, 81% of babies presented during the first week.

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**Figure 40-2** Relationship between diameter of the tricuspid valve (by echocardiography), expressed as z value, and size of the right ventricular cavity (grade estimated subjectively from echocardiographic and cineangiographic studies) in patients with pulmonary atresia and intact ventricular septum (n = 71). (From Hanley and colleagues.)
QRS axis in the frontal plane is usually normal or shows a rightward deviation, and the RV hypertrophy pattern usually present in the neonate is absent. However, electrocardiographic evidence of RV hypertrophy may be present even though the RV cavity is small, precluding its use to predict RV cavity size.

Echocardiography

Two-dimensional echocardiography is diagnostic (Fig. 40-5). Also, dimensions of the tricuspid valve, RV cavity size, and nature of the outflow obstruction (membranous or muscular) can be determined with confidence. Of importance is the fact that RV–coronary artery fistulae can be identified accurately by two-dimensional echocardiography with pulsed Doppler color flow ultrasound imaging (Fig. 40-6). However,
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stenoses, coronary sinusoids, and RV-coronary fistulae. If these are present, extent of LV myocardial dependence on the RV must be established.

Right atrial mean pressure is usually higher than left, and a prominent $a$ wave can be seen on the pressure tracing. RV peak pressure is usually higher than or equal to systemic pressure, although it may be less in association with severe tricuspid regurgitation and a thin-walled RV. Systemic arterial saturation is low, but varies according to flow through the patent ductus arteriosus. Size and configuration of the RV cavity can be displayed by RV angiography (Fig. 40-7). In Ebstein anomaly with severe tricuspid regurgitation presenting in the neonatal period in association with high pulmonary vascular resistance, RV systole may fail to open a normal pulmonary valve; high-quality angiography will prevent the mistaken diagnosis of pulmonary atresia.

Quantitative cineangiographic studies indicate reduced RV function in essentially all cases. LV function and end-diastolic volume are also abnormal unless a normal LV mass is present.

Cardiac Magnetic Resonance Imaging and Computed Tomography Angiography

These imaging modalities are not typically used during the neonatal period. They may, however, be useful in evaluating older patients. Evaluation of cavity size and degree of musculature of the RV can be accurately determined using cardiac magnetic resonance (CMR) imaging (Fig. 40-8). Delayed-enhancement CMR can be used to determine the status of the myocardium as well (Fig. 40-9). Volume-rendered computed tomography (CT) angiography imaging can also accurately define abnormal coronary connections (Fig. 40-10).

NATURAL HISTORY

Pulmonary atresia and intact ventricular septum is an uncommon malformation, occurring in 1% to 1.5% of individuals born with congenital heart disease. It was present in 3% of critically ill infants with congenital heart disease in the New England series. It is highly lethal, with about 50% of individuals dying within 2 weeks of birth and about 85% by age 6 months (Fig. 40-11). Death is caused by severe hypoxia and metabolic acidosis and usually coincides with spontaneous closure of the ductus arteriosus. Rarely, patients survive into young adult life. McArthur and colleagues describe a 21-year-old whose pulmonary blood flow came from a right coronary–pulmonary arterial fistula, and Robicsek and colleagues describe another patient of similar age who survived because of a congenital aortopulmonary window.

TECHNIQUE OF OPERATION

Overview

No single neonatal operation is standard for pulmonary atresia with intact ventricular septum; rather, several surgical procedures, either in isolation or in combination, are indicated based on the details of the morphology in each case (see Indications for Operation later in this chapter for a description of the best initial operation for each morphologic variant). The initial operation most commonly indicated for
patients will ultimately require a bidirectional cavopulmonary shunt as part of their overall surgical management. A prostaglandin E₁ (PGE₁) infusion is started as soon as possible to maintain ductal patency and is continued until after the surgical procedure. The full dose is 0.1 mg · kg⁻¹ · min⁻¹; when the ductus is confirmed to be open, the dose often can be reduced.

Figure 40-7 Cineangiograms in neonates with pulmonary atresia and intact ventricular septum. A, Right ventriculogram, frontal view. Small right ventricle (RV) has smooth borders, infundibular cavity is obliterated, and tricuspid valve shows severe regurgitation. B, Right ventriculogram from another patient in (B1) frontal and (B2) lateral views. The RV is very small, but its walls are trabeculated. Sinusoid channels are connected with coronary circulation. C, Left ventriculogram in frontal view in another patient. The left ventricle (LV) has its usual appearance and supports the aorta. A right Blalock-Taussig shunt has been made. Key: AO, Aorta; IVC, inferior vena cava; RA, right atrium; RPA, right pulmonary artery; RSA, right subclavian artery; SVC, superior vena cava.

this entity is concomitant transanular patching, systemic-pulmonary artery shunting, and ductal ligation. The next most common procedure is an isolated systemic-to-pulmonary artery shunt and ductal ligation.

For all of the procedures described, postnatal preoperative management is similar. Following birth, an arterial pressure monitoring catheter is placed, preferably into the left radial artery. (A right radial artery catheter should be avoided because of the possibility that a systemic-to-pulmonary artery shunt originating from the right subclavian artery will be part of the surgical procedure.) A reliable intravenous line is placed into either the femoral or umbilical vein. In general, deep intravenous lines into the upper body, such as into the subclavian or jugular veins, should be avoided to minimize thrombosis in the upper body venous system, because many patients will ultimately require a bidirectional cavopulmonary shunt as part of their overall surgical management. A prostaglandin E₁ (PGE₁) infusion is started as soon as possible to maintain ductal patency and is continued until after the surgical procedure. The full dose is 0.1 mg · kg⁻¹ · min⁻¹; when the ductus is confirmed to be open, the dose often can be reduced.

Endotracheal intubation and mechanical ventilation are usually necessary, either as part of general resuscitative measures, or as a result of inhibition of intrinsic ventilatory drive due to PGE₁. A low inspired oxygen fraction and controlled hypercarbia are used to counter the tendency for overcirculation through the ductus arteriosus. Low-dose inotropic support with dopamine or milrinone may be needed to support the systemic circulation.
Concomitant Placement of Transanular Patch and Systemic–Pulmonary Artery Shunt

A median sternotomy is made through an incision that is carried a little farther into the neck than usual to provide better exposure of the brachiocephalic trunk and subclavian arteries. After the pericardium is opened and stay sutures applied, the right pulmonary artery between the aorta and superior vena cava is dissected.

A 3.5-mm expanded polytetrafluoroethylene (PTFE) tube (3.0 mm if the neonate is smaller than about 2.5 kg) is cut to proper length. Without giving heparin at this time, a fine...
Cardiopulmonary bypass (CPB) is established, with the perfusate warm and normocalcemic. The neonate’s temperature is maintained at approximately 34°C during CPB. The surgically created shunt is temporarily occluded by placing a vascular clamp on the PTFE tube. The operation may be done with the heart beating, or cold cardioplegia and controlled reperfusion may be used (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).

A longitudinal incision is made in the pulmonary trunk, and the cartilaginous valve plate is incised. The incision is carried proximally onto the RV, taking care to find and stay in the cavity of the infundibulum and to extend it to the sinus portion and distally along the pulmonary trunk, stopping just before the bifurcation. The patch, preferably made from glutaraldehyde-treated autologous pericardium, is sewn into place with 7-0 polypropylene continuous suture. The suture line does not include the full thickness of the incised RV wall, but rather incorporates the epicardium and about 30% of the outer thickness of the RV wall. The foramen ovale must not be closed.

The aortic clamp is released (or controlled reperfusion accomplished), and preparations are made for discontinuing CPB. The vascular clamp is removed from the PTFE tube, and when normothermia is regained, CPB is discontinued and the remainder of the operation completed as usual.

Other Initial Operations

Other initial operations are indicated based on specific morphology. These include isolated placement of a systemic to pulmonary artery shunt and ductal ligation; isolated placement of a transanular patch and ductal ligation using CPB; pulmonary valvotomy, placement of a systemic-to-pulmonary artery shunt, and ductal ligation using CPB; and isolated pulmonary valvotomy and ductal ligation using CPB (Fig. 40-12).

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Postoperative care is the same as described under “Special Features of Postoperative Care” in Chapter 39 for critical pulmonary stenosis in neonates. As in the case with pulmonary stenosis, need for an additional surgical procedure is continually assessed.

**RESULTS**

**Survival**

**Early (Hospital) Death**

Overall hospital mortality of a heterogeneous group of neonates with pulmonary atresia and intact ventricular septum, virtually all of whom have had one or more procedures, has been about 20%.$^{11}$ However, the hazard function for death does not level off appreciably until 3 to 6 months (Fig. 40-13). This plus the wide variability of morphology and of procedures makes the unadjusted figure of little value. More recent studies that have followed, in general, the guidelines described under *Indications for Operation* (see later) show improved early survival. In one study,$^{13}$ there was 1 hospital death among 47 patients (2.1%; CL 0.4%-6.8%), and in another,$^{14}$ 5 early deaths among 44 patients (11%; CL
Survival after initial procedure (performed, on average, at age 3 days) of neonates with pulmonary atresia and intact ventricular septum (n = 171). Circles represent individual deaths, and vertical bars represent 70% confidence limits of non-parametric estimates. Solid line represents parametrically determined continuous point estimates, and dashed lines enclose 70% confidence limits. Excluded were patients having abnormally large right ventricles with or without Ebstein malformation (n = 13, of whom 11 died) and those having no procedure (n = 8, among whom 7 died; 3 are among the 13 just mentioned). Depiction is of 153 patients. A, Survival. B, Hazard function. (From Hanley and colleagues.)

**Figure 40-13** Survival after initial procedure (performed, on average, at age 3 days) of neonates with pulmonary atresia and intact ventricular septum (n = 171). Circles represent individual deaths, and vertical bars represent 70% confidence limits of non-parametric estimates. Solid line represents parametrically determined continuous point estimates, and dashed lines enclose 70% confidence limits. Excluded were patients having abnormally large right ventricles with or without Ebstein malformation (n = 13, of whom 11 died) and those having no procedure (n = 8, among whom 7 died; 3 are among the 13 just mentioned). Depiction is of 153 patients. A, Survival. B, Hazard function. (From Hanley and colleagues.)

**Table 40-3** Incremental Risk Factors for Death in Pulmonary Atresia and Intact Ventricular Septum

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Single Hazard Phase P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td></td>
</tr>
<tr>
<td>(Lower) Birth weight</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>RV-dependent circulation</td>
<td>.03</td>
</tr>
<tr>
<td>(Smaller) Dimension (z value) of tricuspid valve</td>
<td>.03</td>
</tr>
<tr>
<td>If valvotomy or transanular patching performed with a shunt</td>
<td>.001</td>
</tr>
<tr>
<td>Procedural</td>
<td></td>
</tr>
<tr>
<td>(Earlier) Date of shunt alone</td>
<td>.002</td>
</tr>
</tbody>
</table>

Data from Hanley and colleagues. Based on 171 neonates with pulmonary atresia in the Congenital Heart Surgeons Society study (1987-1991). Excluded were patients with Ebstein malformation or right ventricular cavity size greater than normal (n = 13, 11 of whom died) and those having no procedure (8, among whom 7 died; 3 are among the 13 just mentioned), leaving 153 neonates who actually underwent a procedure. Time zero was time of first intervention. Coefficients, their standard deviation, and other details of the multivariable equation resulting from the analysis are in cited article. Key: RV, Right ventricle.

**Figure 40-14** Survival after various initial procedures in a heterogeneous group of patients with pulmonary atresia and intact ventricular septum. In addition, eight patients (seven of whom died) underwent no procedure, and one underwent an unknown procedure. No patient had an initial percutaneous procedure. In general, patients who received a pulmonary-systemic shunt (with or without atrial septectomy) had the smallest tricuspid valves (z value ≤ −3). Key: TAP, Transanular patching. (From Hanley and colleagues.)

**Table 40-3** Incremental Risk Factors for Death in Pulmonary Atresia and Intact Ventricular Septum

6.7%-18%). A 40-year single-institution study of 210 patients also documents that survival has improved over time.

**Time-Related Survival**

Only about 60% of a heterogeneous group of neonates with pulmonary atresia and intact ventricular septum were alive 1 year after entrance into the hospital for treatment, as were 60% at 2 years and 58% at 4 years. The hazard function for death remains high but declining for the first 3 months, but after about 36 months it is only a little higher than that of an age-sex-race-matched general population. Patients with an abnormally large RV, with or without Ebstein malformation, have a particularly poor outlook regardless of treatment; about 85% die within the first year. Excluding this small group of patients, 1-month, 1-year, and 4-year survival has been somewhat better than in the heterogeneous group (see Fig. 40-13). Some recent single-institution reports suggest slightly better long-term outcome.

**Modes of Death**

The most common modes of death are acute heart failure and hypoxia.

**Incremental Risk Factors for Premature Death**

Survival after different initial procedures has varied widely (Fig. 40-14), but prevalence of small tricuspid valves and RV cavities has varied among the procedure groups. A more reliable understanding of the patient-specific and procedural risk factors for death is obtained by multivariable analysis (Table 40-3); validation of the analysis is shown in Appendix Fig. 40B-1.
Early mortality was low and unrelated to RV size. Interestingly, however, they demonstrated that interim mortality (defined as occurring after successful neonatal surgery but before the second-stage operation) was substantial: 15%. Furthermore, when they evaluated only patients with very small RV cavities, interim mortality was 24%.

Right Ventricular–Dependent Coronary Circulation

An RV-dependent coronary circulation is a powerful risk factor for death. In a study among 12 such patients, only 4 (CL 18%-52%) survived 1 or more years. There is evidence, however, that even this powerful risk factor has recently been neutralized to some extent (see Fig. 40-16). In a 2006 study focusing only on patients with RV-dependent coronary circulation, overall mortality was 19%. All patients were managed as neonates with a systemic-to-pulmonary artery shunt only; all deaths occurred within 3 months of the procedure. Notably, all three patients with no coronary-to-aorta connection died. All surviving patients have gone on to a bidirectional cavopulmonary connection or Fontan without further mortality. In another recent study, 2 of 5 patients (CL 14%-71%) with RV-dependent coronary circulation died.

The severity of coronary abnormalities and fistulae affect more than survival; they are also associated with reduced LV function at late follow-up.

Systemic–Pulmonary Artery Shunt

In the past, systemic–pulmonary artery shunting alone has been associated with lower overall survival than when other procedures were used (see Fig. 40-14). More recently, survival with a shunt alone has improved strikingly (see Fig. 40-16). This is the only procedure associated with reasonable survival in patients with very small tricuspid valves.

Birth Weight

As in nearly all types of congenital heart disease requiring treatment early in life, low birth weight is an important risk factor for death.

Interim Interventions after Initial Procedure

This section discusses further interim interventions performed before the definitive intervention leading to a separated two-ventricle system or a single-ventricle Fontan system. Patients whose initial procedure is a transanular patch and a systemic–pulmonary artery shunt generally do not require further interim procedures. This is an important advantage of this operation as the initial procedure. With it, the opportunity for maximal RV (and tricuspid valve) growth exists during the critical early weeks and months of life when myocardial hyperplasia is possible.

Among patients whose initial procedure is pulmonary valvotomy or placement of a transanular patch without a concomitant systemic–pulmonary artery shunt, about half require a systemic-pulmonary shunt within a few weeks (Fig. 40-17). The smaller the dimensions of the tricuspid valve, the greater the probability that a subsequent systemic–pulmonary artery shunt will be needed ($P = .04$) (Fig. 40-18).

Patients whose initial procedure is a pulmonary valvotomy with or without a concomitant shunt often subsequently require placement of a transanular patch (Fig. 40-19). No correlates with subsequent placement of such a patch have been identified. This suggests that a transanular patch should

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**Figure 40-15** Nomogram of a specific solution of a multivariable equation illustrating effects of dimension of tricuspid valve (expressed as $z$ value) and type of initial procedure on survival in neonates with pulmonary atresia and intact ventricular septum (see Table 40-3). Values for other variables entered into equation are birth weight 3.1 kg, right ventricular (RV)-dependent circulation, number, and in the case of a shunt operation, date of operation. This nomogram is a rational basis for therapy. (From Hanley and colleagues.)

**Figure 40-16** Nomogram of a specific solution of multivariable equation (see Table 40-3) demonstrating improvement in survival after an initial shunt procedure that has occurred across time, and effect of a right ventricular (RV)-dependent circulation. Value entered for birth weight is 3.1 kg. (From Hanley and colleagues.)

**Dimensions of Tricuspid Valve**

Small size ($z$ value of diameter) of the tricuspid valve is a strong risk factor for death (Fig. 40-15). An exception is the case of neonates in whom the initial procedure is a systemic–pulmonary artery shunt alone. When that procedure is used, survival is unrelated to dimension of the tricuspid valve (see Fig. 40-15). Survival after shunting appears to have improved recently, probably related to increased experience with making systemic–pulmonary artery shunts in neonates (Fig. 40-16). The recent two-center study by Fenton and colleagues is relevant to this discussion. They assessed survival among 35 patients who underwent a shunt-alone initial procedure. Although they did not measure tricuspid valve diameter, they evaluated RV cavity size, which is known to correlate with tricuspid valve size. Early mortality was low and
Definitive Procedures

It is not possible at present to know the prevalence of achieving (at some time) a separated two-ventricle repair. It appears to be about 60% to 70% in patients with a tricuspid valve \( z \) value of \(-2\) or greater, and less than 10% in those with very small \( z \) values.\(^{11}\)

Theoretically, in all patients in whom a separated two-ventricle repair cannot be accomplished, a single-ventricle Fontan system should eventually be achievable. The limiting factor in this group is survival to the time of a Fontan operation. Thus, the problem is analogous to that in patients with hypoplastic left heart physiology. Results of the Fontan operation in patients with pulmonary atresia and intact ventricular septum appear to be the same as in patients with other congenital cardiac anomalies.\(^{2,11}\) Patients with severe coronary abnormalities may, however, be at increased late risk.\(^{16}\)

A more difficult question is whether all patients not able to achieve a two-ventricle repair should eventually undergo a Fontan, or whether an alternative procedure should serve as the definitive operation in selected patients. For example, certain patients with tricuspid valve \( z \) values that are moderately small may best be served by a definitive operation consisting of a bidirectional superior cavopulmonary shunt combined with closure of the atrial septal defect and a procedure creating unobstructed RV to pulmonary artery flow, the so-called one-and-a-half ventricle repair.\(^{4,8,10,12,13}\) (see Special Situations and Controversies). In patients in whom the tricuspid valve and RV are functional, procedures may occasionally be necessary to correct tricuspid valve regurgitation.\(^{11}\)

Other Outcomes

Myocardial perfusion has been shown to be abnormal at mid- to late follow-up.\(^{23}\) The abnormalities are not restricted to patients with identified coronary fistulae, but include patients with apparently normal coronary arteries. Exercise capacity is

**Figure 40-17** Freedom from a subsequent shunt operation in neonates with pulmonary stenosis or atresia and intact ventricular septum undergoing an initial valvotomy (balloon or surgical) or insertion of a transanular patch without a concomitant shunt \((n = 105)\). (Format is as in Fig. 40-13.) Patients with Ebstein malformation or with a right ventricular cavity size greater than normal, or both, were not included in this analysis. Key: PA, Pulmonary atresia; PS, pulmonary stenosis. (From Hanley and colleagues.\(^{59}\))

**Figure 40-18** Nomogram of a specific solution of a multivariable equation illustrating the relationship between dimensions of the tricuspid valve (expressed as \( z \) value) and probability of being free of a subsequent shunt operation after initial pulmonary valvotomy or placement of a transanular patch without a concomitant shunt. (From Hanley and colleagues; see citation for coefficients and their standard deviation.)

**Figure 40-19** Freedom from a transanular patch (TAP) in neonates with pulmonary atresia and intact ventricular septum undergoing an initial pulmonary valvotomy with or without a concomitant shunt operation \((n = 46)\). (Format is as in Fig. 40-13.) Patients with Ebstein malformation, right ventricular cavity size greater than normal, or both were not included in this analysis. Multivariable analysis identified no risk factors for this event. (From Hanley and colleagues.\(^{11}\))
INDICATIONS FOR OPERATION

Presence of the malformation is generally an indication for operation because of its high lethality. As soon as the diagnosis is suspected, the neonate is resuscitated and stabilized, as described under Technique of Operation. Once the diagnosis is established and the baby is stabilized and in good condition, operation is undertaken, but in view of the favorable effect of PGE₁, it is not done as an emergency.

Selection of the initial intervention is based in large part on the estimated probability that a separated two-ventricle system will ultimately be possible. Indications given in this section are based on the work of de Leval and colleagues and on the findings of the Congenital Heart Surgeons Society study, (see Table 40-3 and Figs. 40-15 to 40-19). These two studies are entirely consistent with each other, as are those of other recent studies.

The inference from all available information is that the best guide to the type of initial operation is size of the tricuspid valve. A z value equal to or less than −4 (and by implication a very small RV chamber) makes probability of death after placement of a transanular patch with a concomitant shunt greater than after a systemic–pulmonary artery shunt alone (see Fig. 40-15). Furthermore, an achieved separated two-ventricle system has been extremely uncommon when the original z value of the tricuspid valve has been less than −3. This line of reasoning could be altered were it to be shown that growth of the hypoplastic tricuspid valve could be made disproportionally greater than that of the body as a whole.) Thus, in patients with pulmonary atresia and a z value of the tricuspid valve equal to or less than −4, an initial systemic–pulmonary artery shunt is indicated.

At age 3 to 6 months, a bidirectional superior cavopulmonary shunt is performed, followed by a Fontan operation (see Indications for Operation in Chapter 41). So long as a total cavopulmonary type of connection is used for the Fontan procedure, nothing need be done to the tricuspid valve. Any evident RV–coronary artery fistula should be closed, unless there is RV-dependent coronary circulation. When the z value of the tricuspid valve is greater than −4, the inference is that risk of death will be no greater (see Fig. 40-15), and probability of a separated two-ventricle system greater, when a transanular patch is placed (or, in special circumstances, a pulmonary valvotomy performed) and a concomitant shunt is placed rather than a systemic–pulmonary artery shunt alone.

Ideally, some objective method of determining need for a transanular patch should be available, but the decision must rest on the subjectively evaluated “adequacy” of the infundibular cavity, the “anulus,” and the pulmonary valve tissue itself. In the absence of any clear evidence of a substantial advantage of valvotomy in this setting, and because about 40% of those in whom a valvotomy has been done have required a subsequent transanular patch, a transanular patch should be used whenever doubt arises.

When an RV outflow operation is being performed as described, need for a concomitant systemic–pulmonary artery shunt is moderately related to RV cavity size and thus to dimension of the tricuspid valve (see Fig. 40-18). As a general guide, a concomitant systemic–pulmonary artery shunt should be performed, especially when the z value of the tricuspid valve is less than about −2 (indicating a small RV cavity).

When the initial procedure has been done under the hypothesis that a separated two-ventricle system will be possible, testing of that hypothesis should begin 6 to 12 months after the initial procedure. The shunt is temporarily occluded, ideally percutaneously. If arterial oxygen saturation remains high, the shunt is permanently closed by percutaneous or surgical techniques (for percutaneous technique, see “Percutaneous Closure of Large Aortopulmonary Collateral Arteries” under Special Situations and Controversies in Section II of Chapter 38). The atrial septal defect is temporarily occluded, again ideally by percutaneous techniques. If right atrial pressure remains below 12 to 15 mmHg, cardiac output is adequate, and oxygen saturation of blood in the right atrium is maintained (any decrease in cardiac output is compensated for by rise in arterial oxygen saturation), the defect should be closed permanently by a surgical or percutaneous technique (see “Closure of Atrial Septal Defects by Percutaneous Techniques” under Special Situations and Controversies in Chapter 30).

When the patient does not tolerate shunt closure, a separated two-ventricle system may not be possible, and consideration should be given to beginning the process leading to a Fontan operation or some other definitive procedure, such as the “one-and-a-half ventricle” repair as discussed earlier under “Definitive Procedures.” When closure of the atrial septal defect is not well tolerated, a prolonged period of procrastination may be wise if the patient’s clinical state is good.

Neonates with RV-dependent coronary circulation represent a special problem (see “Right Ventricular–Coronary Artery Fistulae” earlier under Morphology). When after detailed study, a considerable portion of the LV myocardium is judged to be in jeopardy of developing severe ischemia, decompression or thrombolytic exclusion of the RV is contraindicated. The recent study by Calder provides quantitative information on the amount of LV myocardium at risk of ischemia and how it relates to outcome. These patients may be treated the same as other patients with severely hypoplastic tricuspid valves and RVs, so long as the type of Fontan operation allows fully saturated blood to enter the RV. In time, cardiac transplantation may prove the optimal treatment for this small subset of patients.

SPECIAL SITUATIONS AND CONTROVERSIES

Percutaneous Valvotomy

It has been recognized for some time that percutaneous techniques could become the initial procedure for neonates in whom the pathway through the infundibulum is reasonably wide and the atresia “membranous.” In 1991, this was achieved successfully by laser valvotomy followed by balloon dilatation. Other reports have followed, with mixed outcome. Shinebourne and colleagues recommend percutaneous valvotomy in all cases of membranous atresia with an RV and tricuspid valve that have the potential for a biventricular repair. Even in this favorable subgroup, 60% will remain duct dependent and require a systemic-to–pulmonary artery
shunt. Similarly, Humpf and colleagues attempted percutaneous valvotomy in a highly selected subgroup. Of 30 patients, the valve could not be perforated in 3 (10%; CI 4.6%-19%), 14 required a shunt (47%; CI 36%-57%), and 4 (13%; CI 7.1%-23%) required RV outflow surgery. Thus, more than two thirds of the group required surgical intervention. In the study by Hirata and colleagues, only 2 of 17 patients (12%; CI 4.2%-25%) undergoing percutaneous valvotomy did not require an additional neonatal surgical procedure involving either a shunt or the RV outflow tract. Similar outcomes were observed by McLean and Pearl.

In the U.K.-Ireland multicenter study, neonates undergoing percutaneous valvotomy had an increased risk of reintervention to increase pulmonary blood flow relative to those undergoing initial surgery. Thus, this method has the same limitations as surgical valvotomy or transanular patching without a concomitant shunt—particularly the potential delay of weeks or months in maximizing the stimulus to RV growth—and is associated with a higher likelihood of reintervention than these initial surgical procedures (see “Interim Interventions after Initial Procedure” earlier under Results).

**Formalin Infiltration of Ductus Arteriosus**

In 1975, Rudolph and colleagues introduced formalin infiltration of the wall of the ductus via a left thoracotomy as a means of maintaining patency and avoiding need for an artificial shunt. In carefully selected patients with favorable anatomy, this technique may provide outcome similar to that of surgical intervention. Others have observed ductal closure within a few weeks or months of the procedures, and its use is not currently recommended.

**Right Ventricle–to-Aorta Conduit**

Use of an RV-to-aorta conduit for patients with RV-dependent coronary circulation has been used by several groups to limit myocardial ischemia. Although outcomes have been good, the extremely limited use of this procedure prevents adequate assessment of its effectiveness.

**Tricuspid Valve Closure in the Presence of Right Ventricle–Coronary Fistulae**

Several groups advocate closing the tricuspid valve orifice in the setting of RV-coronary fistulae without major coronary abnormalities. Limited experience prevents adequate analysis of this procedure.

**Tricuspid Valve Growth**

The tricuspid valve and RV cavity tend under some circumstances to increase in size as the patient grows. However, there is little evidence that disproportionate enlargement occurs as growth of the child proceeds, no matter what the surgical procedure. The only evidence for disproportionate growth comes from a recent study by Huang and colleagues of 40 patients undergoing initial neonatal surgical pulmonary valvotomy and shunt. They showed that on average, there was no change in tricuspid valve z value over time; however, on an individual patient basis, 32% showed tricuspid valve enlargement of at least +2 z values at follow-up.

There is evidence that the RV cavity increases in size, but this may result from iatrogenic pulmonary or tricuspid regurgitation or both (Fig. 40-20). The tricuspid valve appears to grow proportionally with the child when there is forward flow across the tricuspid and pulmonary valves, but not otherwise (Fig. 40-21). With growth of the RV, right ventricular–coronary artery fistulae may disappear. However, important abnormalities of RV compliance usually remain. Thus, there is at present no basis for determining treatment on anything other than z value of the tricuspid valve before initial therapy.

**Bidirectional Cavopulmonary Shunt in Right Ventricle–Dependent Coronary Circulation**

It is widely acknowledged that the blood entering the RV (and thus perfusing the coronary circulation) following a total cavopulmonary connection type of Fontan in patients with RV-dependent coronary circulation will be fully or almost fully saturated. Miyaji and colleagues recently have shown that the blood entering the RV after a superior cavopulmonary shunt (“bidirectional Glenn”) is also more saturated than that under conditions of a systemic-to-pulmonary shunt. This raises the question of whether there is value...
in performing an early superior cavopulmonary shunt in patients with RV-dependent coronary circulation.

Right Ventricular Sinus Myectomy

Because it is well accepted that the RV in this malformation is intrinsically tripartite and only becomes bipartite or unipartite from muscular ingrowth and cavity obliteration, it is logical to infer that removal of the excess muscle may have therapeutic value in selected cases. Bryant and colleagues studied this in 16 patients. They concluded that the procedure leads to an immediate increase in RV volume and is associated with achievement of a biventricular repair in 87% of selected patients. Of concern, they also noted that tricuspid valve growth in relation to somatic growth was minimal, potentially limiting long-term success of this procedure.

Assessment of Functional Benefit of Biventricular Versus Univentricular Definitive Procedures

Evidence supporting the generally held view that a biventricular repair is superior to a Fontan is limited at best. Redington and colleagues showed that a biventricular repair in patients with this malformation had restrictive RV physiology, with antegrade flow across the pulmonary valve during atrial contraction. This implies limited functional capacity. Exercise capacity was assessed by Sanghavi and colleagues and found to be similar in patients with biventricular repair and Fontan. Patients in both groups had subnormal peak VO₂, with increasing impairment associated with increasing age. Based on these findings, it is not surprising that Numata and colleagues were unable to demonstrate a benefit in exercise capacity of the so-called one-and-a-half ventricle repair over the Fontan.
**Figure 40A-1** Nomogram for conversion of diameter of tricuspid valve (obtained by echocardiography) to $z$ value. Nomogram assumes a circular shape of tricuspid valve, which is usually the case in patients with pulmonary atresia and intact ventricular septum. (For a description of $z$ value and its method of determination, see “Dimensions of Normal Cardiac and Great Artery Pathways” in Chapter 1.)

**Figure 40B-1** Validation of multivariable risk factor equation (see Table 40-3) for death after initial procedure in patients with pulmonary atresia and intact ventricular septum. Patients with Ebstein malformation, right ventricular cavity size greater than normal, or both were not included in this analysis. Symbols represent nonparametric survival estimates, and vertical bars represent confidence limits for each of the three major treatment groups. Solid lines indicate parametrically estimated survival, and dashed lines enclose their 70% confidence limits, which are obtained by averaging parametric estimates for each patient within each group (see “Parametric Hazard Function Regression” in Section IV of Chapter 6). Note close correspondence of average parametric estimate to nonparametric estimate. (From Hanley and colleagues.)
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Section 1  Tricuspid Atresia and Single-Ventricle Physiology

DEFINITION

Tricuspid Atresia

Tricuspid atresia is a congenital cardiac malformation in which the right atrium, in the setting of ventricular D-loop, fails to open into a ventricle through an atrioventricular (AV) valve. Thus, there is univentricular AV connection consisting of a left-sided mitral valve between morphologically left atrium and left ventricle (LV). Atrial situs is almost invariably solitus (normal) in association with ventricular D-loop, and the right ventricle (RV) is hypoplastic. A ventricular septal defect (VSD) usually is present. Ventriculoarterial connection may be concordant or discordant (transposed great arteries). Rarely, tricuspid atresia occurs in situs inversus with ventricular L-loop (mirror-image pattern).

Patients with atrial situs solitus and ventricular L-loop in which the left-sided left atrium is separated from a left-sided hypoplastic morphologically RV by an atretic left-sided (tricuspid) AV valve are excluded from this discussion; they are considered in Chapter 56.

Single-Ventricle Physiology

Single-ventricle physiology is present when there is impossibility or inadvisability of surgically reconstructing a functional two-ventricle heart with separated in-series pulmonary and systemic circulations. The spectrum of surgical management of single-ventricle physiology is generally similar for tricuspid atresia, other types of univentricular AV connection (see Chapter 56), and other anomalies without two adequate ventricles (see “Fontan versus Intracardiac Repair for Complex Morphology” later in this section) and is based on the Fontan operation. All such anomalies have in common the limitation of single-ventricle physiology, regardless of their specific morphology. Therefore, the Fontan operation and all its modifications and applications, as well as the spectrum of pre-Fontan palliative operations, are discussed fully in this chapter.

HISTORICAL NOTE

In 1906, Kuhne apparently recognized the entity of congenital tricuspid atresia and described its two basic morphologic subsets: hearts with concordant ventriculoarterial connection and hearts with discordant connection.31 In 1949, Edwards and Burchell further emphasized these two subsets and added presence or absence of pulmonary stenosis as another categorizing feature.31 Tandon and Edwards added further descriptive features in 1974.72 The clinical features of tricuspid atresia were described by Bellet and colleagues in 1933 and by Taussig and by Brown in 1936.99,23,7a Controversy arose early and continues as to whether tricuspid atresia should be considered a subset of single ventricle (see Historical Note in Chapter 56).83 From a surgical point of view, it is best considered as such, but tradition and its prevalence support presenting it as a separate entity.

Systemic–pulmonary arterial shunts developed in 1945 by Blalock and Taussig and later by Potts and by Waterston (see Historical Note in Section I of Chapter 38) were soon applied to cyanotic patients with tricuspid atresia. In 1958, Glenn specifically applied the superior vena cava–to–right pulmonary artery anastomosis to patients with tricuspid atresia.920 The basis for the classic Glenn shunt was experimental studies reported by Carlton and colleagues in 1951, by Glenn and colleagues, and by Robicsek and colleagues, showing that systemic venous pressure was adequate to drive pulmonary blood flow.6,6,21,20,9,2,4,11 In Moscow, Bakuljev and Kolesnikov independently developed these same concepts.31 In 1966, Haller and colleagues demonstrated experimentally the possibility of performing a bidirectional superior cavopulmonary anastomosis.14 This was applied clinically by Azzolina and colleagues in 1974, and in 1985, Hopkins and colleagues further refined the procedure with an end-to-side anastomosis of superior vena cava (SVC) to undivided right pulmonary artery (RPA).23,14 Abrams and colleagues applied this idea in the form of a side-to-side anastomosis of SVC to undivided RPA.41 In 1984, Kawashima and colleagues added a further improvisation in patients with either one or two SVCs, and azygos or hemiazygous continuation of the inferior vena cava (IVC) into an SVC, with only splanchic and coronary venous blood draining into the right atrium.410 They divided the SVC (both, if there were two), closed its cardiac end, and anastomosed the SVC end to side to the pulmonary artery after closing the pulmonary trunk. This total cavopulmonary shunt was an incompletely Fontan operation in which only splanchic and coronary venous blood drained directly to the systemic arterial circulation.21,10,31,19

Successful repair of tricuspid atresia with separation of right and left circulations was accomplished in 1968 by Fontan and colleagues and was reported in 1971.11,1,16 This was preceded by experimental studies in 1943 by Starr and colleagues, demonstrating that destroying a dog’s RV did not result in systemic venous hypertension;84 in 1949 by Rodbard and Wagner, demonstrating that the RV could be bypassed;1,16 and in 1954 by Warden, DeWall, and Varco, demonstrating the feasibility of bypassing the RV with a right atrial–pulmonary artery anastomosis.83 Based on these experiments, Hurwitt and colleagues reported an unsuccessful attempt to correct tricuspid atresia by a right atrial–to–pulmonary artery anastomosis in 1955.121 Fontan’s procedure involved constructing a cavopulmonary (Glenn) anastomosis with, in
the first patient, a direct anastomosis between right atrial appendage and proximal end of the divided RPA. In the subsequent two patients, one of whom had discordant ventriculoarterial connection, an aortic allograft valved conduit was placed between right atrium and RPA. In all three patients, an allograft valve was inserted into the IVC ostium, foramen ovale closed, and pulmonary trunk ligated or divided. In 1973, Kreutzer and colleagues reported a modification of Fontan’s operation in which the patient’s pulmonary trunk with its intact pulmonary valve was excised from the RV and anastomosed to the right atrial appendage after closing the VSD and atrial septal defect (ASD). A Glenn procedure was not performed, and no IVC valve was used.28

Other early reports of successful repairs were those of Ross and Somerville and of Stanford and colleagues.2,22,23 Fontan subsequently modified the operation that he and Baudet had originally performed,22,23 many others have as well.2,18,21,22,28,29 Bjork described direct anastomosis between right atrial appendage and RV outflow tract in patients with a normal pulmonary valve, using a roof of pericardium to avoid a synthetic tube graft.9,15 Direct right atrial–pulmonary artery connection, used by Fontan in his first case, has been modified and widely used.14,22,26,63

The extracardiac conduit Fontan modification, in which the IVC is disconnected from the right atrium and connected by a prosthetic tube to the RPA outside the heart, has become popular. A bidirectional superior cavopulmonary connection completes the procedure. This was first described by Humes for use only in special cases of complex venous anatomy.120 It was subsequently modified for use as the procedure of choice for all Fontan candidates by Marcelletti and colleagues and further modified as a closed heart, partial bypass, or off-bypass procedure by Petrossian and colleagues.89,41

Choussat and Fontan and colleagues formalized a set of risk factors (“ten commandments”) for the Fontan operation in 1979.21 In 1988, Laks and colleagues introduced the concept of deliberately making the separation between caval and pulmonary venous pathways incomplete, and then adjusting or closing the communication early postoperatively by percutaneous manipulation of a snare.81,1,3,1,6 Bridges and colleagues modified this approach by closing the residual aperture using catheter techniques late postoperatively.129 Although the Fontan operation was introduced as a treatment for tricuspid atresia, it was soon realized that it was applicable to many other forms of univentricular AV connection. In 1976, Yacoub reported its use for single ventricle,80 and pulmonary venous pathways incomplete, and then adjusting or closing the communication early postoperatively by percutaneous manipulation of a snare.81,1,3,1,6 Bridges and colleagues modified this approach by closing the residual aperture using catheter techniques late postoperatively.129 Although the Fontan operation was introduced as a treatment for tricuspid atresia, it was soon realized that it was applicable to many other forms of univentricular AV connection. In 1976, Yacoub reported its use for single ventricle,80 and by 1980, for many other anomalies with one severely hypoplastic ventricle.310 The Fontan operation has subsequently been used to treat a group of patients who have two adequate ventricles and AV valves but who are judged by some surgeons to have intracardiac morphology too complex for biventricular repair.224

MORPHOLOGY AND MORPHOGENESIS

In tricuspid atresia, there is no direct connection between right atrium and RV, but the left atrium connects through the mitral valve to the LV. Atria is usually muscular (75% of cases), meaning the AV connection is absent; it may be membranous with an imperforate AV connection.17,54 In the muscular type, presence of a tiny dimple in the right atrial floor may or may not represent the atretic valve. The dimple has been said to lie above the LV or ventricular septum in most cases and may then transilluminate from the LV.17,15,11,20,36 In such instances, it may represent a remnant of membranous AV septum.18

The membranous type has three variants. In one, a fibrous diaphragm blocks the AV orifice, and remnants of the valvar apparatus are occasionally found beneath the membrane in the RV. This has been called tricuspid atresia with imperforate valve membrane.16,54 It is often associated with left-sided juxtaposition of atrial appendages and discordant ventriculoarterial connection.71 Overall, juxtaposed atrial appendages are found in 11% of patients with tricuspid atresia.17 In a second, there is classic Ebstein anomaly (see Chapter 42) that is imperforate because of completely fused leaflets that are also fused to the wall of a small RV9,41,36 (Fig. 41-1). In a third and rarer variant, there is an AV septal defect in which the right-sided valve is imperforate and blocks the opening between right atrium and RV (Fig. 41-2). An autopsy series, focused on left-sided structures in tricuspid atresia, identified a high prevalence of mitral valve and LV abnormalities, including cleft mitral valve, muscularized subvalvar apparatus, and abnormal muscle bundles.73

There are two major morphologic subsets of tricuspid atresia:

■ Origins of great arteries are normal (concordant ventriculoarterial connection; 60% to 70% of cases).
■ Origins of great arteries are transposed (discordant ventriculoarterial connection; about 30% to 40% of cases).80,1,25

Rarely, the ventriculoarterial connection is double outlet right ventricle (DORV) or double outlet left ventricle (DOLV) or single outlet with truncus arteriosus.17 Other rare variants exist, and it has been estimated that only about 80% of patients diagnosed as having tricuspid atresia actually have the typical two morphologies.16,17

Tricuspid Atresia and Concordant Ventriculoarterial Connection (Normally Related Great Arteries)

This form of tricuspid atresia was referred to as type I by Edwards and Burchell and by Vlad.1,16,11 Atria are usually in situ solitus. The right atrium and its appendage are enlarged and thick walled, and an interatrial communication is present, usually through a fossa ovalis ASD (Fig. 41-3). The valve of the fossa ovalis may be redundant and bulge into the left atrium and contain multiple fenestrations. The ASD is generally large; by hemodynamic studies, Dick and colleagues found that only 4% of patients had a restrictive ASD.516 Uncommonly, the defect is an ostium primum ASD in association with a cleft left AV valve, and rarely there is a common atrium (see Morphology in Chapter 34).

The eustachian valve is often prominent, and in about 5% of cases it extends superiorly to form a veil or partition across the right atrium, so-called cor triatriatum dexter (see Morphology in Chapter 32).15,73 At operation, this may be confusing to the unprepared surgeon.

The left atrium is morphologically normal but enlarged from obligatory shunting of systemic venous blood across the ASD. The mitral valve is usually larger than normal, as is the LV, because both systemic and pulmonary venous return pass through them. The LV is also hypertrophied and its
Figure 41-1  Specimen and cineangiogram of tricuspid atresia coexisting with Ebstein malformation. A, Exterior view of heart shows displaced left anterior descending coronary artery (LAD) and small right ventricle (RV) to its right. Cordlike pulmonary trunk remnant wraps around proximal aorta where it arises from left ventricle (LV). B, Interior of RV and right atrium (RA). Septal and posterior leaflets are downwardly displaced from tricuspid anulus (dotted line). All three leaflets are loosely adherent to RV wall and join to form an imperforate membrane. Aneurysmal bulge of septal leaflet covers a potential ventricular septal defect. The blind RV is markedly hypertrophied. C, Cineangiogram frame from a similar patient in right anterior oblique projection shows site of tricuspid anulus (arrow) and blind diverticulum formed by fused leaflets. Key: A, Anterior leaflet; AN, aneurysm, septal leaflet; Ao, aorta; D, diverticulum; FO, fossa ovalis; LAA, left atrial appendage; P, posterior tricuspid leaflet; PT, pulmonary trunk; RAA, right atrial appendage; S, septal tricuspid leaflet; SVC, superior vena cava.

Figure 41-2  Specimen of tricuspid atresia with an atrioventricular (AV) septal defect. A, Frontal view with thin-walled, small right ventricle (RV) and pulmonary trunk (PT) open. Rightward portions of AV valve are fused to form an imperforate fibrous membrane. Note large, thick-walled left ventricle (LV). Pulmonary valve is normal. Ventricular septal defect (VSD) is not visible in this view. B, View of opened LV to show typical scooped-out ventricular septal crest and superior and inferior leaflets of left side of AV valve. VSD is adjacent to inferior leaflet. Key: A, Imperforate membrane; AML, left AV valve leaflets; Ao, aorta; RAA, right atrial appendage.
PART VII  Congenital Heart Disease

size and position and is sometimes multiple. In general, the larger the VSD, the larger the RV. The VSD usually lies below the infundibular (conal) septum, and from the LV side is separated from the noncoronary aortic cusp by infundibular muscle. When the VSD is large, it may extend inferiorly to the membranous septum, or it may be entirely muscular, lower in the septum, and sometimes slit-like. The VSD and trabeculated portion of the RV into which it opens are frequently separated from the smooth-walled distal portion by a narrow opening that looks like an os infundibulum (see “Infundibulum” under Morphology in Section I of Chapter 38). Like other VSDs, it frequently narrows spontaneously and is therefore often small and may close completely. In some hearts, the RV is large and has a true sinus portion (Fig. 41-5).

In 85% to 95% of patients, pulmonary blood flow is obstructed. Obstruction most commonly occurs at the os infundibulum, or it may occur at the VSD or throughout the entire infundibulum (Fig. 41-6). The pulmonary valve is bicuspid in about 20% of cases, but usually it and the “anulus,” trabeculations typically fine, although anomalous muscle bands near the posterior papillary muscle are occasionally present.

The normally positioned RV is highly abnormal and typically similar to the small RV of double inlet left ventricle (DILV; see Morphology in Chapter 56). In most hearts it consists of a distal tubular smooth-walled portion with a thin free wall and a smaller proximal trabeculated portion into which a VSD usually opens (Fig. 41-4). The VSD varies in

Figure 41-3  Cineangiogram frame in tilted left anterior oblique projection in tricuspid atresia that shows right-to-left atrial shunt through a stretched patent foramen ovale (large arrow). Valve of fossa ovalis is outlined by small arrows. There is no right ventricular filling. Key: LA, Left atrium; RA, right atrium.

Figure 41-4  Cineangiogram of tricuspid atresia and concordant ventriculoarterial connection in four-chamber view. Injection is into left ventricle, which is mildly enlarged. Severely hypoplastic sinus portion of right ventricle is evident, as is the infundibular outlet portion. Pulmonary valve “anulus” and pulmonary arteries are slightly small but not restrictive. Bifurcation of pulmonary trunk is normal, as is usually the case.

Figure 41-5  Cineangiogram in left anterior oblique projection of tricuspid atresia and a reasonably large right ventricle (RV). A, Systolic frame shows a large ventricular septal defect (VSD) entering RV and a wide channel to pulmonary trunk (PT). B, Enlargement of both right and left ventricles in diastole and large mitral valve orifice. Key: Ao, Aorta; LV, left ventricle; M, mitral orifice.
although a little smaller than normal, are not obstructive (diameter usually within 1 standard deviation of normal). The pulmonary trunk and branch pulmonary arteries are usually a little small, but only uncommonly (about 5% of patients) are they severely hypoplastic and restrictive to flow.\textsuperscript{B15, C33}

In about 10% of cases in this subset, the pulmonary valve is atretic. Under these circumstances, trunk and branch pulmonary arteries are usually small, and pulmonary blood flow (Qp) is via a patent ductus arteriosus or aortopulmonary collateral artery. The RV is usually extremely small, represented only by a minuscule endothelium-lined slit that is often inapparent on gross examination.\textsuperscript{B15} The same is usually true when a VSD is absent. However, an RV chamber may be found in tricuspid atresia without a VSD.\textsuperscript{E1, M12, M44}

\textit{Absent pulmonary valve} is rarely described with type 1 tricuspid atresia. In a report documenting three newly described cases, it was noted that only 24 previous cases had been described.\textsuperscript{L22} A number of associated lesions that are atypical for the more usual forms of tricuspid atresia are commonly found when there is absent pulmonary valve, including absence of a VSD, RV myocardial dysplasia, and abnormalities or even absence of the right coronary artery.

Some 5% to 15% of cases have no infundibular or pulmonary stenosis and normal or increased Qp.\textsuperscript{S25} The VSD is larger than usual. Coronary arteries are normally distributed, and the system is usually right dominant. The well-formed anterior descending coronary artery is displaced rightward by the large LV. The conduction system is basically normal but is affected by abnormalities present. Thus, the AV node is in its usual position in the AV septum between coronary sinus and dimple of atretic tricuspid valve.\textsuperscript{B13, D18} It penetrates the abnormally formed central fibrous body to the left side of the ventricular septum and becomes the branching bundle in the lower confines of the pars membranacea.\textsuperscript{B14, G26} Here it gives off most of the posterior radiation of the left bundle branch. Bifurcation of the bundle and formation of the right bundle branch occur at the posteroinferior angle of the VSD on the LV side. The right bundle branch proceeds here on the LV side and then intramyocardially along the inferior (caudal) border of the VSD. Then it emerges on the RV side and proceeds along the hypoplastic trabecula septomarginalis (septal band) (Fig. 41-7).

Major associated anomalies in this subset of tricuspid atresia are uncommon, but a persistent left SVC entering the coronary sinus occurs in about 15% of cases. Partially unroofed coronary sinus with coronary sinus–left atrial communication (see Morphology in Chapter 33) occurs in 1% to 5% of patients. This is important for the atriopulmonary type of Fontan repair, when high right atrial pressure will produce an important right-to-left shunt through it, even though a shunt was not apparent preoperatively.

\textbf{Tricuspid Atresia and Discordant Ventriculoarterial Connection (Transposed Great Arteries)}

In this tricuspid atresia subset (called \textit{type 2} by Edwards and Burchell\textsuperscript{E1}), the aorta arises from the RV, and the pulmonary trunk from the LV (Fig. 41-8). Generally, the aorta is anterior and to the right of the pulmonary trunk (D-malposition) in the position characteristic of transposition of the great arteries (see Morphology in Chapter 52), but uncommonly there is L-malposition.\textsuperscript{S2, T3}

Atrial anatomy is generally similar to that described in the preceding text. However, left juxtaposition of the atrial...
Tricuspid atresia and discordant ventriculoarterial connection. Injection is into left ventricle (LV) in this long axis view; aorta is seen to arise from right ventricle (RV), which is usually larger than when aorta arises from LV. Single ventricular septal defect is large and subaortic in position. There is moderate subpulmonary stenosis (poorly seen in this view) in LV outflow tract, and LV is typically larger than normal.

apparatus occurs in about 10%, and in about half, the ASD is small.215,216

The RV is larger and thicker walled than usual. It tends to be a single smooth-walled cavity without a proximal trabeculated portion and is, in actuality, a subaortic outlet chamber. The VSD is usually subaortic in position. Commonly it is small, or becomes small, and then represents important subaortic stenosis. In one series, aortic or subaortic stenosis was present in 40%.215 The VSD, however, may be large and unobstructive.

The LV is normal although enlarged. Pulmonary valve and anulus are usually normal or as large as the pulmonary trunk. Thus, Qp is usually large. Subpulmonary stenosis in the LV occurs in about 20% to 30% of cases, and occasionally pulmonary atresia is present. These conditions result in low Qp and hypoxia.

Coronary arteries usually arise from the posterior aortic sinuses of Valsalva, those facing the pulmonary trunk, as in transposition of the great arteries (see “Coronary Arteries” under Morphology in Chapter 52). Associated cardiac anomalies usually involve the aortic arch. Obstruction coexists in about 25% to 35% of cases, with coarctation occurring more frequently than interrupted aortic arch.

Other Aspects of Single-Ventricle Physiology

Wolff-Parkinson-White syndrome is associated with tricuspid atresia.11 The morphology that results in single-ventricle physiology has other systemic effects. For example, levels of natriuretic peptides (both atrial natriuretic peptide and B-type natriuretic peptide) are abnormal; furthermore, they are distinctively abnormal compared with other forms of heart disease, including congenital defects with biventricular physiology.140

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Symptoms and Signs

Tricuspid Atresia and Concordant Ventriculoarterial Connection

Patients in this subset of tricuspid atresia are usually cyanotic from birth because of limited Qp from RV outflow obstruction. Dick and colleagues reported that in 50% of patients, congenital heart disease is recognized on the first day of life.216 Cyanosis is severe, progressive, and often accompanied by hypoxic spells characterized by increased cyanosis, dyspnea, and occasionally syncope. These spells may occur in the first 6 months and are a grave prognostic sign. In patients with increasing obstruction to pulmonary blood flow from progressive infundibular stenosis or VSD closure, cyanosis becomes rapidly more severe, and those who were previously acyanotic may become cyanotic in a matter of a few months. Clubbing of the fingers is common in children who survive beyond the first 2 years, but it may occasionally develop as early as 3 or 4 months. Squatting is uncommon, but dyspnea is often apparent with crying or feeding.

Most patients have loud, harsh, ejection systolic murmurs that are loudest over the lower left sternal border; these may be associated with an apical mid-diastolic rumble from large mitral valve flow. In cases of progressive obstruction to pulmonary flow, murmurs decrease or disappear. A continuous ductus arteriosus murmur may also be heard in patients with pulmonary atresia and occasionally in infants with pulmonary stenosis.

A minority of patients have no obstruction to pulmonary blood flow and a nonrestrictive VSD. These patients may present in infancy with signs and symptoms of excessive pulmonary blood flow, or they may have more or less normal Qp and only mild cyanosis. In the latter, physical findings, chest radiograph, and electrocardiogram (ECG) are similar to those of other patients with normal origin of the great arteries.

Tricuspid Atresia and Discordant Ventriculoarterial Connection

Patients in this subset of tricuspid atresia often present in early life with symptoms and signs of excessive pulmonary blood flow (see “Clinical Findings” under Clinical Features and Diagnostic Criteria in Section I of Chapter 35). Usually an apical mid-diastolic rumble is heard, and there is fixed splitting of the second heart sound at the base. However, moderate subvalvar pulmonary stenosis occasionally results in either mildly increased or normal Qp. Such patients usually present after the neonatal period and sometimes after infancy, with mild cyanosis and few if any symptoms. Physical findings are similar to those in patients with tricuspid atresia and concordant ventriculoarterial connection. If aortic coarctation or interrupted aortic arch is present, the neonate presents with a duct-dependent systemic circulation and pulmonary overcirculation.
Chest Radiography

Chest radiography is usually characteristic of reduced $Q_p$ and RV hypoplasia in typical pulmonary undercirculated patients with tricuspid atresia and concordant ventriculoarterial connection. Pulmonary vascular markings are reduced and hilar shadows diminutive. The left apical heart border may be rounded, forming a high, arched contour. The vascular pedicle is narrow, and the left border in the area of the pulmonary trunk is usually concave. Radiographic appearance of the heart may resemble that of tetralogy of Fallot or occasionally appear normal.

Chest radiography in patients with tricuspid atresia and discordant ventriculoarterial connection usually shows pulmonary plethora and cardiomegaly, and the narrow supracardiac waist and LV contour make it resemble simple transposition.

Electrocardiography

The ECG in the subset with concordant ventriculoarterial connection demonstrates left axis deviation ($0^\circ$ to $-90^\circ$) in about 90% of patients, LV hypertrophy in virtually all, and abnormalities of the P wave,\(^{266,268}\) which is frequently tall (>2.5 mV) and notched.

The ECG may show left axis deviation in the subgroup with discordant ventriculoarterial connection, but a normal QRS axis between 0 and +90 degrees is present in more than half of patients.

Two-Dimensional Echocardiography

Echocardiography with color flow Doppler interrogation confirms the clinical impression of tricuspid atresia and usually provides definitive diagnosis (Fig. 41-9). Position of the great arteries and size and position of the diminutive RV and large LV can be determined (Fig. 41-10). In discordant ventriculoarterial connection, size of VSD relative to aortic “anulus” must be determined because this importantly affects the surgical procedure chosen. The aortic arch is examined for obstruction. RV size is determined because in this setting, it is functionally a subaortic outlet chamber. LV contractility is assessed. Flow across the atrial septum is assessed, which is unobstructed in most but not all cases.

Cardiac Catheterization and Cineangiography

Cardiac catheterization and cineangiography are not routinely performed. Indications for catheterization include inadequate echocardiographic evaluation, suspicion of inadequate or abnormal pulmonary arteries, concerns about pulmonary vascular resistance ($R_P$), and need for catheter-based intervention (e.g., restrictive atrial septum).

Computed Tomography and Magnetic Resonance Imaging

Computed tomography (CT) and magnetic resonance imaging (MRI) are rarely indicated in the newborn period. They can, however, be of great value at subsequent stages to assess valve abnormalities, complex subaortic obstruction, arch obstruction, ventricular mass, ventricular function, peripheral and central vascular dynamics, and abnormal venous and arterial connections associated with chronic single-ventricle physiology.\(^{212}\)

**NATURAL HISTORY**

Tricuspid atresia occurs more commonly than any other type of univentricular AV connection and accounts for 1% to 3% of congenital heart disease. The early natural history is determined primarily by presence and severity of obstruction to pulmonary blood flow and later by LV cardiomyopathy that develops in response to volume overload (see “Cardiomyopathy” later in this section).

Tricuspid Atresia and Concordant Ventriculoarterial Connection

Patients in this subset usually have important RV outflow obstruction and are cyanotic at birth. In most, the VSD narrows rapidly (in common with the general tendency of muscular VSDs to close spontaneously [see “Spontaneous Closure” under Natural History in Section I of Chapter 35]), $Q_p$ diminishes still further, cyanosis worsens, and hypoxia increases, causing the death of 90% of surgically untreated patients by age 1 year\(^{24,81}\) (Fig. 41-11).

When these patients have a normal or increased $Q_p$, natural history is more favorable than in any other subset (see Fig. 41-11). Some die in early infancy of heart failure secondary to large $Q_p$, but spontaneous VSD narrowing and progression of infundibular narrowing usually produce a more balanced flow and better hemodynamic state within a few months of birth. Mild cyanosis and mild to moderate exercise intolerance persist at a plateau level for several years. Spontaneous narrowing of most VSDs continues, however, and

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*Figure 41-9* Four-chamber echocardiogram view of tricuspid atresia and concordant ventriculoarterial connection. Note restrictive ventricular septal defect (VSD) and hypoplastic right ventricular (RV) chamber. There is platelike tricuspid atresia present, with an atrial septal (S) defect and bowing of atrial septum from right to left. Pulmonary veins (PV) can be seen draining to back of left atrium. Left atrium (LA), mitral valve (MV), and left ventricle (LV) are of normal size. Key: RA, Right atrium.
approximately 90% of patients are dead by age 10 years.\textsuperscript{R1,R2} A few survive into their second and third decades and even beyond, presumably because neither VSD nor RV outflow tract continues to narrow.

In patients who survive into the second decade and longer, chronic LV volume overload usually produces a secondary LV cardiomyopathy and reduced systolic function (Fig. 41-12), and mitral regurgitation may develop. These factors produce a lower LV output and consequently increasing cyanosis and heart failure.

Tricuspid Atresia and Discordant Venticuloarterial Connection

Surgically untreated patients in this subset usually have markedly increased Qp, because the LV ejects directly and without restriction into the pulmonary trunk. Any tendency to VSD closure worsens the pulmonary plethora and, by producing subaortic stenosis, reduces systemic blood flow (Qs). This unfavorable situation results in death of most babies by age 1 year (see Fig. 41-11). If there is coexisting important aortic

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**Figure 41-10** Subcostal echocardiogram view of tricuspid atresia and concordant ventriculoarterial connection, demonstrating ventriculoarterial connection. Right atrium (RA), right ventricle (RV), left ventricle (LV), and ascending aorta (Ao) are shown. Aorta is aligned with LV without obstruction. Ventricular septal defect (VSD) is small and restrictive, and RV cavity is hypoplastic.

**Figure 41-11** Free-hand representation of life expectancy of surgically untreated patients with tricuspid atresia. a), Patients with concordant ventriculoarterial connection and reduced pulmonary blood flow at birth. b), Patients with concordant ventriculoarterial connection and normal or increased pulmonary blood flow at birth. c), Patients with discordant ventriculoarterial connection (transposition) and increased pulmonary blood flow at birth. d), Patients with discordant ventriculoarterial connection and decreased or normal pulmonary blood flow at birth. (Data in part from Vlad\textsuperscript{V10} and Dick and colleagues.\textsuperscript{D16})

**Figure 41-12** Left ventricular ejection fraction in patients with tricuspid atresia (TA) and surgically created systemic–pulmonary arterial shunts (solid squares) compared with normal subjects (shaded area). Note that it becomes progressively more depressed as patients age. (From LaCorte and colleagues.\textsuperscript{L1})
coarctation or interruption, natural history is heavily influenced by duct-dependent systemic perfusion. The majority of such infants suffer circulatory collapse and death in the first weeks of life within hours or days of ductal closure.

A few patients have mild or moderate LV (subpulmonary) outflow narrowing at birth and decreased Qp. Progression of VSD narrowing (and RV outflow obstruction) is slower in this subset, so approximately 50% of patients survive to about age 2 years (see Fig. 41-11). Hypoxia worsens with time, however, and about 90% of surgically untreated subjects are dead by age 6 or 7 years.

Cardiomyopathy

The volume-overloaded LV, receiving both pulmonary and systemic venous return in patients with tricuspid atresia, plays an important role in natural history. Surgically untreated infants with diminished Qp have depressed LV systolic function (reduced ejection fraction) and end-diastolic volume larger than normal. Reduced ejection fraction at this young age may be related to hypoxia. In patients who live beyond about age 5 years, ejection fraction becomes progressively more depressed (see Fig. 41-12) and LV volume progressively larger. This is related to progression of LV cardiomyopathy secondary to chronic volume overload. In some patients, this leads to gradual development of mitral regurgitation in the second, third, and fourth decades. Recent evidence suggests the cardiomyopathy is due to a combination of volume overload and ischemia, with the ischemia partially due to an inadequately developed capillary network within the LV.

**Figure 41-13** Left ventricular end-diastolic volume (LVEDV) in patients with tricuspid atresia (TA) and systemic–pulmonary arterial shunts. Presentation is as in Fig. 41-12. Note progressive increase with time in LV size. Key: pts., Patients; yr, years. (From LaCorte and colleagues.)

Physiology and presentation, technique of operation, special features of postoperative care, results, indications for operation, and special situations and controversies of each palliative stage are discussed in separate sections that follow.

### Specific Techniques of Operation

Morphologic variations of tricuspid atresia encompass most of the physiologic circumstances encountered when managing all other forms of single-ventricle physiology; therefore, specific discussion of the surgical management of tricuspid atresia presents an excellent opportunity to outline most techniques for managing all forms of single-ventricle physiology, from birth to Fontan completion. Several unique exceptions exist and are discussed in Chapters 49 and 58.

#### RESULTS

Results of first-stage palliation are presented in Section II, those of second-stage palliation in Section III, and those of third-stage palliation (Fontan operation) in Section IV.

Overall outcome for single-ventricle patients followed from early infancy was assessed in 405 patients by Lee and colleagues. These patients had the entire spectrum of single-ventricle morphology, but included only 14 with hypoplastic left heart physiology; thus, this relatively high-risk lesion did not have a major influence on overall results. Tricuspid atresia, double inlet ventricle, DORV, and unbalanced

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**TECHNIQUE OF OPERATION**

**General Plan for Surgical Management of Single-Ventricle Physiology**

The Fontan operation is considered the surgical end point for patients whose cardiac anomalies do not allow a two-ventricle circulation. The original Fontan operation was performed exclusively in patients with tricuspid atresia, but it is now applied to all forms of univentricular AV connection (see Chapters 40, 49, and 56), as well as to a number of other conditions in which complete two-ventricle circulations cannot easily be achieved (see Chapter 58). Soon after the original operative description, Fontan himself modified the procedure; it therefore seems unnecessary to term each subsequent modification a “modified Fontan.” All forms of Fontan operation aim to divert systemic (with or without coronary) venous return to the pulmonary arterial circulation (either directly or by pathways through the heart), leaving one ventricle to provide essentially all energy driving blood flow in an in-series circulation. Each of the various techniques of achieving this separated pulmonary and systemic in-series circulation has advantages and disadvantages. Widely used techniques are described in sections that follow, and techniques that may be useful in specific cases are described under Special Situations and Controversies in Section IV.
A7 Kaplan-Meier survival from birth of 140 patients

**Figure 41-14** Surgical management and current status of 405 single-ventricle patients. Key: BCPS, Bidirectional cavopulmonary shunt; F/U loss, lost to follow-up; PAB, pulmonary artery band; SV, single ventricle; waiting, waiting for Fontan. (From Lee and colleagues.135)

AV septal defect accounted for 379 of the 405 cases. Patients were managed with a variety of surgical procedures (Fig. 41-14), but the goal was to achieve a Fontan circulation. Survival was thus influenced by operative mortality at each operation, interstage mortality, and mortality following the Fontan operation. The study showed a 10-year survival of 60%. Lan and colleagues examined 140 cases of DILV or tricuspid atresia. (From Lan and colleagues.19)

**Figure 41-15** Kaplan-Meier survival from birth of 140 patients with transposed great arteries and either double inlet left ventricle or tricuspid atresia. (From Lan and Lakes.19)

INDICATIONS FOR OPERATION

Patients in whom only one ventricle has an AV connection and is of sufficient size and power to provide energy for generating in-series pulmonary and systemic blood flows are considered for the Fontan operation. In most of these patients, the heart has a univentricular AV connection (see “Atrioventricular Connection” under Morphology in Chapter 56), one subset of which is tricuspid atresia. The Fontan operation may also be indicated for a few patients with concordant or discordant AV connections in whom one ventricle is too small or dysplastic, or both, to provide sufficient energy for generating adequate blood flow in a two-ventricle circulation (see Chapters 40, 49, and 58). Also, there are some cases in which two adequately sized and functioning ventricles exist in association with adequate inlet valves, but they cannot be septated because of complex relationships among the ventricles, great arteries, and VSDs. Such patients may best be treated with a Fontan procedure (see Chapter 53).24

Some data suggest that a hypoplastic RV of less than 30% normal size does not contribute to the circulation, indicating that the Fontan operation should be performed if this threshold value is met.14

SPECIAL SITUATIONS AND CONTROVERSIES

Moderately Hypoplastic Ventricle

If the RV is hypoplastic but greater than 30% normal size, then it may be of benefit to incorporate it into the right-sided circulation with a functioning inlet and outlet valve and a superior cavopulmonary anastomosis.25-28 This procedure has been called the one-and-a-half ventricle repair.

Although definite proof of its efficacy is lacking, the one-and-a-half ventricle repair, used both to avoid the Fontan operation and to unload the normally developed but failing RV, has gained fairly wide acceptance as a useful procedure in both settings.25,27,38,69,95

Fontan versus Intracardiac Repair

for Complex Morphology

Under certain morphologic circumstances, biventricular repair, although theoretically possible, may not be advisable, and consideration should be given to performing the Fontan operation. These circumstances include but are not limited to:

- Unbalanced AV septal defect
- Moderate right heart hypoplasia
- Moderate left heart hypoplasia
- DORV with uncommitted VSD
- Tricuspid atresia with VSD and moderately developed RV
- Pulmonary atresia with intact ventricular septum with moderate RV hypoplasia or dysfunction
- Ebstein anomaly with moderate RV hypoplasia or dysfunction
- Marked straddling of one AV valve, with AV and ven-triculoarterial discordant connections, in association with VSD and pulmonary atresia or stenosis

In these anomalies, there may be two reasons to question a standard biventricular repair:

- Concern about ability of the hypoplastic ventricle or AV valve to function adequately
- Overall complexity of the procedure required to achieve a standard biventricular repair

Occasionally, both ventricles and inlet valves are of normal size and morphology is not particularly complex, but one ventricle demonstrates marked dysfunction (e.g., tetralogy of Fallot with markedly reduced RV function). In these circumstances, biventricular repair, Fontan operation, superior cavopulmonary anastomosis with intracardiac repair (one-and-a-half ventricle repair) and transplantation are...
Some patients will not meet physiologic criteria for the definitive operation for patients with single-ventricle physiology. Alternative definitive operations prior to development, or at least wide acceptance, of the Fontan operation.

The operation is followed in many patients by redistribution of pulmonary blood flow in the right lung. Using ventilation/perfusion lung scans, Cloutier and colleagues demonstrated a decreased ratio of upper lobe–to–lower lobe pulmonary blood flow. Presumably as a more advanced manifestation of the same underlying process, right-sided pulmonary arteriovenous fistulae form late after the Glenn procedure, generally confined to the right lower lobe. In Kopf and colleagues’ 30-year follow-up study, pulmonary arteriovenous fistulae developed in the right lung of 33% of patients. They found that a longer interval between operation and observation increased the probability of these fistulae being present. Right-to-left shunting and cyanosis usually develop with sufficient severity to warrant therapeutic fistula embolization in about one third of patients. Right-to-left shunting and cyanosis usually develop with sufficient severity to warrant therapeutic fistula embolization in about one third of patients. Right-to-left shunting and cyanosis usually develop with sufficient severity to warrant therapeutic fistula embolization in about one third of patients. Right-to-left shunting and cyanosis usually develop with sufficient severity to warrant therapeutic fistula embolization in about one third of patients.
delay placing the band until $Q_p/Q_s$ increases somewhat, in concert with the normal postnatal decrease in pulmonary resistance ($R_p$) (see “Timing of Pulmonary Trunk Banding” under Indications for Operation later in this section).

**Technique of Operation**

**Preoperative Management**

Before undertaking any surgical procedure, overall cardiopulmonary stability should be ensured. These neonates are typically stable and come to the operating room breathing spontaneously and on little pharmacologic support other than, in some cases, prostaglandin $E_1$ ($PGE_1$) infusion to maintain ductal patency. However, if they present in an uncompensated state, either with overcirculation of the pulmonary circuit or with undercirculation and profound cyanosis, it is prudent to resuscitate them aggressively before operation. This may include use of $PGE_1$, inotropic agents, diuretics, mechanical ventilation with appropriate manipulations, nutritional support, and treatment of sepsis. Following stabilization, a period of observation is usually beneficial to allow recovery of systemic end-organ damage before surgical intervention. However, circumstances may require urgent operation despite inadequate resuscitation. For example, a previously undiagnosed and stable infant may present at several weeks of life with a recently closed ductus, resulting in ongoing critical cyanosis.

**Systemic–Pulmonary Arterial Shunt**

After anesthesia induction, an indwelling arterial catheter is placed, preferably in the left radial artery. Reliable intravenous access is achieved, preferably via peripheral extremity vein; subclavian and internal jugular veins should be specifically avoided because they tend to develop deep venous thrombosis that can importantly complicate subsequent management at the time of superior cavopulmonary shunt (see Section III). It is similarly important to avoid femoral vein cannulation, because most patients with univentriicular AV connection require multiple cardiac catheterization evaluations, preferably via the femoral vein.

The preferred incision for performing a systemic–pulmonary arterial shunt is median sternotomy. This incision has multiple advantages over traditional lateral thoracotomy:

- Both lungs can be completely ventilated throughout the procedure. This can be especially important in unstable infants.
- The shunt can be placed more centrally on the left or right branch pulmonary artery, thereby reducing prevalence of right or left upper lobe pulmonary artery branch stenosis.
- Maximal flexibility is achieved.
- If the ductus arteriosus is to be ligated during the shunt procedure, it can be accomplished effectively.
- If central pulmonary artery stenosis at the site of ductus insertion is present or suspected, pulmonary arterioplasty can be performed.
- If the patient becomes unstable during the procedure and requires cardiopulmonary bypass (CPB), there is access for cannulation.
- Occurrence of musculoskeletal deformities induced by a lateral incision, such as scoliosis, is eliminated.

The single disadvantage of median sternotomy is risk of hemorrhage from inadvertent cardiotomy on repeat sternotomy at subsequent procedures. This can be minimized by leaving intact the anterior aspect of the pericardial sack overlying the ventricular mass at the first procedure.

Median sternotomy is performed (see “Incision” in Section III of Chapter 2). The typically large thymus gland is mobilized or partially removed, and only the upper pericardial reflection over the great arteries is opened, leaving intact the portion overlying the ventricular mass. Sites on both systemic and pulmonary circuits are chosen for placing the shunt (see “Systemic–Pulmonary Arterial Shunt” under Special Situations and Controversies later in this section). Usually a modified Blalock-Taussig shunt is performed (Fig. 41-16) using an expanded polytetrafluoroethylene (PTFE) vascular graft of specified internal diameter, placed between the brachiocephalic–right subclavian artery junction, and central portion of the RPA (see “Systemic–Pulmonary Arterial Shunt” under Special Situations and Controversies later in this section). Systemic and pulmonary arterial sites are prepared using sharp dissection. The patient is heparinized ($3 \text{ mg} \cdot \text{kg}^{-1}$ intravenously). An appropriately sized partial occlusion vascular clamp is used to isolate the brachiocephalic–right subclavian arterial segment, which is incised over a length appropriate to create an orifice that matches the expanded PTFE graft.

Focus on detail is necessary to create a functional and reliable shunt. Attention is given to the angle of takeoff of the brachiocephalic artery origin and brachiocephalic-subclavian arterial junction. The expanded PTFE graft is tailored with a bevel to maximize laminar flow at the arterial graft anastomosis. Anastomosis is then performed with running 7-0 nonabsorbable monofilament suture.

After the anastomosis is completed, the partial occlusion clamp on the arterial segment is removed and replaced with a small clamp occluding the graft. This allows the arterial segment to assume its natural position, thereby permitting the surgeon to judge exactly the length of the graft in preparation for its anastomosis to the RPA. Attention to detail is necessary because a graft tailored to an inappropriate length may kink or distort the involved arteries. Typically, no bevel is necessary at the graft-RPA connection, and end-to-side anastomosis is performed at a 90-degree angle. After trimming the graft to an appropriate length, a partial occlusion clamp is placed on the central portion of the RPA that lies to the right of the ascending aorta and left of the SVC; it should not involve the right upper pulmonary artery. An incision of appropriate length is made in the sequestered segment of RPA, and anastomosis proceeds using a technique similar to that of the previous anastomosis. Before completing it, heparinized saline may be infused into the graft and pulmonary artery segments to flush remnants of blood that may have accumulated. The clamp is then removed from the RPA.

Before removing the clamp on the shunt, the ductus arteriosus (if present) is exposed, and a heavy silk ligature with a snare is placed around it. The clamp is then removed from the shunt, and the snare on the ductus is gently tightened to occlude it.

A period of hemodynamic adjustment then ensues. The surgeon should pay careful attention to change in systemic arterial oxygen saturation ($S_aO_2$) as indicated by pulse oximetry and by change in hemodynamics as indicated by heart rate and systolic, diastolic, and mean blood pressures. New
Figure 41-16  Right modified Blalock-Taussig shunt through median sternotomy. Although either anastomosis can be performed first, here the graft–right pulmonary artery (RPA) anastomosis is performed first, followed by the graft–subclavian artery anastomosis. (See text for description of procedure in opposite order.) A, After median sternotomy, thymus gland is subtotally resected and pericardium opened along its upper aspect. Aorta is retracted to left side, and superior vena cava to right side, exposing RPA. Brachiocephalic artery and its bifurcation into right subclavian and carotid arteries are dissected cephalad to brachiocephalic vein. B, Side-biting vascular clamp is placed on RPA in such a way that clamp itself holds aorta to patient’s left. Care is taken that incision in superior aspect of RPA does not encroach on its bifurcation into upper and lower branches, but is kept as central as possible. An appropriately sized polytetrafluoroethylene (PTFE) tube graft is then connected to RPA incision, using a continuous suture technique and 7-0 nonabsorbable monofilament suture (see text for a more detailed discussion of factors involved in determining choice of shunt size). Posterior aspect of anastomosis is performed first, followed by anterior aspect. C, After the graft to pulmonary artery anastomosis is completed, a side-biting vascular clamp is placed on exposed right subclavian artery or right subclavian–brachiocephalic artery junction. Sequestered segment of artery is incised over an appropriate length to match circumference of PTFE tube graft. Graft is tailored to an appropriate length and beveled to avoid kinking or distorting subclavian and right pulmonary arteries. Anastomosis is performed using a technique similar to that described for graft-to–pulmonary artery anastomosis (B). D, Shunt is shown with anastomoses completed and aorta and superior vena cava in their normal positions. Additionally, ductus arteriosus has been ligated with a 5-0 polypropylene suture following blunt circumferential dissection with a small right-angled clamp.
steady-state values for these variables are judged against baseline conditions, which may vary among infants. In general, \(\text{SaO}_2\) between 75% and 85% is considered acceptable. \(\text{SaO}_2\) below this range should raise concerns about a technical problem with the shunt, an inadequately sized shunt, or unsuspected distal pulmonary artery problems. \(\text{SaO}_2\) above this range should raise concern that the shunt is too large. This latter concern is heightened if systemic arterial diastolic blood pressure is less than 25 to 30 mmHg.

Once stability has been achieved, the snare is removed from the ductus, and it is permanently ligated. PGE\(_1\) infusion is stopped. Mediastinal drainage and closing the median sternotomy are as usual (see “Completing Operation” in Section III of Chapter 2).

**Pulmonary Trunk Banding**

Pulmonary trunk banding is usually performed via median sternotomy, lateral thoracotomy, or anterior parasternal incision. Median sternotomy is preferred for the same reasons described in the preceding text for placing a systemic–pulmonary arterial shunt; patient preparation is also similar. If the surgeon prefers a lateral thoracotomy or anterior parasternal incision, it is performed on the left side. In other patients with univentricular AV connection with conotruncal abnormalities that result in position of the pulmonary trunk to the right of the aortic root, a right lateral incision is chosen.

Preferred median sternotomy is performed as described in Chapter 2, and the thymus gland is mobilized or partially removed. The pericardium is opened only at its superior border over the great arteries, with care taken to leave it intact over the ventricular mass. The tissue plane between ascending aorta and pulmonary trunk is developed over a limited area halfway between the sinutubular junction of the pulmonary trunk and origin of the RPA (Fig. 41-17, A).

Aggressive dissection in this area is discouraged because it increases the chances of migration of the band over time. Once circumferential access to the pulmonary trunk is achieved, the band is placed around it. Choice of band material may vary; however, material that prevents important fibrosis and calcification and has a low risk of erosion into the pulmonary trunk should be chosen. Width of band material should be broad (at least 2.5 mm) to minimize erosion. Preferred choice of band is a 3-mm-wide strip fashioned from a relatively thick (0.3 to 0.4 mm) silicone rubber sheet. This material incites minimal reaction in surrounding tissues.

After placing the band around the pulmonary trunk (Fig. 41-17, B), its free ends are secured together to create a circumferential ring (Fig. 41-17, C). Formulas can be used to estimate the appropriate circumferential length, but individual physiologic variability usually dictates adjustments be made. Free ends of the band are initially secured together at a point that allows only minimal circumferential narrowing of the pulmonary trunk. Following this initial placement, two sutures are placed at points 180 degrees opposite each other on the circumference of the band, attaching the band to the adventitia of the proximal portion of the pulmonary trunk (see Fig. 41-17, C). These sutures prevent pressure-driven distal band migration on the pulmonary trunk. Migration is common if the band is not secured.

Once the band is positioned, but before it has been adjusted to its final circumference, it is prudent to temporarily place a catheter into the distal pulmonary trunk to measure pressure distal to the band. Difference in systemic arterial and
distal pulmonary artery pressure provides an accurate assessment of band gradient. The surgeon then gradually reduces band circumference, evaluating both band gradient and $\text{Sao}_2$ as end points. Both vary depending on physiologic circumstances; however, a typical band gradient in a neonate will be in the range of 40 to 70 mmHg, and $\text{Sao}_2$ should range between 75% and 85%. Band circumference is adjusted by placing metal clips in the vicinity where the two free ends of the band were initially secured together (see Fig. 41-17, C). These clips are placed sequentially, with each subsequent clip placed just below the most recently placed one, gradually approaching the physiologic end points just described. Appropriately adjusting $\text{Qp}$ with a pulmonary trunk band can be somewhat difficult. This is because pulmonary blood flow occurs only in systole, and the band is a two-dimensional resistor with little length. As a result, small changes in band circumference result in marked resistance changes and, therefore, marked $\text{Qp}$ changes. Because flow across the band occurs only in systole, $\text{Qp}$ varies with changes in systemic arterial pressure. It is therefore critical that the anesthesiologist create circumstances during band adjustment such that systemic blood pressure approximates that expected in the awake infant. This can usually be achieved by appropriate choice of anesthetic and volume management.

Once the band is appropriately adjusted, an indwelling right atrial catheter and atrial and ventricular pacing wires are placed as described earlier in this section for the systemic–pulmonary arterial shunt. Mediastinal drainage and median sternotomy closure are as described in “Completing Operation” in Section III of Chapter 2.

**Special Features of Postoperative Care**

**Systemic–Pulmonary Arterial Shunting Procedures**

After completing the procedure, it is not necessary to reverse the heparin with protamine; instead, the heparin is allowed to metabolize slowly. Beginning on the first postoperative night, aspirin is given rectally (1 mg·kg$^{-1}$·day$^{-1}$) to prevent thrombus formation in the shunt.

Some degree of hemodynamic instability and modest metabolic acidosis are common in the first few postoperative hours. It is prudent to support the patient over the first postoperative day with mechanical ventilation and close observation. Occasionally, low-dose inotropic support is indicated.

**Pulmonary Trunk Banding**

As $\text{Rp}$ gradually decreases after placement of a pulmonary trunk band, it is occasionally necessary to reoperate to tighten the band further. Need for readjusting it can be minimized by appropriately timing the initial banding (see “Timing of Pulmonary Trunk Banding” under Indications for Operation later in this section).

**Results**

**Systemic–Pulmonary Arterial Shunting Procedures**

Early mortality for patients with tricuspid atresia and other types of univentricular communications and reduced $\text{Qp}$ is low (Tables 41-1 and 41-2) and similar to that for shunts performed for palliation of tetralogy of Fallot (see “Interim Results after Classic Shunting Operations” in Section I of Chapter 38). As expected, early mortality from multi-institution reports is somewhat higher than in the single-institution reports cited in these tables. A three-institution report revealed 3 early deaths in 23 cases (13%; CL 6%-24%).$^{97}$ Under most circumstances, pulmonary artery distortion by the shunt is uncommon. $^{33}$

In patients who cannot subsequently have a Fontan operation, palliation has been good, and 5-year survival without definitive operation is about 90%. $^{33}$ Intermediate time-related survival, including mortality of subsequent interventions, is about 85% at 10 years when the shunt is initially performed after the first few months of life. $^{2,3,5,7,11,19}$ (Fig. 41-18). However, substantially worse survival was reported by Franklin and colleagues for a patient group in which many required operation early in life; this may be more representative $^{18,8,19}$ (Fig. 41-19). Risk of dying is highest in the first few months following the shunt procedure (Fig. 41-20). Then, after 5 to 10 years, many patients begin to deteriorate. This is related to cyanosis, which is due to relative narrowing of the Blalock-Taussig shunt commensurate with patient growth, as well as to LV cardiomyopathy secondary

### Table 41-1 Hospital Mortality after Surgical Procedures for Tricuspid Atresia

<table>
<thead>
<tr>
<th>Operation</th>
<th>$n$</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
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<tbody>
<tr>
<td>Systemic–pulmonary artery shunting</td>
<td></td>
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<tr>
<td>Blalock-Taussig</td>
<td>69</td>
<td>5</td>
<td>7</td>
<td>4-12</td>
</tr>
<tr>
<td>PTFE interposition</td>
<td>31</td>
<td>2</td>
<td>6</td>
<td>2-15</td>
</tr>
<tr>
<td>Others</td>
<td>13</td>
<td>1</td>
<td>8</td>
<td>1-24</td>
</tr>
<tr>
<td>Glenn operation</td>
<td>25</td>
<td>2</td>
<td>8</td>
<td>3-18</td>
</tr>
<tr>
<td>Revisions of shunts</td>
<td>11</td>
<td>2</td>
<td>18</td>
<td>6-38</td>
</tr>
<tr>
<td>Open palliative procedures</td>
<td>8</td>
<td>2</td>
<td>25</td>
<td>9-50</td>
</tr>
<tr>
<td>Pulmonary trunk banding</td>
<td>7</td>
<td>1</td>
<td>14</td>
<td>2-41</td>
</tr>
<tr>
<td>Coarctation repair and pulmonary</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>0-27</td>
</tr>
<tr>
<td>trunk banding</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0-86</td>
</tr>
<tr>
<td>Miscellaneous other palliative</td>
<td>6</td>
<td>1</td>
<td>17</td>
<td>2-46</td>
</tr>
<tr>
<td>procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>108</td>
<td>11</td>
<td>10</td>
<td>7-14</td>
</tr>
</tbody>
</table>

Data from Cleveland and colleagues.$^{23}$ Key: CL, 70% confidence limits; PTFE, polytetrafluoroethylene.
Table 41-2 Hospital Mortality after Initial and Subsequent Palliative Operations for Single Ventricle

<table>
<thead>
<tr>
<th>Operation</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
<th>Key: CL, 70% confidence limits; PTFE, polytetrafluoroethylene.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic–pulmonary artery shunting</td>
<td>73</td>
<td>6</td>
<td>8</td>
<td>5-13</td>
<td>1/55, 2%; CL 0.2%-6%</td>
</tr>
<tr>
<td>Blalock-Taussig</td>
<td>41</td>
<td>1</td>
<td>2</td>
<td>0.3-8</td>
<td></td>
</tr>
<tr>
<td>PTFE interposition</td>
<td>14</td>
<td>0</td>
<td>0</td>
<td>0-13</td>
<td></td>
</tr>
<tr>
<td>Other shunts</td>
<td>18</td>
<td>5</td>
<td>28</td>
<td>16-43</td>
<td></td>
</tr>
<tr>
<td>Pulmonary trunk banding</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0-38</td>
<td></td>
</tr>
<tr>
<td>Atrial septectomy</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0-19</td>
<td></td>
</tr>
<tr>
<td>Repair only of associated cardiac anomaly</td>
<td>7</td>
<td>2</td>
<td>29</td>
<td>10-55</td>
<td></td>
</tr>
<tr>
<td>Combined closed palliative procedures</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0-19</td>
<td></td>
</tr>
<tr>
<td>Othersa</td>
<td>9</td>
<td>2</td>
<td>22</td>
<td>8-45</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>111</td>
<td>10</td>
<td>9</td>
<td>6-13</td>
<td></td>
</tr>
</tbody>
</table>

aSeven exploratory cardiotoomies, including or not including pulmonary valvotomy or a valved extracardiac conduit (seven cases, one hospital death), and two revisions of previous procedures (one hospital death).

Data from Stefanelli and colleagues.335

to chronic volume overload, which worsens with time (see "Cardiomyopathy" under Natural History in Section I).

Pulmonary Trunk Banding

Early mortality after pulmonary trunk banding has been reported to be substantial—25% to 35%.113,113,335 This high mortality likely reflects that this information spans many years and thus includes many patients receiving bands in the 1970s, when mortality in general was high for complex cases. It may also reflect difficulty of achieving physiologic balance of Qp and Qs compared with a systemic–pulmonary arterial shunt. In the current era, mortality of less than 5% should be expected (see Tables 41-1 and 41-2). Low mortality (no early deaths in 10 cases) (0%; CL 0%-17%) in the current era is confirmed even in multi-institutional reports.111

Outcome following pulmonary trunk banding, like systemic–pulmonary arterial shunting, is somewhat influenced by intracardiac anatomy. For example, with tricuspid atresia or DILV and discordant ventriculoarterial connection, the tendency for subaortic stenosis to develop or progress is a frequent and unfavorable sequel to the banding procedure (see "Physiology and Presentation" under Discordant Ventriculoarterial Connection later in this section).220,222,225,23,17,229 Subaortic stenosis not only increases risk of death before definitive repair but also after the Fontan operation; this is due to the resulting increase in main ventricular chamber muscle mass and corresponding decrease in ventricular compliance.312
Indications for Operation

**Systemic–Pulmonary Arterial Shunt**
Presence of severe cyanosis (SaO₂ < 70%-75%) early in life or of duct dependency are indications for performing a systemic–pulmonary arterial shunt. Causes for cyanosis other than restrictive Qp (e.g., reversible lung disease, anemia, obstructive pulmonary venous connection) must be ruled out.

The shunt does not facilitate later decision making about a Fontan operation, and it somewhat complicates its later performance.

**Pulmonary Trunk Banding**
When Qp is large enough to produce serious heart failure early in life, the pulmonary trunk should probably be banded. If increased Qp is insufficient to produce important heart failure in the early weeks of life, banding is not performed.

**Timing of Pulmonary Trunk Banding**
If a pulmonary trunk band is placed too early following birth when distal Rp is still high, the surgeon will be limited by the patient’s cyanosis when attempting to tighten the band to an appropriate level. As Rp gradually decreases after placing such a band, it is commonly necessary to reoperate to tighten the band further. Need for readjusting the band can be minimized by appropriately timing the initial banding. The ideal time varies based on individual physiologic characteristics, but the procedure is usually best performed in the second, third, or fourth week of life. In the physiologic setting of low distal Rp and relatively high Qp, the situation is optimal for placing the band with an appropriate tightness that ensures long-term balance between Qp and Qs.

**DISCORDANT VENTRICULOARTERIAL CONNECTION**

**Clinical Features and Diagnostic Criteria**

In this subset, neonates typically present a different set of physiologic considerations from those with concurrent ventriculoarterial connection. Because the pulmonary valve is in fibrous continuity with the mitral valve and arises directly from the LV, obstruction to pulmonary blood flow is unusual and unrestrictive Qp the rule. The aorta arises from the hypoplastic RV, and as a result, the LV must eject through the VSD (bulboventricular foramen) and underdeveloped RV into the aorta. If the outflow tract from LV to aorta and the aortic arch are well developed, the patient can be managed effectively in a fashion similar to that described for tricuspid atresia and concordant ventriculoarterial connection with excessive Qp using a pulmonary trunk band as described in the preceding text.

Tricuspid atresia and discordant ventriculoarterial connection, however, commonly manifests with important obstruction in the systemic circulation.⁷ Obstruction typically occurs at two levels: subaortic and aortic arch. **Subaortic obstruction** is due to a combination of restrictive VSD and muscular obstruction in the underdeveloped incomplete RV. Any type of coexisting aortic arch obstruction increases by sevenfold the probability that severe subaortic stenosis will be present.⁸ Any type of coexisting aortic arch obstruction increases by sevenfold the probability that severe subaortic stenosis will be present.⁸ Narrowing may be accelerated by maneuvers that reduce volume load on the heart, such as pulmonary trunk banding or takedown of a systemic–pulmonary arterial shunt at the time of a bidirectional superior cavopulmonary shunt or Fontan procedure. Some studies suggest that subaortic stenosis will ultimately develop in up to 80% of such patients who undergo pulmonary banding early in life.⁹,¹⁰,¹¹,¹²

Even when the VSD is large at the time of a Fontan operation, it may narrow thereafter and subaortic stenosis may appear.²⁵ Narrowing may occur immediately at the time of the Fontan operation if important volume unloading occurs, either by removing a pulmonary artery band with pulmonary trunk occlusion or by removing a systemic–pulmonary arterial shunt. However, if the patient is undergoing three-stage palliation, it is more likely for the volume load to be dramatically reduced at the time of second-stage bidirectional superior cavopulmonary shunt, and subaortic stenosis is more likely to develop at that time.

In summary, subaortic stenosis is a potential problem in patients in whom the aorta arises above an incomplete ventricle (or outlet chamber). Probability of its appearance is increased by smallness of the VSD (bulboventricular foramen), coexisting aortic arch obstruction, and maneuvers that reduce ventricular volume load. Even in the absence of associated factors, it may still develop. Subaortic stenosis is least likely to occur when the aortic valve is large, the VSD is large, and no arch obstruction is present.

**Technique of Operation**

**Preoperative Management**
Neonates with this morphology have the potential to be acutely ill in a manner similar to those with hypoplastic left heart physiology; therefore, preoperative stabilization should be similar to that for patients with hypoplastic left heart physiology (see Box 49–1 under “Definition,” and
“Preoperative Management” in Chapter 49). Even when the VSD is large at birth, it may spontaneously narrow, and subaortic obstruction then becomes apparent.

**Pulmonary Trunk Banding and Aortic Arch Reconstruction**

This technique is described for tricuspid atresia and discordant ventriculoarterial connection with aortic arch obstruction, but is applicable to any patient with univentricular AV connection, aortic arch obstruction, and excessive Qp (Fig. 41-21). The patient is positioned in right lateral decubitus position, and a standard left posterolateral thoracotomy is made through the fourth intercostal space [see “Alternative Primary Incisions” under Incisions in Section III of Chapter 2]. Description of the arch repair is similar to that for isolated coarctation in the neonate [see Technique of Operation in Section I of Chapter 48 for details].

Following arch reconstruction, a longitudinal incision in the pericardium is made 1 cm anterior to the left phrenic nerve. Depending on extent of the thymus gland, modest mobilization of its left lobe may be necessary. Once the pericardium is opened, the pulmonary trunk is identified in the transposed position, posterior and to the left of the ascending aorta. (In patients with DILV and L-transposition, the pulmonary trunk is posterior and to the right.) The plane between adjacent walls of ascending aorta and pulmonary trunk are carefully dissected, gaining circumferential access around the pulmonary trunk midway between its sinutubular junction and origin of the RPA. The RPA origin is particularly difficult to visualize through a left thoracotomy incision; however, it must be carefully located before positioning the band. Following this, details related to placing and adjusting the band are similar to those described previously [see “Pulmonary Trunk Banding” under Technique of Operation earlier in this section] for placing a pulmonary artery band through a median sternotomy [see Fig. 41-17].

**Proximal Pulmonary Trunk to Aortic Connection with Arch Repair**

This technique is described for tricuspid atresia and discordant ventriculoarterial connection with subaortic and arch obstruction, but is applicable to all forms of univentricular AV connection with subaortic and arch obstruction34 (Fig. 41-22). After anesthesia induction, placing indwelling peripheral arterial and venous catheters, and supine positioning, a median sternotomy is performed [see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2]. The thymus gland is subtotally removed and the pericardium opened anteriorly over the heart. The plane between pulmonary trunk and ascending aorta is carefully dissected and the entire aortic arch mobilized, including the first 1 to 2 cm of each arch vessel. The central pulmonary artery, ductus arteriosus, and descending aorta to the level of the first pair of intercostal arteries are also mobilized. The patient is then prepared for CPB. If the aortic arch is hypoplastic but not preocclusive (>2-3 mm in diameter), adequate perfusion on CPB can be achieved by cannulating the aortic system alone using a 6F or 8F aortic cannula.27 If the ascending aorta is of adequate size, it can be cannulated directly (as shown in Fig. 41-22), or alternatively, if it is hypoplastic, the base of the brachiocephalic artery can be cannulated. The arterial cannula (or cannulae) is secured in place with standard purse-string sutures and snares. If the aortic arch is interrupted, or

is in continuity but with preocclusive narrowing at the isthmus and coarction, dual arterial cannulation of the proximal pulmonary trunk and the aortic system is performed. (This variation is not shown in Fig. 41-22, but see Technique of Operation in Chapter 48 for a detailed description of cannulation technique and CPB management when the arch is interrupted.) Temporary occlusion of branch pulmonary arteries is achieved either with snares or vascular clamps if perfusion is performed through the pulmonary trunk and ductus arteriosus to the descending thoracic aorta.

Venous cannulation is through a purse string in the right atrial appendage. After cannulation, CPB is instituted and preferably carried out using continuous antegrade cerebral perfusion [see Fig. 41-22]. Alternatively, some surgeons prefer to use circulatory arrest [see “Technique in Neonates, Infants, and Children” in Section IV of Chapter 2]. These CPB management techniques are also discussed in detail in the description of the Norwood procedure for hypoplastic left heart physiology [see “Norwood Procedure Using Continuous Perfusion” under Technique of Operation in Chapter 49]. In particular, the techniques described in Chapter 49 for performing continuous antegrade cerebral perfusion are widely applicable to all forms of neonatal arch obstruction with associated hypoplastic arch and ascending aorta. Once the target perfusion temperature is reached, antegrade cerebral perfusion established, and cardiac arrest induced with cardioplegia, the obstructed aortic arch is addressed, as described in Fig. 41-22.

If the aortic arch is in continuity but hypoplastic, the aortic isthmus is ligated with a 5-0 polypropylene suture, and ductus and coarctation tissue distal to it are removed [see Fig. 41-22, A]. A small vascular clamp can be placed across the descending aorta at the level of the first set of intercostal vessels to stabilize the aorta and deliver it into the anterior mediastinum. A longitudinal incision is made in the posterior aspect of the upper ascending aorta and proximal aortic arch [see Fig. 41-22, B], and the descending aorta is anastomosed to this incision with a running 7-0 monofilament absorbable suture, thereby repairing the arch obstruction [Fig. 41-22, B]. In the case of true aortic arch interruption, the isthmus ligature is not necessary, and arch repair otherwise proceeds as described.

With the arch obstruction addressed, antegrade cerebral perfusion is terminated and full-body bypass is again established [see “Norwood Procedure Using Continuous Perfusion” under Technique of Operation in Chapter 49]. Attention is turned to the proximal pulmonary trunk–aortic anastomosis. This can be accomplished in several ways, one of which is described in detail in Fig. 41-22, B. Although unusual in neonates with tricuspid atresia, if preoperative evaluation suggests that potential or real obstruction exists at the atrial septum, the right atrium is opened during continuous bypass, and the septum primum is removed to create an unobstructed atrial communication. During this maneuver, the single venous cannula in the right atrium must be temporarily clamped, and cardiomyopathy suction devices used within the two veno caval orifices to provide exposure for the atrial septal resection. The right atriotomy is then closed with a running 6-0 polypropylene monofilament suture. Venous drainage via the right atrial cannula is then reestablished and rewarming begun.

An appropriately sized expanded PTFE tube graft is then used to create a modified Blalock-Taussig shunt [see Fig.
Chapter 41  Tricuspid Atresia and Single-Ventricle Physiology

Figure 41-21  Repair of hypoplastic aortic arch and pulmonary trunk band placement via left thoracotomy. A, Standard left posterolateral thoracotomy is performed through fourth intercostal space, and ribs are retracted. Adventitia overlying distal aortic arch and left pulmonary artery is shown. Positions of phrenic and vagus nerves are indicated. Large ductus arteriosus is noted, along with severe hypoplasia of aortic isthmus and moderate hypoplasia of distal aortic arch. Great arteries are in transposed position, with aorta anterior and pulmonary trunk posterior. Left lung has been deflated and retracted in an inferior direction. B, Adventitia overlying distal aortic arch is opened and retracted with sutures. Aortic arch obstruction is managed in standard fashion for neonatal aortic coarctation (see Section I of Chapter 48 for full discussion of technical and management issues related to aortic arch obstruction in the neonate). After appropriate dissection of aorta and ductus, vascular clamps are placed, and ductus arteriosus is ligated and divided, as is hypoplastic aortic isthmus. All remaining ductal tissue is removed from descending aorta, and a longitudinal incision is made on undersurface of aortic arch (dashed lines). Descending aorta is connected end to side to undersurface of aortic arch between left subclavian and brachiocephalic arteries. C, Repaired arch with ligated and divided hypoplastic aortic isthmus and ligated and divided ductus arteriosus. D, Inferiorly retracted lung is now repositioned with more direct posterior retraction to better expose proximal intrapericardial great arteries. Incision in pericardial sack is made anterior and parallel to phrenic nerve to expose proximal pulmonary trunk in preparation for placing pulmonary trunk band. Pulmonary trunk is carefully dissected in limited fashion just above tops of pulmonary valve commissures and below origin of right pulmonary artery (see Fig. 41-17). Identification of right pulmonary artery origin may be difficult from the left thoracotomy perspective. Using a small right-angled clamp, circumferential dissection is achieved and a 3-mm-diameter band, taken from a sheet of reinforced silicone rubber, is placed around proximal pulmonary trunk. Band is then tightened and secured to prevent migration, as described in Fig. 41-17.

Details of the shunt procedure are similar to those described earlier in this section for isolated neonatal systemic–pulmonary arterial shunt.

Principles of rewarming and separation from bypass are those described in “Completing Cardiopulmonary Bypass” in Section III of Chapter 2. Following separation from CPB, management considerations with regard to pharmacology, physiology, and sternal wound (immediate or delayed sternal closure) are the same as described in the management of hypoplastic left heart physiology following the Norwood procedure (see “Special Features of Postoperative Care” in Chapter 49).
**Modified Norwood Anastomosis**

The Norwood anastomosis used in this setting is a slight modification of the procedure used in first-stage repair of patients with classic hypoplastic left heart physiology. It combines the Damus-Kaye-Stansel anastomosis with extensive augmentation (enlargement) of the hypoplastic aortic arch and upper descending thoracic aorta (see Chapter 49). It is important to emphasize that the augmentation patch used is of a slightly different shape from that described for the typical patient with hypoplastic left heart physiology. This is necessary because with either tricuspid atresia and discordant ventriculoarterial connection, or with double inlet ventricle with L-loop and discordant ventriculoarterial connection, orientation of the great arteries is different from that in patients with normally related great arteries (i.e., found in aortic atresia and other classic forms of hypoplastic left heart physiology).

**Muscular Resection to Relieve Subaortic Obstruction**

This technique is described for patients with tricuspid atresia and discordant ventriculoarterial connection with subaortic obstruction at the bulboventricular foramen (VSD) or incomplete RV, but is applicable to all patients with univentricular AV connection in whom the aorta arises from an incomplete ventricle. Other lesions that result in a similar problem include DILV with discordant ventriculoarterial connection, and mitral atresia with concordant ventriculoarterial connection (see Chapter 56).

Patient preparation, median sternotomy, and cardiac exposure are similar to that described in the preceding text. In the unusual case that there has been no previous surgery, upon opening the pericardium, it is immediately noticed that aorta and diminutive RV are anterior. More commonly, previous surgery (including previous median sternotomy) has been performed. Caution should be exercised upon repeat median sternotomy, because the anterior aorta may be in close proximity to the posterior sternal table. The patient is prepared for CPB by placing purse strings in the ascending aorta just below the brachiocephalic artery origin and in SVC and IVC. Aortic and bicaval cannulation is then performed in standard fashion, the patient is placed on CPB, and moderate hypothermia is achieved. The aorta is clamped, and cardioplegia is administered through the aortic root (see “Single-Dose Cold Cardioplegia in Neonates and Infants” in Chapter 3).

The VSD is best approached through an incision in the incomplete ventricle (outlet chamber) just below the aortic
valve (Fig. 41-23, A). This incision is later closed by an enlarging patch. Alternatively, the VSD may be approached through the aorta; however, this exposure may be limited because the aortic valve and aorta are typically hypoplastic. Some have considered the risk of surgically induced heart block to be high in this procedure, but risk is substantially reduced using currently available knowledge about the location of the conduction tissue. When the VSD is observed through an incision in the outlet chamber (morphologic RV), the relationship of the conduction system to the VSD is the same as with any conoventricular VSD, with the conduction tissue at the posterior inferior rim of the defect. This is true whether the underlying morphology is tricuspid atresia and discordant ventriculoarterial connection, or double inlet single LV and discordant AV and ventriculoarterial connections. Confusion regarding this issue has arisen because the conduction system appears to be positioned on the “anterior” rim of the VSD when viewed from the perspective of the main ventricular chamber of either tricuspid atresia and discordant ventriculoarterial connection or DILV and discordant AV and ventriculoarterial connections. This confusion is the result of difficulty in conceptualizing the spatial arrangement of the two ventricular chambers and ventricular septum with this exposure, which involves an atrial incision, substantial rotation of the heart, and visualization of the VSD through an AV (typically mitral) valve.

The preferred approach is a vertical incision made in the outlet chamber free wall directly in line with the course of the ascending aorta (see Fig. 41-23, A). This incision should be made only after all major coronary artery branches are identified, because the incision should not cut across any of these. Once the outlet chamber has been entered, the VSD is identified and a full-thickness wedge of septum is removed from the anterior and anterior apical aspects of the rim of the defect (Fig. 41-23, B).

Obstructing muscle bundles within the outlet chamber are excised. The outlet chamber is enlarged by closing the ventriculotomy with an enlarging patch, typically of polyester or glutaraldehyde-treated pericardium, using running monofilament suture (Fig. 41-23, C). The process of separation from bypass and chest closure is standard.

**Special Features of Postoperative Care**

These are detailed under Special Features of Postoperative Care in Chapter 49.

**Results**

**Pulmonary Trunk Banding and Aortic Arch Reconstruction**

In early-era reports, both early and intermediate-term survival have been unfavorable in patients with single-ventricle physiology following initial coarctation repair, with or without pulmonary trunk banding (see Fig. 41-19) (see “Results of Repair of Coarctation in Patients with Other Major
Coexisting Intracardiac Anomalies” in Section I of Chapter 48). Risk of death early after the procedure has been particularly high (see Fig. 41-20). This may be due to associated instability that accompanies single-ventricle physiology. Although these data are for patients with DILV with arch obstruction, it is likely that similar outcomes pertain to patients with tricuspid atresia and discordant ventriculoarterial connection with aortic arch obstruction. More recent reports show better early and midterm outcomes. Odim and colleagues reported no early mortality (0%; CL 0%-12%) and an 87% survival at mean follow-up of 68 months in 15 patients undergoing aortic arch reconstruction and pulmonary trunk banding.38

Proximal Pulmonary Trunk to Aortic Connection with Arch Repair

This procedure carries a substantial early mortality (=35%).325 Although limited data are available for evaluating it, certain insights can be gained by comparing the Damus-Kaye-Stansel and shunt procedure with the Norwood procedure, because there are important parallels between them (see “First-Stage Reconstruction [Norwood Procedure]” under Results in Chapter 49). Regurgitation of the original aortic or pulmonary valve, either immediate or delayed (perhaps due to distortion of the great arteries), and hemodynamic instability relating to a pulmonary circulation arising from a systemic–pulmonary arterial shunt all can be problems if the Damus-Kaye-Stansel procedure is used in this setting. Despite high early mortality, intermediate-term results in hospital survivors appear to be good.7,8,12,21,27

Modified Norwood Anastomosis

Early mortality ranges from 0% to 35%.24,25 Reports with better outcomes tend to be from more recent series.24 It should be expected that outcomes from the modified Norwood procedure will be somewhat better in this morphologic population compared with patients with aortic atresia and other forms of hypoplastic left heart physiology because of fewer morphologic risk factors.

Muscular Resection to Relieve Subaortic Obstruction

Knowledge of results of this operation is incomplete because of the great heterogeneity of patients receiving it, relatively small experience with it, and lack of complete and long-term follow-up.1,5,17,13,23,28 Hospital mortality of 11% (CL 1%-33%) has been reported by Cheung and colleagues among 9 patients.17 The death occurred in a patient operated on in the first year of life at the time of VSD enlargement. One patient required repeat surgical enlargement. Deaths after hospital dismissal were related to subsequent procedures. More recently, Cerillo and colleagues reported no early mortality after 6 resections (0%; CL 0%-27%).59

Indications for Operation

When designing the appropriate operative procedure, the status of the aortic arch must be assessed. If the ascending aorta and arch are widely patent, associated subaortic obstruction is less likely. If obstruction is identified at the aortic arch, the subaortic region must be carefully evaluated because obstruction at this level is commonly present. Accurately evaluating the subaortic region may be difficult in the preoperative setting of a patent ductus arteriosus, because the LV ejects only part of the systemic cardiac output (upper-body component) across the VSD to the aortic valve; the remainder (lower-body output) is delivered from the LV directly across the pulmonary valve and ductus arteriosus to the thoracic aorta. As a result, absence of a gradient (determined either by echocardiography or cardiac catheterization) between LV and aorta is an unreliable gauge of future outflow tract adequacy once the aortic arch is repaired and the ductus arteriosus removed. Under these circumstances, the entire systemic

Figure 41-23  Direct relief of subaortic obstruction in univentricular hearts with transposed great arteries. A, Median sternotomy exposure and standard cardiopulmonary bypass technique using moderate hypothermia and cardioplegic myocardial protection are utilized. Longitudinal incision in subaortic area of incomplete right ventricular (RV) chamber is used to expose subaortic obstruction. B, Internal anatomy of incomplete and hypoplastic RV chamber is shown. Dashed lines show incisions used to resect muscle that result in enlarging the ventricular septal defect (VSD). Wedge of full-thickness septal muscle between these two incisions is removed, taking care to avoid injury to adjacent aortic valve and underlying atrioventricular valve. Position of wedge resection is also designed to avoid conduction tissue positioned along posteroinferior rim of VSD, represented by open circles. C, Incision in free wall of incomplete RV is closed with a patch designed to augment subaortic chamber. Patch material can be polyester, glutaraldehyde-treated autologous pericardium, or polytetrafluoroethylene. Care is taken to avoid injury or obstruction to major coronary branches running along free wall of incomplete RV during incision closure.

A

B

Conduction tissue

C

PART VII  Congenital Heart Disease
cardiac output must cross the VSD and subaortic region. Because physiologic variables are unreliable, one must rely on morphologic details of the sizes of the VSD, subaortic region, and aortic valve itself in judging adequacy of the LV-to-aortic outflow tract. Echocardiographic characterization of VSD size has been suggested as a predictor of long-term adequacy of the LV outflow tract.\textsuperscript{M18}

However, if obstruction is documented preoperatively in this setting, then the systemic LV outflow tract will be clearly inadequate. If so, the operative procedure entails repair of the obstructed aortic arch, creating a proximal pulmonary trunk–to-aortic anastomosis (Damus-Kaye-Stansel procedure) and a systemic–pulmonary arterial shunt. This combination essentially achieves the same result as that achieved by aortic arch reconstruction in the Norwood procedure for hypoplastic left heart physiology (see Indications for Operation in Chapter 49). The Damus-Kaye-Stansel procedure with aortic arch reconstruction, or modifications of Norwood aortic arch reconstruction that some surgeons prefer, can be applied to other forms of univentricular AV connection in the setting of aortic arch and subaortic obstruction, most commonly DILV with discordant ventriculoarterial connection and mitral atresia with VSD and concordant ventriculoarterial connection (see Indications for Operation in Chapter 56).\textsuperscript{R26,V4}

For a detailed description of aortic arch reconstruction in hypoplastic left heart physiology, see the description of the Norwood operation under Technique of Operation in Chapter 49. Most forms of aortic arch obstruction in combination with subaortic obstruction occur in the setting of ventriculoarterial discordant connection. Orientation of the great vessels, therefore, is quite different from that in typical hypoplastic left heart physiology. As a result, the Norwood type aortic arch reconstruction is somewhat modified.

### SPECIAL SITUATIONS AND CONTROVERSIES

#### Concordant Ventriculoarterial Connection

**Systemic–Pulmonary Arterial Shunt**

**Site** Systemic–pulmonary arterial shunts can be placed at sites on the systemic and pulmonary arterial systems other than that described previously in this chapter. These alternative sites may be chosen for practical reasons relating to individual anatomy or simply surgeon preference. Anatomic variations that may determine site of the shunt include situs inversus, atrial isomerism, right-sided aortic arch, and abnormal arch branching patterns. In patients with small central pulmonary arteries, it may be wise to site the pulmonary arterial anastomosis on the pulmonary trunk segment, if one is present, to avoid distorting or occluding either left or right pulmonary arteries. Regardless of site, the systemic–pulmonary arterial connection is performed using a specific length and diameter of extended PTFE tube graft (see text that follows).

**Size** Diameter of the expanded PTFE graft is the most important determinant of resistance within a systemic–pulmonary arterial connection and therefore is the prime regulator of $Q_p$. Other factors, such as graft length and site of origin on the systemic circulation, also influence resistance but to a lesser degree (Poiseuille resistance relationships). Once the appropriate diameter is chosen for the graft, these other factors can be used in individual patients to help further regulate pulmonary blood flow to create the ideal balance between $Q_p$ and $Q_s$. A 3.5-kg infant is typically well served using a 3.5-mm-diameter graft connected to the brachiocephalic–right subclavian arterial junction. A larger infant, or one who has particularly small pulmonary arteries or manifests physiology indicative of elevated $R_p$, might best be served by a similar 3.5-mm tube graft connected directly to the brachiocephalic artery or even ascending aorta. With these adjustments, resistance in the artery giving rise to the tube graft is reduced, and therefore overall resistance across the connection is less, compared with a graft constructed with a more distal (smaller diameter) systemic connection. On the other hand, a smaller infant or one who manifests physiology indicative of very low $R_p$ preoperatively may best be served by a 3.5-mm-diameter graft connected entirely to the right subclavian artery. In this case, the subclavian artery contributes additional resistance to that of the tube graft. A 3-mm-diameter tube graft may be considered in particularly small infants, such as those with a body weight 2.5 to 3 kg or less (see “Type” in text that follows).

**Type** Technique of Operation in this section describes the preferred modified Blalock-Taussig shunt using an expanded PTFE tube graft. Systemic–pulmonary arterial shunts using direct arterial tissue-to-tissue connection, such as end-to-side connection of the subclavian artery to the RPA (classic Blalock-Taussig shunt),\textsuperscript{T2} direct ascending aorta–to-RPA connection (Waterston shunt), descending aorta–to-left pulmonary artery connection (Potts shunt), and central ascending aortic–to-pulmonary trunk connection, are rarely if ever used in the setting of normally developed branch pulmonary arteries. These connections all have disadvantages of unreliable regulation of $Q_p$ or high prevalence of pulmonary artery distortion.

There is no foolproof formula for choosing optimal shunt diameter and connection to create perfectly balanced $Q_p$. Careful evaluation of patient size, pulmonary arterial anatomy, and physiologic behavior of the pulmonary vasculature preoperatively, and the surgeon’s own experience, all are considerations when choosing size, site, and type of shunt that will best serve an individual patient. A surgeon who typically uses precise and accurate surgical technique will achieve a 3.5-mm orifice at systemic and pulmonary artery anastomoses when a 3.5-mm tube graft is used; one who typically uses less precise and accurate technique will likely create anastomoses at both sites that are smaller than the 3.5-mm tube graft. In this case, a surgeon may come to realize over time that a larger-diameter graft provides the appropriate degree of pulmonary flow.

**Aspirin Use** Although the use of aspirin following shunt placement is widely practiced, until recently there has been little documented evidence of its efficacy. The recent multicenter study by Li and colleagues\textsuperscript{L20} shows that risk of thrombosis and death are both lower when aspirin is used. The study involved a wide range of morphologic lesions, and aspirin daily dosage varied, with 80% of patients receiving 20 to 40 mg · day\textsuperscript{−1}. The efficacy of aspirin did not vary with dosage.

**Left Pulmonary Artery Stenosis** Occasionally, infants with this subset of tricuspid atresia have either hypoplasia or a discrete stenosis in the proximal left pulmonary artery in the region of the ductus arteriosus. This lesion will almost certainly become rapidly progressive once PGE\textsubscript{2} infusion is stopped. It is usually prudent to address it at the initial shunt procedure. Individual judgment is required regarding the method of relieving the stenosis. A patch can
Repair of periductal left pulmonary artery (LPA) stenosis in neonate.  

To achieve satisfactory reconstruction, the pulmonary trunk–to-aortic connection (Damus-Kaye-Stansel anastomosis) with arch reconstruction, or a modified Norwood procedure can be performed without using CPB, allowing the shunt to perfuse the right lung only during left pulmonary artery reconstruction. Occasionally with more complex central pulmonary artery stenosis, CPB support is necessary to achieve satisfactory reconstruction.

Discordant Ventriculoarterial Connection  
Aortic Arch Obstruction without Apparent Subaortic Obstruction  
When this subset of tricuspid atresia exists with important aortic arch obstruction but without evidence of clear subaortic obstruction, surgical management in the neonatal period is controversial. Some surgeons prefer to act on the established observation that presence of aortic arch hypoplasia increases the likelihood of subaortic obstruction, and in all such cases they perform a proximal pulmonary trunk–to-aortic connection (Damus-Kaye-Stansel anastomosis) with arch reconstruction, or a modified Norwood procedure. This approach has the advantage of removing uncertainty related to adequacy of LV systemic outflow. Its disadvantages are magnitude and risk of the procedure, which usually involves a prolonged period of CPB, myocardial ischemia, and in many hands, cerebral ischemia. This risk is warranted if subaortic obstruction exists; it may not be warranted if in fact the equivocal subaortic region is adequate.

Thus, some surgeons prefer to make an individual evaluation of the subaortic region. If its morphologic characteristics suggest the LV-to-aortic outflow tract will be adequate, an isolated arch repair and pulmonary trunk band is performed. The advantage of this approach is that CPB and organ ischemia are avoided, and complexity of the procedure minimized. Acute morbidity and mortality with this operation are clearly lower than with the former approach. The disadvantage, however, is that the subaortic region remains a concern. Therefore, careful and frequent evaluation of the subaortic region, beginning in the immediate postoperative period, must be undertaken.

Mild subaortic obstruction for a short period may not negatively affect function of the single ventricle. Recent evidence suggests that patients with subaortic gradients up to 40 mmHg for up to about a 6-month duration, who initially underwent pulmonary artery banding and only later DKS procedures, did not have negative effects on ventricular function or reduced candidacy for later Fontan.  

Assessment of the subaortic area must be ongoing over the course of the patient’s life. If LV-to-aortic outflow obstruction develops, the patient must undergo one of several subsequent procedures to relieve it. If subaortic obstruction occurs in the first several months following aortic arch repair and pulmonary trunk banding, the most appropriate procedure is a proximal aortic–to–pulmonary trunk connection (Damus-Kaye-Stansel anastomosis) and systemic–pulmonary artery shunt. Before this procedure is done, the banded pulmonary trunk must be assessed carefully to confirm that no damage to the pulmonary valve has occurred from the band. Distortion or damage to the pulmonary valve resulting from the banding procedure may increase the chances of important neoaortic regurgitation following the proximal pulmonary trunk–to-aortic connection. When careful attention is given to technical details, competence of the native pulmonary valve can usually be preserved. If the pulmonary valve is
regurgitant, the only remaining surgical alternative is to incise and excise the obstructing subaortic muscle at the level of the VSD and hypoplastic RV chamber. Such a procedure, however, carries an important risk of morbidity in the small infant or neonate with respect to ventricular function and conduction integrity.

If subaortic obstruction develops later in infancy following neonatal arch reconstruction and pulmonary trunk banding, proximal aortic to pulmonary trunk connection (Damus-Kaye-Stansel anastomosis) can be performed at the time of superior cavopulmonary connection, obviating need for a systemic–pulmonary artery shunt. Again, careful evaluation of the adequacy of the pulmonary valve must be undertaken, and the alternative of a subaortic muscle resection must be given consideration.

If subaortic obstruction develops in a patient who previously received arch reconstruction and pulmonary trunk banding as a neonate, and who has subsequently undergone either a superior cavopulmonary shunt or a Fontan procedure, risk/benefit analysis of each of the two procedures that can be used to relieve the obstruction is substantially altered. Forward flow across the pulmonary valve is eliminated or markedly reduced at the time of the superior cavopulmonary shunt and must be eliminated at the time of the Fontan. If subaortic obstruction develops subsequently, long-standing lack of flow across the pulmonary valve, with stasis of the valve cusps, increases concern about its long-term function in the systemic circulation. Muscle resection to enlarge the VSD and subaortic region, although never without morbidity, becomes a more attractive option under these circumstances. In the larger patient, accurate resection at the level of the VSD may relieve obstruction with less risk of injuring the conduction system or major coronary branches in the septum.

**Arterial Switch Operation**

The technique used for neonates with simple transposition of the great arteries (see “Arterial Switch Operation” under Technique of Operation in Chapter 52) has been described in a limited number of patients with subaortic obstruction complicating the various forms of univentricular AV connection described in this chapter. This technique has one major disadvantage and as a result is not commonly used. Although the arterial switch itself relieves subaortic obstruction completely, restriction at the VSD and outlet chamber regulates Qp. Obstruction can be quite variable and, as a result, regulation of Qp can be unpredictable, resulting in patient instability or need for further procedures to stabilize or rebalance Qp.

A single report is the basis for assessing risk of the procedure in this setting. From this experience, 5 of 6 (83%; CL 54%-98%) critically ill neonates were hospital survivors of the arterial switch procedure (accompanied by aortic arch repair and atrial septectomy), and 4 of the 6 (67%; CL 38%-88%) were still awaiting definitive Fontan operation at the time of the report. No late follow-up of this experience is available.

**Other Palliative Operations**

Early mortality after palliative procedures discussed in the text that follows should be low. Procedures should not interfere with, and indeed should facilitate, later Fontan operation, and they should provide good long-term palliation for patients in whom the completed Fontan operation is not possible.

**Atrial Septectomy**

Atrial septectomy, usually performed for patients with mitral atresia, can be performed with low mortality either as an isolated procedure or combined with pulmonary trunk banding or a systemic–pulmonary arterial shunt procedure (see Table 41-2). This success, however, is not universal. Shore and colleagues report a high mortality (23%; CL 10%-41%).

**Hybrid Palliation**

The hybrid procedure, initially designed as a neonatal alternative to the Norwood operation for patients with aortic atresia and other forms of hypoplastic left heart physiology (see Chapter 49), has occasionally been applied to other single-ventricle patients with systemic outflow obstruction and unobstructed pulmonary blood flow.

**Other Operations in Neonatal Period**

Other operations are indicated for specific physiologic circumstances. These primarily include anomalous pulmonary venous connection and occasionally AV valve regurgitation. Outcomes after surgical management of single-ventricle patients with associated anomalous pulmonary venous connection, especially when obstructed, are poor. Sznizobahmya and colleagues report 1-year actuarial survival of 31%. Lodge and colleagues report 1-year survival of 53%, but when transplantation is included, midterm survival without need for transplant is about 25%.

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**Section III Second-Stage Palliation**

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

The second stage of the three-stage management plan for patients with tricuspid atresia and other forms of single-ventricle physiology has three purposes:

- Eliminate inefficiencies of the completely mixed circulation as early in life as possible
- Correct or eliminate existing morphologic abnormalities before Fontan operation
- Allow for ventricular remodeling in response to the acute reduction in volume load

Eliminating physiologic inefficiencies of the completely mixed circulation is accomplished by partially separating pulmonary and systemic venous circuits. By directing desaturated SVC blood exclusively into the pulmonary arteries, using a superior cavopulmonary shunt or hemi-Fontan connection, efficiency of gas exchange is improved such that the systemic–pulmonary arterial connection (via either a systemic–pulmonary arterial shunt or pulmonary trunk band) can be eliminated or markedly reduced. This results in dramatic reduction in workload of the single ventricle to a level that approaches that in an intact normal circulation. The new physiology has important positive implications for
improved functional status and long-term preservation of the myocardium. This is an important consideration because failure of the myocardium is one of the most important causes of long-term morbidity and mortality in single-ventricle patients, both with and without Fontan physiology (see “Cardiomyopathy” under Natural History in Section 1). \(^{(15, 22)}\) Reduction in ventricular work is accomplished without compromising gas exchange or \(\text{SaO}_2\), which typically remains above 80%. Additionally, diastolic shunt runoff is eliminated, increasing aortic diastolic pressure and improving coronary perfusion.

Considering the beneficial effects of the physiology associated with the superior cavopulmonary shunt compared with that of a completely mixed circulation, it seems prudent to perform the cavopulmonary shunt as soon as it is safe to do so. The major deterrent to performing it in the neonate is elevated pulmonary resistance (Rp) following birth. In theory, the superior cavopulmonary shunt should be possible within 4 to 8 weeks after birth when Rp has decreased to normal. Based on these concepts, there has been a general trend toward performing the superior cavopulmonary shunt in early infancy. \(^{(5, 10, 13, 26, 22)}\) This experience has shown that it can be performed at age 8 to 10 weeks, with morbidity similar to that seen in infants age 6 months and older. However, the experience of one of the authors (Hanley FL: personal communication, 2002) has shown that the procedure is associated with increased morbidity when performed between age 4 and 6 weeks. \(^{(7)}\) This experience shows that the morbidity is not related to persistent elevation inRp, because pressure in the cavopulmonary system is not elevated. Rather, it is related to unacceptable cyanosis. It thus appears that factors other than elevated Rp, such as poor ventilation/perfusion matching or exaggerated responses in the lungs to CPB, may play important roles in determining the lower age limit for safely performing the superior cavopulmonary shunt.

The second purpose for performing the second-stage operation is to correct or eliminate any existing morphologic abnormalities before the Fontan procedure is performed. The second-stage procedure is preventive in this regard. Early removal of the synthetic systemic–pulmonary arterial shunt and creation of a tissue-to-tissue cavopulmonary connection prevent branch pulmonary artery distortion and eliminate any possibility of developing pulmonary vascular obstructive disease. Additionally, the second-stage operation provides the opportunity to correct other malformations such as branch pulmonary artery hypoplasia or stenosis, arch obstruction, subaortic obstruction, AV valve regurgitation, restrictive atrial septum, or anomalous pulmonary venous connection. Careful early attention to these issues preserves and maximizes overall cardiopulmonary function and markedly simplifies the technical procedure at the Fontan operation.

The third purpose of the second-stage operation is to allow for ventricular remodeling, which necessarily occurs with acute reduction in volume loading, to happen prior to the Fontan. Acute volume reduction results in temporary relative ventricular hypertrophy, lower ejection fraction, and diastolic filling abnormalities. \(^{(22, 24)}\) These changes resolve over time. Thus, ventricular mass and function will return toward normal well before the Fontan operation if a second-stage procedure is performed. The acute ventricular changes associated with volume reduction are better tolerated under conditions of the superior cavopulmonary shunt physiology than under conditions of Fontan physiology.

### TECHNIQUE OF OPERATION

#### Preoperative Management

Prior to proceeding with second-stage palliation, assessment with echocardiography, and usually cardiac catheterization, is performed. Echocardiography primarily evaluates existing intracardiac morphologic abnormalities and identifies new or evolving ones, such as AV valve regurgitation or ventricular outlet obstruction. Cardiac catheterization primarily is used to evaluate morphology of pulmonary artery branches and measureRp, a critically important value in determining the advisability of creating a cavopulmonary shunt (see Indications for Operation later in this section). At catheterization, pulmonary artery pressure can accurately be estimated by measuring pulmonary venous wedge pressure, thus simplifying the procedure. \(^{(25)}\) Recently, some have argued that routine catheterization is not necessary and should be performed only when noninvasive evaluation by echocardiography, computed tomography angiography (CTA), or cardiac MRI suggests that abnormalities of ventricular end-diastolic pressure and Rp are likely to be present. \(^{(20, 23, 29, 31, 26, 29)}\)

#### Bidirectional Superior Cavopulmonary Shunt

This palliative operation diverts SVC blood from either one or bilateral superior venae cavea to the pulmonary arteries, with preservation of continuity between right and left pulmonary arteries. Usually, patients will have undergone previous palliative procedures involving either a systemic–pulmonary arterial shunt or a pulmonary trunk band. Operation is typically performed through a median sternotomy with or without CPB.

#### Using Cardiopulmonary Bypass

When CPB is used, the ascending aorta and SVC at the brachiocephalic–jugular vein junction are cannulated, and a calcium-supplemented blood prime is used with either mild or no hypothermia (Fig. 41-25, A). After partial bypass is initiated, the heart is allowed to remain beating, and all sources of systemic-to-pulmonary blood flow are controlled. If the decision is made to remove all extra sources of pulmonary blood flow permanently, it can be done at this point. If a systemic–pulmonary arterial shunt is present, it is ligated either with heavy suture material or metal clips and always divided (see Fig. 41-25, A). If a pulmonary trunk band is present or any forward flow exits from heart to pulmonary arteries, the pulmonary trunk is transected between vascular clamps, and proximal and distal ends are oversewn with running monofilament suture. Care should be taken to avoid creating a blind pouch when the proximal pulmonary trunk is transected, because this pouch may serve as a nidus for thrombus formation, with the potential for systemic embolization. If the decision is made to keep an extra source of pulmonary blood flow, the systemic–pulmonary arterial shunt is temporarily controlled with vascular clamps, whereas a pulmonary trunk band need not be addressed at this time in the procedure.

Vascular clamps are placed across the SVC at the cavoatrial junction and close to the venous cannulation site. The SVC is transected as it crosses the RPA. Theazygos vein is ligated to avoid late decompression of superior cavopulmonary shunt flow into the lower body. The SVC stump attached to the right atrium is oversewn with a running monofilament suture.
suture. An appropriately sized partial occlusion vascular clamp is then placed on the cephalad aspect of the RPA, and it is incised over an appropriate length to accommodate the circumference of the transected SVC. If a systemic–pulmonary arterial shunt has been previously placed into the RPA, all shunt material is completely removed from it before creating the anastomosis between SVC and RPA (Fig. 41-25, B). An end-to-side anastomosis of SVC to RPA is performed using 7-0 absorbable monofilament suture. The patient is then separated from CPB, and cannulae are removed (Fig. 41-25, C). Atrial pressure is monitored with an indwelling catheter, and pulmonary artery pressure is measured before chest closure.

If the patient has a preexisting systemic–pulmonary arterial shunt and the decision is made to allow the shunt to remain patent as an extra source of pulmonary blood flow, it is usually necessary to reduce shunt flow substantially (Fig. 41-25, E). It can be reduced by placing either sutures or

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**Figure 41-25** Creation of right-sided bidirectional superior cavopulmonary shunt. A, Surgical exposure is through a standard median sternotomy as shown. Procedure can be performed on partial cardiopulmonary bypass (CPB), as shown here, by cannulating ascending aorta and cephalad portion of superior vena cava (SVC). At institution of CPB, the dissected and exposed previously placed right subclavian artery–to–pulmonary artery shunt is immediately ligated at its proximal origin and divided. As shown in the two insets, azygos vein is doubly ligated and divided. B, SVC has been divided between clamps and cardiac end oversewn with a continuous monofilament suture. Old polytetrafluoroethylene shunt is completely removed from right pulmonary artery (RPA), and RPA opening is enlarged to accommodate diameter of SVC. Cephalad portion of SVC is then connected to RPA end to side using absorbable fine monofilament suture. Posterior aspect of anastomosis is completed first, as shown, followed by anterior component. SVC clamp is then removed, and patient is separated from CPB in standard fashion. C, Completed procedure.
Exposure is through median sternotomy. Previously placed pulmonary trunk band is shown. After mobilizing SVC and RPA, two appropriately sized right-angled venous cannulae are inserted into SVC at brachiocephalic–jugular vein junction and into right atrial appendage. They are carefully de-aired and connected together following full heparinization to provide continuous SVC-to-right atrial flow while creating the SVC-to-RPA anastomosis. After cannulae are secured and flow established through them, vascular clamps are placed on SVC just inferior to upper cannula and at SVC–right atrial junction. SVC is transected as it crosses over RPA. Transected cardiac end of SVC is oversewn with a continuous monofilament suture. A partial occlusion clamp is placed on superior aspect of RPA, taking care not to disrupt forward flow through pulmonary trunk band site to left pulmonary artery, and an incision is made in sequestered portion of RPA to accommodate circumference of SVC. SVC is connected end to side to RPA using a fine absorbable monofilament suture with continuous technique. Upon completion of anastomosis, SVC and RPA clamps are removed, and caval and right atrial cannulae are clamped and removed, establishing bidirectional superior cavopulmonary shunt-to-pulmonary artery flow. Based on patient’s hemodynamic response, pulmonary trunk band is further tightened, or pulmonary trunk is completely occluded (see text for full discussion of factors involved in this decision). Similar to D, except that existing pulmonary blood source is through a left modified Blalock-Taussig shunt rather than from forward flow across banded pulmonary trunk. Reconstruction proceeds exactly as in D, except that at completion of procedure, after physiologic assessment of patient has been made, shunt is modified appropriately or eliminated using medium-sized metal clips (see text for full discussion of factors involved in shunt management at time of bidirectional superior cavopulmonary shunt). As shown in inset, shunt diameter is narrowed using several metal clips.
metal clips along the length of the shunt to partially reduce its internal diameter. Shunt flow can be reduced in a quantitative fashion by carefully observing changes in hemodynamics as shunt diameter is narrowed, and by adhering to the following process. Preoperative catheterization data are reviewed, and thus the surgeon has a good idea of amount of flow through the shunt under baseline preoperative conditions. After the bidirectional superior cavopulmonary shunt is completed and the patient removed from CPB and in a hemodynamic steady-state, the change in systemic diastolic blood pressure that occurs when the temporarily occluded shunt is opened is observed. This maneuver can be repeated several times to get a reliable measurement. The shunt can then be permanently narrowed to achieve a diastolic blood pressure at a level between the two values observed when the shunt was completely open and when it was occluded. This provides a semiquantitative estimate of reduction in shunt flow. Additional information that can be used to adjust the extra source of flow is absolute pressure within the SVC and pulmonary arteries following the bidirectional superior cavopulmonary shunt. As a general rule, mean pulmonary arterial pressures should be less than 15 mmHg, and pulse pressure in the pulmonary artery should be less than 5 mmHg.

If the preexisting source of pulmonary blood flow was through a pulmonary trunk band or stenotic pulmonary valve and it is decided to leave this as an extra source of flow, it is usually necessary to adjust the band or further narrow the pulmonary trunk after creating the bidirectional cavopulmonary anastomosis. Changes in systemic diastolic blood pressure are insensitive indicators of changes in flow across a pulmonary trunk band; measuring distal mean pulmonary arterial pressure and pulsatility responses with the band site open and with it temporarily occluded is the best way to adjust flow across the pulmonary valve or pulmonary trunk band. The standard method for placing and adjusting a pulmonary trunk band is used (see Fig. 41-21, D).

Without Using Cardiopulmonary Bypass
When CPB is not used, it is prudent to decompress the upper-body venous system while creating the cavopulmonary anastomosis if a single SVC is present. Before placing venous cannulae, the patient is fully heparinized (3 mg · kg⁻¹). Two venous cannulae are placed, one in the SVC and the other in the right atrial appendage, de-air ed, and connected together (Fig. 41-25, D).

If bilateral SVCs are present, decompression is usually not needed. If the preexisting source of pulmonary blood flow is either a right- or left-sided systemic–pulmonary arterial shunt, the operation proceeds by creating the first cavopulmonary anastomosis on the side opposite the preexisting source of pulmonary blood flow. Once this anastomosis is completed, it can serve as an adequate source of pulmonary blood flow while the systemic–pulmonary arterial shunt is removed in preparation for creating the second cavopulmonary connection on the side where the shunt existed.

Hemi-Fontan Operation
The hemi-Fontan operation is physiologically similar to a bidirectional superior cavopulmonary shunt, but important differences exist. The hemi-Fontan requires hypothermic CPB and cardiac arrest because it is an open cardiac procedure, technical details of the operation are more complex, and potential for sinoatrial node injury is increased. Some surgeons prefer the hemi-Fontan operation because it is believed that this procedure makes a subsequent lateral tunnel Fontan simpler to perform. Others who use the lateral tunnel Fontan prefer the bidirectional superior cavopulmonary shunt. If the subsequent Fontan operation will be an extracardiac conduit Fontan, the hemi-Fontan operation provides no advantage.

The hemi-Fontan operation consists of diverting SVC flow to the pulmonary arteries by creating a right atrial–to-RPA anastomosis. After CPB, hypothermia, and cardiac arrest are achieved in standard fashion, an incision in the roof of the right atrium is spiraled onto the back of the SVC (Fig. 41-26, A). A complementary incision is made on the caudad aspect of the RPA, and the two structures are sewn together to complete the anastomosis (Fig. 41-26, B-C). A right atrial free-wall incision is made, and a pulmonary allograft patch is placed inside the superior aspect of the right atrium, partitioning the inferior vena caval, coronary sinus, and pulmonary venous flow from the hemi-Fontan anastomosis (Fig. 41-26, D). A large atrial septal opening is created if necessary, and any central pulmonary artery abnormalities may be corrected at the same procedure. Managing preexisting sources of pulmonary blood flow is similar to that described in the preceding text for the bidirectional superior cavopulmonary shunt. Upon completion of the Fontan operation, if a lateral tunnel Fontan is to be used, the intraatrial patch is removed, and the lateral tunnel baffle can be easily placed while working solely within the right atrium.

The hemi-Fontan operation can be simplified by performing a standard bidirectional superior cavopulmonary shunt and connecting the cardiac stump of the transected SVC into the caudad surface of the RPA. The procedure is completed within the right atrium by placing a patch over the right atrial–SVC orifice. Although this modification simplifies the surgical anastomosis, it also requires hypothermic CPB and cardiac arrest, because it is an open cardiac procedure. At the time of the Fontan operation, the intraatrial patch is removed.

SPECIAL FEATURES OF POSTOPERATIVE CARE
In general, care is routine. Hemodynamics are typically stable. The patient should be positioned with the head elevated 30 degrees because of the elevated SVC pressure. Aggressive pulmonary toilet is particularly important because important desaturation can occur with this physiology if gas exchange is not efficient. The hematocrit should be maintained at 45% at least. Duration of mechanical ventilation should be minimized; however, while the patient is mechanically ventilated, care should be taken to keep PaCO₂ at approximately 45 mmHg.

RESULTS
Bidirectional Superior Cavopulmonary Shunt
Hospital mortality is about 5% to 10%. However, this may partly reflect additional risk from concomitant procedures. Early palliation has generally been excellent, with SaO₂ averaging 85%. Midterm results can be estimated from only limited data, because currently
most patients receiving a bidirectional Glenn procedure go on to a Fontan operation. Available reports suggest 1-year survival of about 90% and 5-year survival of more than 80%. A8, H8, P17 Risk factors for death include elevated pulmonary artery pressure, total anomalous pulmonary venous connection, heterotaxy, RV morphology, AV valve regurgitation, and very young age. A8, R6, S5, S23 Age between 2 and 6 months and bidirectional superior cavopulmonary shunt as a second-stage operation in appropriately selected patients are not risk factors for death. C13, P14, B6

Risk factors for prolonged intensive care and hospital stays include length of CPB, RV morphology, elevated central venous pressure, elevated transpulmonary gradient, and low weight for age at the time of the procedure. A13, E22

The operation facilitates, more so than the classic Glenn operation, a subsequent completed Fontan operation, because the RPA has not been divided. In patients not suitable for the completed Fontan operation, long-term palliation, although not known, will probably be similar to that achieved by the classic Glenn operation (see “Classic Glenn Operation” under Special Situations and Controversies in Section I).

Hemi-Fontan Operation

Early mortality for the hemi-Fontan operation is in the range of 5% to 10%. D23, J6 The operation considerably facilitates the subsequent procedure of conversion to the lateral tunnel form of completed Fontan procedure, but does not facilitate conversion to the extracardiac conduit form. There is evidence that the hemi-Fontan compromises sinus node function at least temporarily. C28
INDICATIONS FOR OPERATION

Second-Stage Palliation

Although there is no absolute indication for the bidirectional superior cavopulmonary shunt or hemi-Fontan as the second stage of a three-stage plan to completion Fontan, it is widely believed that the second-stage procedure is beneficial and therefore indicated in most patients with single-ventricle physiology.215,53,110 (see “General Plan for Surgical Management of Single-Ventricle Physiology” in Section 1). The procedure should be performed between age 3 and 6 months to achieve maximum benefit. The bidirectional superior cavopulmonary shunt and hemi-Fontan achieve the same physiologic result; however, morbidity of the procedures may be different (see “Hemi-Fontan Operation” under Technique of Operation in this section). If an extracardiac conduit Fontan is contemplated, the bidirectional superior cavopulmonary shunt is the clear choice for the second-stage procedure, whereas if a lateral tunnel Fontan is contemplated, the hemi-Fontan may produce certain technical advantages.

Generally accepted contraindications to the procedure are:

- Age younger than 6 weeks
- Mean pulmonary artery pressure greater than 30 mmHg regardless of Rp
- Rp greater than 4 units · m²
- Pulmonary venous obstruction

These must be eliminated or corrected, sometimes with interim surgical or interventional procedures, before proceeding with the superior cavopulmonary shunt or hemi-Fontan. A recent study suggests that patients with baseline (room air) Rp as high as 6 units · m² can successfully undergo a superior cavopulmonary anastomosis if the Rp falls to less than 3.5 units · m² in 100% oxygen, albeit with increased risk of death.122 Inhaled nitric oxide may be beneficial in such high-risk cases.3

Bidirectional Superior Cavopulmonary Shunt as Primary Procedure

Patients who are not dependent on the ductus arteriosus for pulmonary blood flow, who maintain SaO₂ greater than 70% to 75%, and who do not have excessive Qp with pulmonary hypertension (mean pulmonary artery pressure > 25 mmHg) or failure to thrive may be considered for a primary bidirectional superior cavopulmonary shunt at about age 8 weeks.

SPECIAL SITUATIONS AND CONTROVERSIES

Three-Stage Palliation Plan

The three-stage surgical plan is neither mandatory nor universally practiced. Some centers selectively choose patients for the Fontan procedure following neonatal (first-stage) palliation only, whereas others routinely follow the three-stage plan. Currently, however, it is most commonly held that advantages of the second-stage bidirectional superior cavopulmonary shunt outweigh its disadvantages.215,517 Its main advantages are described at the beginning of this section. Additionally, evidence suggests that other complex measures of ventricular mechanics improve following the second-stage procedure.74,75 Disadvantages cited by some include acute surgical risks of an additional procedure, inadequate pulmonary artery growth under conditions of low Qp, development of aortopulmonary collateral vessels in response to low Qp and cyanosis, development of abnormal venovenous channels, and formation of intrapulmonary arteriovenous malformations.212,48,31,32,35 Important controversy exists regarding the clinical relevance of many of these disadvantages. It is generally believed, however, that the mortality risk (which is low) associated with the bidirectional superior cavopulmonary shunt is outweighed by its benefits, pulmonary artery size (diameter) may not correlate with Fontan outcome, and pulmonary artery growth may continue relatively normally following the shunt. Also, it is recognized that both acquired aortopulmonary collaterals and intrapulmonary arteriovenous malformations usually form gradually and in a small fraction of patients.14,35 As a result, interventional catheterization or an early Fontan procedure, when necessary, can eliminate or minimize these developments in most patients.829

Retaining Additional Source of Pulmonary Blood Flow

Another important management issue at the time of the second-stage procedure is whether to retain an additional source of pulmonary blood flow along with the bidirectional superior cavopulmonary shunt.229 Proponents of this practice argue that a controlled extra source of flow can provide a “normal” (Qp/Qs of 1) or close to normal amount of flow to the lungs, promoting normal pulmonary artery growth and possibly providing necessary humoral or hemodynamic factors (flow and pulsation) to eliminate or reduce the tendency for developing aortopulmonary collaterals and intrapulmonary arteriovenous malformations, with few or no ill effects.310,7,37,36 Opponents make two points:

- Even if the extra flow causes pulmonary artery growth and reduces collateral formation, there is no clinical benefit in terms of eventual Fontan candidacy or outcome.24,23,56
- Evidence exists that morbidity is increased and that an extra source of flow continues to place an increased, albeit limited, volume load on the single ventricle.7,18

Although the controversy is unresolved, a middle ground with appropriate patient selection and operative management might well maximize overall outcome. For example, patients with RV morphology, reduced ventricular function, or a common or regurgitant AV valve might best be managed without an extra source of pulmonary blood flow, based on careful risk/benefit analysis. On the other hand, patients with normal ventricular function, especially those with LV morphology or two ventricles, normally formed and competent AV valves, small pulmonary arteries, or certain forms of heterotaxy syndrome (that predispose to forming intrapulmonary AV malformations) might benefit from a carefully constructed extra source of pulmonary blood flow that augments Qp/Qs by an accurately determined additional 0.3 to 0.5.

Use of Cardiopulmonary Bypass

It has been shown that the superior cavopulmonary anastomosis can be created safely without the use of CPB.212,1,23 The decision regarding use of CPB is based on several practical
considerations. Avoiding CPB is an option if an existing source of pulmonary blood flow can be maintained while the bidirectional superior cavopulmonary shunt is being constructed, such as when the original source of pulmonary blood flow is a pulmonary artery band, central shunt, or shunt placed on the opposite side of the proposed bidirectional superior cavopulmonary shunt, or when bilateral superior venae cavae are present. When one of these exists, surgeon preference determines whether to use CPB or to avoid it. Even when these conditions do not exist, techniques have been devised to avoid bypass (see Fig. 41-25, D-E). The only situation in which CPB is absolutely necessary is when there is a single source of preexisting pulmonary blood flow through a systemic–pulmonary arterial shunt that is positioned such that the shunt must be completely removed to perform the bidirectional superior cavopulmonary shunt. This situation is commonly present when the SVC is unilateral and on the right side and the patient has received a previous right-sided modified Blalock-Taussig shunt.

**Section IV  Third-Stage Palliation (Fontan Operation)**

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

In typical three-stage surgical palliation for patients with tricuspid atresia, as well as for other forms of single-ventricle physiology, the patient presents for the Fontan procedure having already undergone a bidirectional superior cavopulmonary shunt or a hemi-Fontan procedure. At the time of the Fontan operation, all IVC blood flow is directed into the pulmonary circulation, leaving only pulmonary venous blood and coronary sinus blood to return to the common atrial chamber and single ventricle. Thus, this operation achieves almost complete separation of systemic and pulmonary circulations. Some centers routinely create a separate communication between systemic and pulmonary venous circulations (adjustable ASD, or fenestrated Fontan). In certain circumstances, this may provide a hemodynamic benefit, although it is achieved at the expense of increased mixing of desaturated blood with pulmonary venous return, thereby reducing SaO2.

At the time of the Fontan operation, other morphologic and hemodynamic issues may also require attention. If any systemic–pulmonary arterial connections exist, either natural or surgically created, every effort must be made to eliminate them, either at operation or by the interventional cardiologist at the time of preoperative cardiac catheterization. Additionally, other issues such as distortion or hypoplasia of branch pulmonary arteries, AV valve regurgitation, obstruction at any level in the systemic circulation, and abnormal systemic venoatrial connections should be addressed at the time of the Fontan.

In some cases, patients have not previously undergone typical first-stage neonatal palliation and second-stage bidirectional superior cavopulmonary shunt. Sometimes only one or the other of these procedures has been performed, and occasionally no previous surgical intervention has been required. If a bidirectional superior cavopulmonary shunt has not been performed, it is performed at the Fontan operation along with the IVC-to–pulmonary artery connection.

**Preoperative Evaluation**

Standard preoperative evaluation involves cardiac catheterization and echocardiography. Echocardiography is performed primarily to evaluate ventricular function and define details of intracardiac anatomy and physiology such as AV valve morphology and function. Cardiac catheterization is performed for two reasons:

- As a diagnostic study to evaluate morphology and hemodynamics that cannot be directly assessed by echocardiography. These include morphology of the distal pulmonary arterial system, which is assessed by angiography, and hemodynamic variables, including atrial filling pressure, ventricular end-diastolic pressure, pulmonary artery pressure, Qp : Qs, and systemic vascular resistance (Rs) and pulmonary vascular resistance (Rp). These data are used to select appropriate patients to undergo the Fontan operation and provide details for designing the operation. The specific physiologic data used to select patients for the Fontan operation are discussed under Indications for Operation later in this section.
- To determine whether any cardiac intervention will be needed before surgery. Potential interventional procedures include closing systemic–pulmonary arterial shunts, systemic–pulmonary artery collateral vessels, and systemic venoatrial connections, as well as balloon dilation or stenting of peripheral pulmonary arteries or aortic coarctation.

Recently, some have argued that routine catheterization is unnecessary; in their view, catheterization should be performed only when noninvasive evaluation by echocardiography, CT, angiography, and cardiac MRI suggest that abnormalities of end-diastolic pressure and pulmonary vascular resistance are likely to be present. Currently, this approach is taken by only a small minority of programs that manage Fontan patients. (The approach is taken somewhat more frequently during preoperative evaluation prior to the superior cavopulmonary anastomosis.) An important argument for preoperative catheterization is that acquired aortopulmonary collaterals develop in essentially all patients with single-ventricle physiology and present a potential volume load on the single ventricle. These can be coil occluded at the time of catheterization. Although there is universal acknowledgment of the development of these collaterals, opinions differ regarding their clinical significance.

In patients with prior atriopulmonary Fontan and atrial dysrhythmias, formal electrophysiologic evaluation is performed preoperatively.

**TECHNIQUE OF OPERATION**

Fontan connection can be achieved in a number of ways. Currently, the two most frequently used methods are the extracardiac conduit and lateral tunnel total cavopulmonary connections. The Society of Thoracic Surgeons (STS) Congenital Heart Database indicates that as of 2009, about two thirds of Fontans are of the extracardiac conduit type. In their classic forms, both include a bidirectional superior
cavopulmonary shunt or hemi-Fontan. The *atriopulmonary* connection, formerly the most frequently performed Fontan variant, is no longer considered a first-line option because of its related complications.

Other recently described techniques for creating the IVC-to-pulmonary artery connection are options. They include the extracardiac lateral tunnel technique, 

extracardiac pericardial tube technique, and direct IVC-to-pulmonary trunk connection. The latter is applicable only in a limited number of patients who have morphology favorable for a direct tissue-to-tissue connection. These procedures are not yet widely embraced.

Experimental evidence using computational fluid dynamics suggests that a Y-graft extracardiac conduit demonstrates better flow characteristics, during both rest and exercise, than a single tube either with or without an offset between IVC and SVC connections. 

This design has not been tested clinically, and concerns about thrombosis in the smaller-diameter limbs of the graft remain a concern at present.

**Extracardiac Conduit Fontan Operation**

Preparations for operation and median sternotomy are generally as described under “Incision” in Section III of Chapter 2. Operative technique is described for the patient with tricuspid atresia who has previously undergone neonatal palliation and subsequent second-stage palliation with a bidirectional cavopulmonary shunt. However, the general operative plan can be applied to all patients with single-ventricle physiology who have undergone similar neonatal and second-stage palliation. Details of the procedure require modifications appropriate to morphology, such as atrial isomerism, situs inversus, interrupted IVC, and distortions in pulmonary artery, systemic venous, or pulmonary venous systems. Techniques applicable to these morphologic variations are discussed in other chapters.

It is particularly important for the skin overlying the femoral vessels to be prepped into the surgical field. This is prudent for the usual reasons relating to reoperative sternotomy, but also because in some patients, especially those weighing more than 20 kg, peripheral venous cannulation may simplify the surgical procedure (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2).

After median sternotomy, complete dissection of the previously created superior cavopulmonary shunt and pulmonary artery system out to the hilum bilaterally is performed, including the pulmonary artery segment under the ascending aorta (Fig. 41-27, A). It is important to mobilize any adhesions around right-sided pulmonary veins as they enter the left atrium. The RPA is mobilized beyond the origin of the right upper lobe pulmonary artery such that it and lower-lobe pulmonary arteries are clearly identified circumferentially (see Fig. 41-27, A). A standard arterial purse string is placed in the ascending aorta and, in patients weighing less than 20 kg, a purse string is placed in the IVC at the reflection of the ascending aorta (Fig. 41-27, B). This completely isolates the central pulmonary artery system. In some cases, it may be necessary to disconnect the pulmonary trunk from the heart if this has not been done previously. The inferior (caudal) surface of the central pulmonary trunk and RPA is then opened, beginning in the periphery at approximately the level of the previously placed bidirectional superior cavopulmonary shunt and extending it centrally to the pulmonary trunk beneath the ascending aorta.

A PTFE tube graft is then selected to create the extracardiac conduit. The tube graft should be at least 2 cm in diameter and larger if possible, to accommodate growth to adulthood. Placing large conduits in small children may create IVC–conduit diameter mismatch, raising concerns about flow disruption and thrombosis. A 2-cm graft generally fits nicely in children who weigh 15 kg or more, although there can be wide variation in IVC diameter for the same body surface area. Akio and colleagues have reported a series of extracardiac conduits in patients weighing less than 10 kg without an increase in morbidity (see “Timing of Fontan Operation” under Indications for Operation later in this section). In patients who weigh more than 20 kg, a 22- or even 24-mm PTFE tube graft can easily be accommodated. Itatani and colleagues argue that smaller-diameter conduits (16 to 18 mm) provided superior flow characteristics when studied 1 year postoperatively in 3-year-old patients, however, there are concerns that these conduits may be of inadequate size as these children grow.

Before creating the proximal anastomosis, the PTFE graft is beveled such that the free edge of the graft matches the length of the extensive incision in the right and central pulmonary arteries. In this way, the proximal anastomosis can also be used to patch-augment any central pulmonary artery distortion or hypoplasia. Occasionally the proximal anastomosis must be extended across the central pulmonary artery to the left pulmonary artery if there is proximal left pulmonary artery stenosis. This can easily be accomplished, because the left pulmonary artery is controlled by a vascular clamp obliquely across the peripheral RPA close to the bidirectional superior cavopulmonary shunt anastomosis, such that a long segment of the inferior (caudal) aspect of the pulmonary trunk and RPA is isolated. The left pulmonary artery is clamped on the left side of the ascending aorta (Fig. 41-27, B). This completely isolates the central pulmonary artery system. In some cases, it may be necessary to disconnect the pulmonary trunk from the heart if this has not been done previously. The inferior (caudal) surface of the central pulmonary trunk and RPA is then opened, beginning in the periphery at approximately the level of the previously placed bidirectional superior cavopulmonary shunt and extending it centrally to the pulmonary trunk beneath the ascending aorta.

The conduit to the right lung is anastomosed end-to-end to the peripheral RPA close to the bidirectional superior cavopulmonary shunt anastomosis. The pulmonary trunk is beveled such that the free edge of the graft matches the diameter limbs of the graft remain a concern at present.

Usually the upper anastomosis of the Fontan connection can be performed before instituting CPB.

A segment of central pulmonary trunk and RPA proximal to the previously placed bidirectional superior cavopulmonary shunt is isolated in preparation for the upper anastomosis. This is accomplished without interrupting flow from the SVC to right lung by placing a vascular clamp obliquely across the peripheral RPA close to the bidirectional superior cavopulmonary shunt anastomosis, such that a long segment of the inferior (caudal) aspect of the pulmonary trunk and RPA is isolated. The left pulmonary artery is clamped on the left side of the ascending aorta (Fig. 41-27, B). This completely isolates the central pulmonary artery system. In some cases, it may be necessary to disconnect the pulmonary trunk from the heart if this has not been done previously. The inferior (caudal) surface of the central pulmonary trunk and RPA is then opened, beginning in the periphery at approximately the level of the previously placed bidirectional superior cavopulmonary shunt and extending it centrally to the pulmonary trunk beneath the ascending aorta.

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On rare occasions, the appropriate length of pulmonary artery cannot be cannulated without causing either hemodynamic instability or inadequate oxygenation, and CPB must be instituted to create the proximal anastomosis of the conduit to the RPA. When this is necessary, a separate purse string is placed in the SVC, and normothermic CPB is initiated after cannulating the ascending aorta, SVC, and IVC in standard fashion. A calcium-supplemented blood prime allows the heart to remain beating throughout the procedure.
Figure 41-27 Extracardiac conduit Fontan operation. A, Exposure is through standard median sternotomy. Most often this a reoperative median sternotomy, because most patients will have undergone several previous procedures. Typically, a bidirectional superior cavopulmonary shunt has been previously performed, as shown here. In this case, there is no additional source of pulmonary blood flow. Once sternum is opened, adhesions are dissected in order to completely mobilize previous superior vena cava (SVC)-to-right pulmonary artery (RPA) anastomosis. Pulmonary artery system is dissected from right upper and lower arterial branch junction to pulmonary trunk, working from right to left under ascending aorta. Occasionally, proximal left pulmonary artery (LPA) is dissected as well, working on left side of ascending aorta. Goal of this dissection is to mobilize an extensive length of RPA and pulmonary trunk for proximal Fontan anastomosis. B, Patient is heparinized, and central portion of pulmonary artery is isolated by placing two vascular clamps, one obliquely across RPA close to previously constructed bidirectional superior cavopulmonary shunt, and the other on the central or LPA as far to the left as possible. In this depiction, LPA is controlled on left side of ascending aorta. Inferior surface of right and central pulmonary artery is incised (dashed line) over an appropriate length to accept the circumference of a sharply beveled 20-mm-diameter expanded polytetrafluoroethylene (PTFE) tube graft. Care is taken that clamp adjacent to previously placed superior cavopulmonary anastomosis does not obstruct SVC flow to RPA, which is required for systemic oxygenation. C, Anastomosis between graft and pulmonary artery is performed using nonabsorbable fine monofilament suture and a continuous technique, beginning with posterior aspect and finishing with anterior aspect of anastomosis.

Assuming that CPB is not used, after the proximal anastomosis is completed, the graft and pulmonary arteries are de-aired, a vascular clamp is placed across the PTFE graft, and the branch pulmonary artery clamps are completely removed (Fig. 41-27, D). This reestablishes bidirectional superior cavopulmonary flow.

The ascending aorta and IVC are cannulated and connected to a centrifugal pump at approximately 50 mL · kg · min⁻¹ without an oxygenator, to achieve pump-assisted IVC decompression. Two large vascular clamps are placed across the IVC, one at the cavoatrial junction and the other just at the level of IVC cannulation (Fig. 41-27, E-F). If the femoral vein is used for lower body venous cannulation instead of the IVC, the clamp on the IVC is placed at the level of the diaphragm. The IVC is then transected and the cardiac stump oversewn with a running 3-0 polypropylene suture. The PTFE graft is then tailored to the appropriate length and anastomosed end to end to the IVC at the diaphragm with
Proximal anastomosis is completed, and pulmonary artery vascular clamps have been removed. These are replaced with a single clamp on midportion of tube graft. This allows reestablishing bidirectional SVC-to–pulmonary artery flow. Inferior vena cava (IVC) is examined, and PTFE graft is tailored to appropriate length for end-to-end graft to IVC. An IVC purse string is placed at its diaphragmatic reflection. During graft to IVC anastomosis, interruption of caval flow is necessary. During this period, IVC blood can be rerouted into either right atrium or ascending aorta in several ways as described in text. Once IVC decompression is accomplished, two large vascular clamps are placed on it, one at the atrio caval junction and the other just cephalad to venous cannula. IVC is transected between clamps. IVC remnant on right atrium is oversewn with a nonabsorbable heavy monofilament continuous suture technique. PTFE tube is connected end to end to diaphragmatic component of IVC using a nonabsorbable fine monofilament suture and a continuous technique as shown, with anastomosis beginning at posterior aspect of circumference of IVC. Completed extracardiac conduit Fontan with previously placed bidirectional superior cavopulmonary shunt.

a running 5-0 polypropylene suture (Fig. 41-27, G). This anastomosis can typically be performed in about 10 minutes.

Alternative extracorporeal circulation techniques can be used to construct the IVC-to–PTFE conduit anastomosis. One of these eliminates use of the pump described in previous text. Purse strings are placed on the right atrial appendage and IVC, and both are cannulated with large venous cannulae, which are then connected together to provide passive IVC decompression to the right atrium while the IVC is clamped and transected and the PTFE graft–to-IVC anastomosis performed. This technique is currently used by the authors as well as others. Another technique involves
simply clamping the IVC (which completely interrupts IVC flow) while the PTFE-to-IVC anastomosis is performed.\(^{320}\)

Following completion of the anastomosis, the patient is decannulated as needed (Fig. 41-27, H). Pressure-monitoring catheters are placed in the common atrium and IVC at the cannulation site to measure Fontan pathway and left-sided filling pressures and calculate transpulmonary gradient. These catheters are removed as soon as hemodynamic stability is ensured. Temporary atrial and ventricular pacing wires are placed along with appropriately positioned drainage tubes in the pleural and pericardial spaces, and the sternotomy is closed in standard fashion.

Extracardiac Conduit Fontan Operation with Deliberately Incomplete Atrial Partitioning

Incomplete atrial partitioning with the extracardiac conduit Fontan is usually unnecessary, particularly when the procedure is performed without CPB or with minimal CPB.\(^{112}\) (The reasons for this are detailed in “Fontan Operation with Deliberately Incomplete Atrial Partitioning” under Indications for Operation later in this section.) In essence, in creating a complete extracardiac conduit Fontan, the damaging effects of both CPB and myocardial ischemia are avoided, attenuating the transient hemodynamic disturbances that have made incomplete atrial partitioning necessary to ensure superior outcomes.

If hemodynamics following the Fontan procedure requires a communication between the Fontan conduit and atrium, this can be assessed after completing the Fontan as described; the connection can be accomplished without CPB. With the patient still heparinized, side-biting clamps are placed on the free wall of the right atrium and adjacent conduit, and a connection is made between these structures in one of two ways. First, a carefully controlled punch incision of predetermined diameter can be made in the conduit to regulate size of the fenestration. A second larger incision can be made in the sequestered segment of atrial wall, and free edges of the atrial incision can then be sewn widely around the punch hole in the conduit to create a fenestration. Second, small incisions can be made in both conduit and right atrial free wall, and a PTFE tube graft of approximately 8-mm diameter can be sewn between the two structures to create a tunnel-like communication. One of the authors (FLH) has used both of these techniques since 1992.\(^{113}\) Either communication can be regulated with a large snare if the surgeon prefers. The tube graft fenestration can also be closed using interventional catheterization.\(^{325}\)

Lateral Tunnel Fontan Operation

Preparation for operation and median sternotomy incision are generally those described in “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2. After anesthesia induction, a short double-lumen catheter is inserted percutaneously into the right internal jugular vein and advanced centrally (see subsequent text about early removal). In small patients, it may extend too far, interfering with SVC cannulation or with a total cavopulmonary connection; in that case the surgeon cuts off excess length. Inserting a polyvinyl catheter through the right superior pulmonary vein into the left atrium to measure ventricular loading is particularly important.

Risk of thrombosis around catheters in caval veins and their branches is increased in patients undergoing a Fontan operation (or bidirectional superior cavopulmonary shunt); therefore, any inserted for operation should be removed early postoperatively as soon as hemodynamic stability is achieved.

Aortic cannulation and cardioplegia purse-string sutures are placed as usual, as are those for direct SVC and IVC cannulation (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2, and Fig. 41-23). However, particular attention is paid to placing the SVC purse string as far cephalad as possible so that it does not interfere with a bicaval-pulmonary connection if chosen. Also, an elliptical shape of the purse string, with the long access of the ellipse oriented longitudinally, is particularly important so that tying it down later only minimally narrows the SVC. Purse string and cannulation may be on the brachiocephalic vein. Any previously made systemic–pulmonary arterial anastomosis is dissected (see “Repair of Tetralogy of Fallot after Blalock-Taussig orPolytetrafluoroethylene Interposition Shunt” under Technique of Operation in Section I of Chapter 38) and closed immediately after start of CPB.

CPB is established, systemic hypothermia achieved, aorta clamped, and cold cardioplegic infusion given. Perfusate temperature is rapidly lowered on CPB by taking the heat exchanger water bath to 4°C. Body temperature is stabilized, usually at 25°C, before administering cardioplegia. The technique of controlled myocardial reperfusion can be used after repair is completed (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).

Although practiced in only a small minority of programs, some surgeons perform the operation using hypothermic circulatory arrest, in which case the body temperature is brought to 15°C to 18°C. During cooling, a left atrial vent may be inserted through the base of the right superior pulmonary vein, or the field may be freed of blood by a pump-oxygenator sump-sucker placed across the foramen ovale after the right atrium is opened.

The pulmonary trunk is completely dissected away from the ascending aorta, and right and left pulmonary arteries are mobilized out to their first branch. This is usually begun before CPB is established, but is completed after establishing CPB and closing any systemic–pulmonary arterial anastomoses (Fig. 41-28, A). To prevent serious bleeding after CPB, meticulous hemostasis must be obtained with electrocautery as dissection is being accomplished.

The right atrium is opened through an oblique incision placed a little more anteriorly than usual (to preserve more posterior right atrial wall to serve as part of the intraatrial tunnel that will be created), and the pump-oxygenator sump-sucker is placed across the foramen ovale into the left atrium (see Fig. 41-28, A).

The pulmonary trunk is transected as close to the valve as convenient, and the proximal end is closed with two rows of continuous 4-0 polypropylene sutures (Fig. 41-28, B). During dissection, division, and closure of the pulmonary trunk, care is taken not to disturb the left coronary artery. It is tempting to leave the distal end of the pulmonary trunk open for later anastomosis to the cardiac end of the transected SVC, but this anastomosis can rarely be performed without tension and angulation of the trunk and first part of the left pulmonary artery. Therefore, the distal end of the pulmonary trunk is usually closed with two rows of continuous 6-0
Lateral tunnel Fontan operation. Operation is shown for tricuspid atresia and normally related great arteries with well-developed main and branch pulmonary arteries. A, Exposure is through a standard median sternotomy, and standard cardiopulmonary bypass (CPB) with moderate hypothermia and cardioplegia is used. In this case, a bidirectional superior cavopulmonary shunt has not yet been performed. Dashed line indicates incision to be made in right atrial appendage. Operation proceeds by separating pulmonary trunk from aorta using sharp dissection. B, Right and left pulmonary arteries are dissected to their first branches in a manner similar to that used for arterial switch operation. After separating ascending aorta and pulmonary trunk, superior vena cava (SVC) is mobilized andazygos vein identified. CPB is then instituted with aortic cannulation and separate high SVC and inferior vena cava (IVC) cannulae. If any systemic–pulmonary arterial connections exist, these are also taken down immediately upon institution of CPB. Pulmonary trunk is transected at level of pulmonary valve, and each end is oversewn with a continuous monofilament suture. Dashed line on SVC shows point of eventual transection required to completed Fontan procedure. Somewhat anteriorly placed incision on right atrial free wall is also shown. Entry into right atrium provides access to left side of heart, allowing a pump sump-sucker to be placed across foramen ovale to decompress it. C, Anastomosis between cephalad portion of divided SVC and an incision in the superior surface of right pulmonary artery (RPA) is performed as shown, using a continuous 7-0 monofilament absorbable suture. This is performed exactly as shown in technique used for bidirectional superior cavopulmonary shunt (see Fig. 41-22). Cardiac end of divided SVC is connected to incision in inferior aspect of RPA as shown, using a continuous 7-0 monofilament absorbable suture.

polypropylene sutures placed as a whip stitch (see Fig. 41-28, B). However, if the distal pulmonary trunk segment has little length (which may be the case when a pulmonary trunk band has previously been placed too far distally), a patch of pericardium or allograft pulmonary artery is used for closure to maintain a wide pathway between right and left pulmonary arteries.

Success requires that the central unbranched hilar portions of right and left pulmonary arteries be enlarged if they are small. This can be accomplished by making a long incision in the midportion of the anterior wall of the left and right pulmonary arteries extending to the area of origin of the first branch on both sides. Inserting a widening patch-graft is accomplished with continuous 6-0 polypropylene sutures. If available, a pulmonary arterial allograft serves best as the patch-graft material. Otherwise, aortic allograft or autologous pericardium, untreated or treated with glutaraldehyde, may be used. Incision for anastomosis to the right atrium or cavae is then best made in the native pulmonary arterial wall rather than in the patch. This procedure can neutralize the incremental risk of small central right and left pulmonary arteries only if the branching portions of these arteries are of reasonable size.

If a previous bidirectional superior cavopulmonary shunt has not been performed, the SVC is transected at the point where it crosses the RPA; the transection is usually
just proximal to the azygos vein, which is divided between ligatures to help mobilize the cephalic end of the SVC. A longitudinal incision is made along the superior surface of the RPA, and the cephalic end of the SVC is anastomosed to this opening (Fig. 41-28, B-C). A longitudinal incision is made along the inferior surface of the RPA, a little more medially placed than the previous incision, and anastomosis made between the central end of the divided SVC and this opening (see Fig. 41-28, C). In most cases the sinus node artery can be seen and avoided.

A tunnel within the right atrium is required to conduct IVC and hepatic venous blood to the cardiac end of the SVC; generally, some heavy atrial trabeculations must be excised to clear that pathway. The ASD may need to be enlarged, particularly if the right AV valve will be the main pathway for pulmonary venous blood to reach the systemic ventricle (Fig. 41-28, D). A patch cut from a PTFE tube is selected, trimmed, and sewn into place. The suture line is started between the coronary sinus and IVC orifices and continued cephalad along the atrial septum as near the ASD as possible until the leftward edge of the SVC is reached. With the other arm of the suture, the suture line is carried over the IVC orifice, along the inside of the right atrial wall, and then over the SVC (Fig. 41-28, D-E).

The coronary sinus, as with the extracardiac conduit Fontan, now drains into the low-pressure left atrium; this arrangement is physiologically preferred, in contrast to an atroipulmonary Fontan, in which the coronary sinus drains to the high-pressure systemic venous circuit. Ilbawi and colleagues have shown that coronary sinus pressure greater than 15 mmHg depresses systemic ventricular output, although Ward and colleagues’ and Eicken and colleagues’ data appear to disprove this.\textsuperscript{3,13,15,20}

Collateral blood flow to the pulmonary circulation is often large in patients undergoing the Fontan operation, and particular care must be taken to avoid overdistention of the left atrium (and pulmonary veins) and systemic ventricle during final stages of repair. This can be accomplished by suction on the vent placed across the foramen ovale into the left atrium and by free drainage of blood from the pulmonary arteries into the right atrium through the anastomoses. The vent can be conveniently introduced through the right atrial appendage. In any event, as the right atrium is being closed, necessitating removal of the pump sump-sucker, care must be used
to prevent undue elevation of left atrial and ventricular pressure until cardiac action has returned. Toward this end, the caval tapes may be released before the atrium is closed, and suction on the caval cannulae can help decompress the pulmonary arteries and thereby the left atrium. After the heart is closed, aortic root reperfusion is established and de-airing begun. The remainder of operation is completed in the usual manner (see “Completing Operation” in Section III of Chapter 2).

At times, it may be more convenient to use a right atrial flap as the inner part of the wall of the tunnel.\(^\text{19}\) Depending on the anatomic situation in the individual patient, this atrial inner wall may be made from either anterior or posterior portions of right atrial wall.

Some prefer not to use the orifice of the cardiac end of the transected SVC to make the anastomosis to the RPA, but rather to close the central end and use a separate incision in the superior aspect of the right atrium for the anastomosis. A roof for the anastomosis is then made with allograft pulmonary arterial wall or pericardium. The intraatrial baffle is constructed so that it conducts IVC blood to the new opening.

When possible, as the repair is being completed, provision is made for measuring pressure in the pulmonary artery, venae cavae, and left atrium. Sites of insertion of fine polyvinyl catheters depend on the specific procedure used. Two right atrial and two RV myocardial electrodes are placed at the end of operation.

Provision for adequate drainage of the pericardium is particularly important. While the patient is still on CPB, a large window is made between the pericardial and right pleural spaces by excising a large piece of pericardium anterior to the phrenic nerve. A window is made between the pericardial and left pleural spaces by tilting the heart up anteriorly and making a large incision in the posterior pericardium well behind the phrenic nerve from within the pericardium. One posteriorly placed and one anteriorly placed drainage tube is brought out from each pleural space.

Lateral Tunnel Fontan Operation with Deliberately Incomplete Atrial Partitioning

Under some circumstances (see Indications for Operation later in this section), incomplete atrial partitioning is considered advantageous in performing the Fontan operation.\(^\text{G13}\) This has been accomplished in two ways in the setting of the lateral tunnel procedure.

Laks and colleagues leave a small defect in the suture line that attaches the PTFE to the atrium. They place one pledgeted polypropylene mattress suture through the edge of the PTFE at the site of the defect, bring the suture outside the heart through the posterior atrial wall, and pass the ends through another pledget and secure them on a snugger (a section of an 8F pediatric suction catheter)\(^{L3,L4,P6}\) (Fig. 41-29, A). The end of the suture is left beneath the closure of the linea alba (Fig. 41-29, B). Pushing the snugger down makes

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**Figure 41-29** Lateral tunnel Fontan operation with deliberately incomplete atrial partitioning using “adjustable atrial septal defect.” **A**, After intraatrial polytetrafluoroethylene (PTFE) lateral tunnel baffle is placed, a small (approximately 6 mm) aperture is left in midportion of baffle suture line where baffle is attached to right atrial free wall, as shown. This aperture is controlled by a mattress suture using heavy 2-0 polypropylene suture with felt pledgets placed on both sides, connected to a snare. Length of snare is tailored to reach subxyphoid area prior to closure of right atrium. Snare is tested to demonstrate effectiveness of mechanism for opening and closing the aperture. Right atrium is then closed and patient separated from cardiopulmonary bypass in standard fashion. Prior to closing sternal incision, hemodynamics are assessed and aperture adjusted to maximize early hemodynamics. **B**, Prior to closing sternum, snare length is carefully determined to reach the subcutaneous position in subxyphoid region. Snare is secured at determined level of aperture patency that results in ideal early hemodynamics by placing multiple large metal clips at subcutaneous end of snare. This allows easy access to snare either early or late postoperatively for further aperture adjustment. Metal clips serve not only to stabilize snare but also as a convenient radiologic and tactile landmark, should early or late aperture adjustment be necessary.
the interatrial communication smaller. The residual aperture is adjusted to an appropriate size before closing the chest. In the intensive care unit (ICU), the aperture is made larger, smaller, or nonexistent by simply removing a few sutures from the skin and linea alba closure, removing clips holding the snagger in position, and repositioning and securing the snagger.

An alternative is a fixed fenestration in the lateral tunnel PTFE baffle. At operation, after the tunnel is placed in the atrium, a hole is made in equidistant from the two suture lines and somewhat inferior to the center of the tunnel. The hole is made with a 4-mm aortic punch for patients weighing less than about 12 kg, with a 5-mm punch for those weighing about 12 to 30 kg, and with a 6-mm punch for larger patients.\textsuperscript{524} Postoperatively, the patient is evaluated continuously for the possibility and proper time, if at all, for closure of the interatrial communication (see Special Features of Postoperative Care later in this section). When the time is appropriate, the patient is taken to the cardiac catheterization laboratory, where the communication is temporarily closed by a percutaneously inserted balloon; if the hemodynamic state remains good, the communication is closed permanently with a percutaneously inserted occlusion device.\textsuperscript{526} Otherwise, the communication is left open and closure is reconsidered later.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Care usually given after intracardiac operations is appropriate (see Section IV of Chapter 5). However, some aspects of care are of particular importance.

Monitoring

The patient leaves the operating room with catheters in the IVC and left atrium as well as the usual arterial catheter. Not only are these devices useful in general management of patients after a complete or partial (bidirectional superior cavopulmonary shunt, hemi-Fontan, or fenestrated) Fontan operation, they also provide information critical to making rational decisions for patients who are not convalescing normally. Catheters in caval veins are removed as soon as possible.

General Measures

The patient is nursed in semi-Fowler’s position, and positive end-expiratory pressure is not used.\textsuperscript{911} Because of the adverse effect of positive intrathoracic pressure on $Q_p$, inspiratory ventilation pressures are kept as low as possible, and spontaneous breathing is encouraged as early as possible.\textsuperscript{78,810} Extubation is usually accomplished within 2 to 48 hours of operation. Stay in the ICU is usually 48 to 72 hours, rather than the usual 24 hours, because cardiac physiology is not fully normalized.

There is more than the usual tendency for fluid to leave the intravascular compartment and pass into the interstitial space and into the pleural, pericardial, and peritoneal cavities. The cause is multifactorial and includes increase in microvascular permeability resulting from CPB (if used), and at least mild increase in right atrial and caval pressures.\textsuperscript{\textsuperscript{510,14,227}} Because of this tendency for transcapillary fluid loss, 5% albumin or stable plasma protein solution may be necessary to maintain adequate ventricular loading.

Every effort is made to keep body cavities free of fluid and atrial and caval pressures low. Pleural effusions drain through the tubes placed at operation, and the wide opening made between the pericardial space and both pleural spaces prevents pericardial tamponade. On occasion, a peritoneal catheter may have to be inserted in the ICU to drain rapidly developing ascites.

Occasionally, serous drainage may insidiously become chylous, perhaps because the leaking microvascular pores gradually enlarge with time with passage of macromolecules, such that ultimately chylomicrons can pass.\textsuperscript{527} In any event, when the fluid becomes chylous, ligation of the thoracic duct rarely is useful, and surgical attempts to promote pleural symphysis often fail. Adequate tube drainage, high caloric intake, fluid restriction, and aggressive use of diuretics are the mainstays of treatment (see “Chylothorax” in Section II of Chapter 5). In cases of persistent chylous effusion, more aggressive measures can be effective in eliminating it. These include nothing by mouth (NPO) status, with all nutrition provided parenterally, and administration of synthetic somatostatin analogs such as octreotide.\textsuperscript{\textsuperscript{5}26,511}

Careful follow-up is required for at least 3 to 6 weeks. The tendency to fluid retention, hepatomegaly, and ascites may persist for most of this time, making sodium and fluid restriction and diuretic therapy necessary. Also, fluid retention and even chylous accumulations may appear to be mild during hospitalization, but with increased activity after hospital dismissal, larger accumulations of fluid or chyle may develop in body cavities. This may be recognized only when pulmonary or cardiac dysfunction appears to develop rather suddenly. If this occurs, immediate hospitalization and intensive treatment are necessary; these late accumulations can be rapidly fatal if untreated.

**Preventing Atrial Thrombosis**

Although atrial or Fontan pathway thrombosis is uncommon (see “Thromboembolic Complications” under Results later in this section), it is a serious complication warranting special consideration. It appears reasonable to believe that this is more apt to occur in patients with elevated Fontan pathway pressures or in those who are slow to recover because of chronic effusions or some other complication. Thus, patients in these categories are placed on warfarin therapy beginning about 3 days postoperatively and continuing for 6 to 12 weeks. Thereafter, lifelong therapy with aspirin (80 mg · day\textsuperscript{-1}) is advisable. It should be noted that for the atrio pulmonary Fontan, Fontan pathway thrombosis is atrial thrombosis; for the lateral tunnel Fontan, atrial thrombosis may be in the Fontan pathway or in the systemic side of the atrium; and for the extracardiac conduit Fontan, the atrium is completely excluded from the Fontan pathway and is not at risk for thrombosis.

Should acute thrombosis occur early postoperatively, particularly if it causes obstruction or is associated with pulmonary embolization, immediate surgical exploration, or in some cases thrombolytic therapy, is indicated.\textsuperscript{522}

**Strategic Importance of Fontan Pathway Pressure**

Patients often have a Fontan pathway pressure of 16 mmHg or less a few hours after entering the ICU, and they generally convalesce well. When pressure is higher than this, and
particularly when it progressively increases—often as a result of a need to augment blood volume to maintain cardiac output—a potentially lethal situation may be developing, and a thoughtful and prompt analysis is indicated. When a fenestrated Fontan operation has been performed, the warning sign may be severe arterial desaturation rather than elevation of Fontan pathway pressure. Narrowing the fenestration may simply substitute elevation of pressure for arterial desaturation; therefore, treatment strategies for these two developments are similar.

Treatment strategy for these patients first considers left atrial pressure (LA). If it is elevated to within a few mmHg of Fontan pathway pressure and if it too rises as the hours pass, main chamber ventricular dysfunction or AV valve dysfunction (regurgitation or stenosis) is probably etiologic to the poor hemodynamic state. PLA greater than 10 mmHg is not well tolerated, because this results in unacceptably high Fontan pathway pressure, even in the face of a normal Rp and transpulmonary pressure gradient. Two-dimensional echocardiographic examination in the ICU is indicated. If ventricular dysfunction is present, an increase in inotropic support may improve the hemodynamics. If new-onset AV valve regurgitation is present, reoperation and valve repair should be considered. If these efforts are unsuccessful or are not feasible, the only option is mechanical ventricular support in preparation for transplantation (see Chapter 21).

If Fontan pathway pressure remains 12 mmHg or more higher than PLA, and pulmonary arterial pressure is similarly elevated, then pulmonary vascular disease, pulmonary arteriolar spasm, or small size of pulmonary arteries may be responsible. The patient is hyperventilated to an arterial PaO₂ of 25 to 30 mmHg, arterial PaO₂ is maximized (short of having an FiO₂ of 1.0), and inhaled nitric oxide is initiated in a dose of 20 to 40 ppm. If these do not soon bring about improvement, it must be concluded that the problem is pulmonary vascular disease or small pulmonary arteries, and not pulmonary arteriolar spasm. Modification or takedown of the Fontan operation must be considered. Improved knowledge of stress-related metabolic and hormonal changes, and of inflammatory responses to surgery, may provide additional modes of therapy. Aprotinin has been associated with reduced Fontan pathway pressure.

If Fontan pathway pressure is high and left atrial and pulmonary artery pressures are not, then an obstruction exists in the newly created pathways. If Fontan pathway pressure is greater than 16 mmHg or if pressure increases as the hours pass, serious consideration must be given to reoperation for obstruction of the pathway. Echocardiographic or angiographic study may be desirable before the final decision is made.

Takedown or Modification of Fontan Operation

Under certain circumstances, and usually within 12 hours of operation, the hemodynamic state of the patient may be sufficiently poor that probability of survival seems low, and modification or takedown of the Fontan operation is advisable as an emergency procedure.

When a completed Fontan operation has been performed, takedown should be done as soon as circumstances requiring it are identified. These are a poor hemodynamic state and presence of an elevated pulmonary arterial pressure (greater than 18 mmHg) and elevated PLA (>10 mmHg) with a relatively normal transpulmonary pressure gradient. In the case of a lateral tunnel Fontan, after CPB and cardioplegia are established, the right atrium is opened and the patch placed to form the intraatrial tunnel is removed, resulting in a wide open interatrial communication. The cardiac end of the SVC is closed by a patch placed from within the right atrium. Essentially, this is conversion of a completed Fontan operation to a hemi-Fontan. The extracardiac conduit Fontan can be taken down simply by removing the conduit from the undersurface of the pulmonary artery and connecting it to the side of the right atrium. This procedure is performed using normothermic, beating-heart CPB with aortic and IVC cannulation. A large partial-occlusion vascular clamp is used to sequester the portion of the right atrial wall that will receive the IVC conduit.

When a poor hemodynamic state exists in the setting of elevated pulmonary artery pressure and low PLA—that is, an elevated transpulmonary pressure gradient—establishing a fenestration if one is not present or enlarging an existing fenestration or adjustable ASD may be beneficial. Following a complete lateral tunnel Fontan, this requires return to CPB, opening the right atrium, and creating an appropriately sized hole in the PTFE patch. If a complete extracardiac conduit Fontan exists, the communication can be performed without return to CPB by placing an 8-mm-diameter PTFE tube graft between the extracardiac conduit and right atrial appendage using partial occlusion vascular clamps to isolate segments of the conduit and the right atrium (see “Extracardiac Conduit Fontan with Deliberately Incomplete Atrial Positioning” under Technique of Operation earlier in this section). If an incompletely Fontan with an adjustable ASD had been performed originally, then opening the skin and fascia overlying the controlling snare around the ASD is performed and ASD size adjusted. If these maneuvers fail to improve the hemodynamic state, Fontan takedown is undertaken.

Fontan Operation with Deliberately Incomplete Atrial Partitioning

It has been hypothesized that some failures and deaths after a completed Fontan operation are due to temporary pulmonary vascular or parenchymal dysfunction (presumably related to the damaging effects of CPB) and to temporary myocardial dysfunction (presumably related to inadequate myocardial management). This hypothesis is supported by the finding of increased ventricular wall thickness (myocardial edema) and decreased ventricular compliance and volume immediately after the Fontan operation, with regression of these responses to surgery over the several weeks or months thereafter.

Thus, in the early postoperative period, when SaO₂ increases to 85% or greater and Fontan pathway pressure decreases to 15 mmHg or less, closure of the aperture by snugging down the suture controlling the adjustable ASD or by a percutaneously placed device may be considered. A valuable indicator that the incompletely Fontan operation can be made complete is cessation in formation of pleural effusions. With closure of the residual aperture, SaO₂ should approach 100%, but Fontan pathway and PLA responses can be variable. Fontan pathway pressure may increase to greater than 15 mmHg, PLA may decrease to less than 7 to 8 mmHg, and the cardiac index may fall, evidence that the aperture should be reopened. When Fontan pathway pressure
pressure remains at or less than 15 mmHg, and PLa remains sufficiently high that cardiac output remains good, the residual aperture can be permanently closed.

Although this general plan has often been successful, at times morbidity is increased by closing the residual aperture. In the early postoperative period, timing of atrial communication closure remains controversial. Delayed closure several months after the Fontan operation is practiced at many centers, and this strategy may be more prudent than one that attempts to close the communication in the postoperative period. In essence, there is little reason to close the communication early unless SaO2 decreases to unacceptable levels (<75%) in association with low pressure (<15 mmHg) in the pulmonary arteries, indicating that the communication is too large. Regardless of timing of closure, assessing hemodynamic consequences of closure should be made by temporarily closing the communication first. In some cases, hemodynamic response will suggest that the communication be left open permanently. Fenestration closure may benefit patients at midterm follow-up, however, others argue that patients are better off with the fenestration left open.

RESULTS

Completed Fontan Operation

A considerable body of knowledge is available about early and late results after completed Fontan operation. Effects of temporary or permanent partial Fontan operations, of lateral tunnel and extracardiac conduit variations, and of minimal use or avoidance of CPB have been documented at early but not late follow-up.

Survival

Early (Hospital) Death Thirty-day or hospital mortality has improved over the past decade and currently is 0% to 4%, substantially better than earlier reports of about 20% in heterogeneous groups of patients. Improvement in survival is documented both in series that report Fontan operations performed exclusively in more recent calendar years and in series that cover a wider range of calendar years in which improved survival is documented for more recent calendar years. Equal results have been achieved with extracardiac conduit and lateral tunnel techniques, and with the entire spectrum of CPB management techniques, from off-pump series to series using hypothermic circulatory arrest.

Time-Related Survival Overall, in heterogeneous groups of patients undergoing completed Fontan operation in the time period from approximately 1970 to 1985, 5-, 10-, and 15-year survivals, including early mortality, were about 70%, 65%, and 50%, respectively. In a series of 216 tricuspid atresia patients undergoing the Fontan over a 25-year period at the Mayo Clinic, overall survival was 79%.

Outcomes improved substantially within each decade of this experience, with 56/59 patients alive from the final decade. Long-term follow-up is becoming available for more recent patients who have undergone a bidirectional superior cavopulmonary shunt (bidirectional Glenn or hemi-Fontan) followed by a lateral tunnel or extracardiac conduit total cavopulmonary Fontan. Midterm survival is markedly improved, with 1- to 5-year survival approaching and exceeding 90%.

Survival after a “Perfect” Fontan Operation Because many deaths after the Fontan operation have been due to circumstances that can be avoided in the present era, the persistent and rising hazard function for death (see Fig. 41-30, B) could be a result of now avoidable circumstances. However, analysis of survival under circumstances that can be considered ideal indicates that the late, slow-rising phase of hazard is still present (Fig. 41-32, A). Under ideal circumstances, 15-year survival is predicted to be 73% (Fig. 41-32, B), a prediction supported by the experience of others.

A recent analysis revisiting the idea of the perfect Fontan shows that in the modern era, using an extracardiac conduit for the Fontan, outcomes equal to that predicted by Fontan and colleagues.
colleagues’ original “perfect Fontan” equations can be achieved routinely in all patients. Other recent series document 10-year survival superior to that achieved with the classic “perfect Fontan” (see Fig. 41-31). These data simply reflect the gradual improvement in outcome that has occurred over the last 2 decades.

Declining survival late postoperatively and rising late hazard for death under good circumstances are different from those after repair of tetralogy of Fallot (see “Time-Related Survival and the Question of ‘Cure’” under Results in Section I of Chapter 38), as is the gradually declining functional capability after the Fontan operation (Fig. 41-33). These suggest that the Fontan operation should be considered an excellent palliative operation but not a curative one. The fact that no risk factors (other than older age at operation) have been identified for the late phase of hazard suggests that this is related to the circulatory state after the Fontan operation. This state may predispose to subtle morphologic and functional changes in the pulmonary circulation similar to those that occur after the bidirectional superior cavopulmonary shunt. Also, there may be gradual deterioration of structure and function of the congenitally abnormal ventricular chamber. The latter could be contributed to by high coronary sinus pressure, unless it has been diverted into the left atrium. Also, additional congenital cardiac and myocardial anomalies are common in the univentricular hearts of patients who undergo the Fontan operation, and these may gradually impair cardiac function as time passes. It remains to be seen whether the proposed advantages of the extracardiac-conduit Fontan procedure—which removes the atrium from the Fontan circuit, avoiding right atrial foreign material and suture, eliminating myocardial ischemia at operation, and removing the coronary sinus from the Fontan circuit—will result in improved laminar flow, reduced dysrhythmias, preserved ventricular function, and reduced thrombotic and obstructive complications, thereby reducing the slope of the late hazard phase.

**Figure 41-31** Freedom from Fontan failure, including death, take-down, and transplantation, after 216 extracardiac conduit Fontan procedures. Vertical bars are 70% confidence limits. (From Petrossian and colleagues.)

**Figure 41-32** Survival after a “perfect” Fontan operation. Solid lines are parametric estimates enclosed between 70% confidence limits. Dash-dot-dash line represents estimates for a matched general population. A, Nomogram of predicted hazard function for death. Equation for nomogram is based on multivariable risk factor equation (see Table 41-4), entering optimal values within the realm of realism for each risk factor. Details are described in the publication. Note that greatly expanded vertical axis makes hazard function appear to be higher than that of Fig. 41-30, B; in fact, it is lower. B, Corresponding predicted survival. (From Fontan and colleagues.)

**Figure 41-33** Time-related New York Heart Association (NYHA) functional class of patients after Fontan operation. Parentheses enclose number of patients followed up within intervals. Squares, circles, and triangles represent actual percentages; solid lines are parametrically determined percentages, with dashed lines enclosing 70% confidence limits around the percentages for NYHA classes I and III (see “Longitudinal Outcomes” in Section IV of Chapter 6). (From Fontan and colleagues.)
Modes of Death
For patients undergoing the Fontan operation in the 1970s and 1980s, acute cardiac failure early postoperatively was the most common mode of death. Chronic cardiac failure, which first appears several years before death, and sudden death are the most common modes late postoperatively.

Assigning a mode of death after a Fontan operation is difficult because of frequent occurrence of fluid retention, which may have obvious hemodynamic causes (e.g., myocardial failure, elevated Rp, Fontan pathway obstruction) or may occur in the absence of any specific hemodynamic abnormality other than the existence of the Fontan itself. This fluid retention often appears primarily as persistent accumulations of pleural fluid or, less often, of ascitic or pericardial fluid. This tendency has been shown to be considerably less when a bidirectional superior cavopulmonary shunt has preceded the Fontan procedure.\(^2\) In any event, in only about 10% of patients who die does persistent fluid accumulation in pericardial, pleural, or peritoneal spaces without hemodynamic insufficiency appear to be the mode of death (Table 41-3).

Incremental Risk Factors for Death

Acute Ventricular Decompression An important potential risk factor still remains to be investigated: namely, sudden “decompression” of the ventricular chamber by the Fontan operation. Decompression at the time of Fontan can be avoided by surgical staging, as described in this chapter, using one of two techniques: bidirectional superior cavopulmonary shunt or a hemi-Fontan operation.\(^4\) In this case, decompression is achieved at the time of second-stage palliation (see Section III), not at the time of the Fontan operation. It has not been shown definitely that avoiding ventricular decompression at the time of the Fontan improves outcome.

Deterioration The incremental risk factor for a late rising phase of hazard for death may be the post-Fontan state. It may result from:

- Long-standing nonpulsatile pulmonary artery flow generated by the systemic venous pressure
- Abnormality of the dominant ventricle per se

The latter may be an immutable congenital anomaly or may be acquired during postnatal life, either from the abnormal hemodynamic state existing before Fontan repair or from myocardial ischemia at previous operations. (A similar late-rising phase of hazard occurs in patients with discordant AV connection undergoing a two-ventricle repair.)

Younger Age at Operation In older studies, younger age at time of the Fontan operation was a risk factor for death (or complete takedown of a Fontan operation) early after operation\(^6,26,F14,E20\) (Table 41-4). The nature of the relationship was such that risk of death (or takedown) early postoperatively began to increase as age of operation approached 3 years, and then increased more steeply as age was reduced to younger than 2 years\(^6,F14,M23\) (Fig. 41-34). Good results can be obtained from performing the Fontan operation in infants and children younger than 2 years, yet the probability of surviving has been documented to be less than in older patients\(^,M23,M24,W5\). It should be emphasized, however, that this documentation is now 15 to 20 years old.

Certainly, mortality of 55% for patients younger than 4 years\(^M24\) in older reports is no longer the case.\(^M23,M58,S37\) The incremental risk of young age may have been neutralized by staged, fenestrated, incompletely Fontan operations, and by avoiding use of CPB, although this is not yet fully documented\(^E4,M50\).

Older Age at Operation Older age at operation is not a risk factor for death early postoperatively.\(^H20\) Burkhardt and colleagues\(^B33\) report an 8.3% operative mortality, Otrovskii and colleagues\(^G11\) and Veldtman and colleagues\(^V7\) 13%, and Fujii and colleagues\(^F30\) 4%, when operation is performed in

<table>
<thead>
<tr>
<th>Table 41-3</th>
<th>Modes of Death, Both Early and Intermediate Term, after Fontan Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mode of Death</td>
<td>n</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>80</td>
</tr>
<tr>
<td>Acute</td>
<td>50(^a)</td>
</tr>
<tr>
<td>Subacute</td>
<td>23</td>
</tr>
<tr>
<td>Chronic</td>
<td>7</td>
</tr>
<tr>
<td>Acute pulmonary failure</td>
<td>1</td>
</tr>
<tr>
<td>Persistent fluid accumulation</td>
<td>11</td>
</tr>
<tr>
<td>Neurologic dysfunction</td>
<td>9</td>
</tr>
<tr>
<td>Sudden</td>
<td>4</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>2</td>
</tr>
<tr>
<td>Arrhythmic death</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>110</td>
</tr>
</tbody>
</table>

Data from Fontan and colleagues.\(^1\) Three occurred perioperatively after late reoperation for Fontan operation, and two occurred after late reoperation for Fontan pathway obstruction.

<table>
<thead>
<tr>
<th>Table 41-4</th>
<th>Incremental Risk Factors for Death or Takedown after Fontan Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk Factor(^a)</td>
<td>Hazard Phase</td>
</tr>
<tr>
<td></td>
<td>Early(^a)</td>
</tr>
<tr>
<td>Patient</td>
<td></td>
</tr>
<tr>
<td>(Younger) Age</td>
<td>•</td>
</tr>
<tr>
<td>(Older) Age</td>
<td>• •</td>
</tr>
<tr>
<td>(Greater) Morphologic:</td>
<td></td>
</tr>
<tr>
<td>Left AV valve atresia</td>
<td>•</td>
</tr>
<tr>
<td>(Smaller) Dimensions of pulmonary arteries</td>
<td>•</td>
</tr>
<tr>
<td>(Higher) Pulmonary artery pressure</td>
<td>•</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
</tr>
<tr>
<td>Nonuse of cardioplegia</td>
<td>•</td>
</tr>
<tr>
<td>(Longer) Global myocardial ischemic time with cardioplegia</td>
<td>•</td>
</tr>
<tr>
<td>RA-PA (rather than RV) anastomosis</td>
<td>•</td>
</tr>
<tr>
<td>RA-to-PT valved conduit</td>
<td>•</td>
</tr>
<tr>
<td>Direct RA-to-PT anastomosis with linear RA incision</td>
<td>•</td>
</tr>
</tbody>
</table>

Data from Fontan and colleagues.\(^1\) Shaping parameters and coefficients are in original publication.\(^1\) Key: AV, Atrioventricular; PT, pulmonary trunk; RA, right atrium; RV, right ventricle.
selected adults. It slightly increased risk of death late after the Fontan operation (Fig. 41-34, B) in one study, but this was not found by others.\textsuperscript{26,34b,77}

**Cardiac Morphology** Cardiac morphology has been reported to be importantly related to outcome after the Fontan operation; specifically, tricuspid atresia has been found to have more favorable outcomes than other anomalies, and all anomalies with the morphologic LV as the main chamber have been reported to have more favorable outcomes than those with a right or indeterminate main ventricle.\textsuperscript{6,8,26,29,319,24,78} There are exceptions; three studies found no influence of ventricular morphology on outcome.\textsuperscript{41,316,176}

A related morphologic feature that has also been identified as a risk factor is left AV valve atresia.\textsuperscript{12} (see Table 41-4). This may not be a morphologic risk factor per se, but rather a morphologic arrangement that until recently resulted in use of a complex baffle for partitioning the atria. Such baffles often resulted in some obstruction of the pulmonary venous pathway to the right or a common AV valve, and this probably was the true risk factor.\textsuperscript{12} Various forms of total cavopulmonary connection, including the extracardiac conduit and lateral tunnel Fontan techniques (see Figs. 41-27 and 41-28), have overcome this problem, and left AV valve atresia may not be a risk factor in the future.

**Small Size of Central Right and Left Pulmonary Arteries** Small size of central right and left pulmonary arteries has been identified by some as a risk factor for death (or takedown) early after the Fontan operation,\textsuperscript{14} although others have not found this to be so.\textsuperscript{22} As is often the case, the controversy may relate to differing patient populations, patient data, and surgical techniques. In nearly all studies, only the prebranching pulmonary artery dimensions have been studied. If small size is limited to prebranching portions of right and left pulmonary arteries and if these portions are enlarged by patch-grafting at Fontan repair, one may expect to find little relationship between small size and outcome, as was the case in the study of Bridges and colleagues.\textsuperscript{27} Failure to perform surgical enlargement may leave small pulmonary artery size as a risk factor. Thus, according to the combined University of Bordeaux–UAB experience, when the prebranching portions of the right and left pulmonary arteries are small (McGoon ratio less than about 1.5 [see Figs. 1F-1, 1F-2, and 1F-3 in Chapter 1]), a z value of less than about −3.5, or a cross-sectional area index [Nakata index] of less than about 160 mm\(^2\) \(·\) m\(^3\), risk of early death is increased\textsuperscript{14} (Fig. 41-35). Nakata and colleagues suggested, as a more restrictive guideline for considering patients at high risk, an index of less than 250 mm\(^2\) \(·\) m\(^3\).\textsuperscript{22} However, rarely was augmentation of the central pulmonary arteries performed in these patients.

By contrast, the Mayo Clinic group has suggested that size of right and left pulmonary arteries measured in the operating room is not related to outcome, even when augmentation is not done. However, the patients on whom they made measurements were selected based on not having small pulmonary arteries, so inferences about small size are not possible from their data. There are few studies relating size of pulmonary arteries measured after enlargement to outcome.

If pulmonary arterial narrowing extends into more distal portions of right and left pulmonary arteries, their small sizes may be a risk factor for death. Pulmonary artery “distortion” was found to be a powerful risk factor for death, but such distortion has been uncommonly found.\textsuperscript{37,23,148}

**Elevated Pulmonary Artery Pressure and Pulmonary Vascular Resistance** Elevated mean pulmonary artery pressure (Ppa) and Rp have been known to increase risk of the Fontan operation since Choussat and colleagues’ classic paper;\textsuperscript{21} this has been confirmed in subsequent studies.\textsuperscript{8,29,26,24,12} Risk is particularly elevated when Ppa is greater than 15 to 20 mm Hg, unless the elevation is explained by a large Qp or important AV valve regurgitation. Rp would be expected to predict outcome more precisely, but in many patients it is difficult to measure determinants of this value, and the value is not highly sensitive to presence of multiple peripheral thrombi.\textsuperscript{12} Nonetheless, with Rp greater than 2 to 4 units \(·\) m\(^2\), probability of good outcome is less.\textsuperscript{8}

**Advanced Main Chamber Ventricular Hypertrophy** Advanced main chamber ventricular hypertrophy and increased muscle mass is an important risk factor for death,\textsuperscript{26,24,14,50,12} (see Table 41-4). Early survival (out to 6 months) after a Fontan operation in a 5-year-old child with favorable features and mild LV hypertrophy is estimated to be 99%, but it is 78% when moderately severe LV hypertrophy
is present. This risk factor adversely affects ventricular compliance (diastolic function) and, when advanced, systolic function as well. These observations have led to the widely held current practice of aggressive surgical relief of ventricular outflow obstruction in the staging of patients with single-ventricle physiology (see Section III). Although not advisable, relief of ventricular outflow obstruction can be performed simultaneously with the Fontan.

Atrial Isomerism Atrial isomerism (see Chapter 58), with its usually concurrent asplenia or polysplenia, has been identified as a risk factor for death. This risk factor may relate in large part to abnormal systemic venous connections to the heart, and these may be neutralized by modifications of surgical technique (see “Persistent Left Superior Vena Cava with Hemiazygos Extension of Interior Vena Cava” under Special Situations and Controversies later in this section). Recent techniques may have neutralized the risk of heterotaxy. Early mortality in 21 patients undergoing operation from 1995 to 2004 was only 9.5% (2 deaths; CL 3.3%-21%), and 10-year survival of a larger cohort of 142 patients from the same series was 57%. In other studies, recent experience defines the risk of early mortality at 0% to 13%. Risk may also relate to dysfunction of the common AV valve, which is often present.

Functional Status Many patients consider themselves fully active after the Fontan operation; it was previously reported that 94% of patients are in New York Heart Association (NYHA) functional class I or II. Now that intermediate-term follow-up information is available out to at least 20 years, it is known that NYHA functional class gradually deteriorates. Nearly 90% of patients are in NYHA functional class I at 1 year after operation, but this is true in only about 56% of patients at 10 years (see Fig. 41-33). This information supports the inference that the Fontan operation is a palliative procedure, with increasing disability developing in some patients by 10 years and in an increasing percentage thereafter. In patients with lateral tunnel or extracardiac conduit connections, exercise capacity is also well below normal, and
daily activity limitations are related to older age, further supporting this inference.\textsuperscript{244,213,215} Other variables may affect functional status. In a large multicenter study, the extracardiac conduit Fontan was noted to have better functional status than the lateral tunnel Fontan as measured by oxygen consumption during exercise testing.\textsuperscript{214} In the same study, LV morphology also was associated with better functional status than either RV or indeterminate ventricular morphology. In a large multicenter evaluation, the presence of heterotaxy did not affect functional status.\textsuperscript{212} The study by Shiraiishi and colleagues suggests that in patients undergoing an extracardiac conduit Fontan, earlier age at completion of the procedure results in better long-term hemodynamics and exercise capacity.\textsuperscript{216} In contrast, the study by Napoli and colleagues found no differences based on age at which the Fontan was performed.\textsuperscript{217} Whether the RV is incorporated into the Fontan circuit or not, pharmacologic afterload reduction does not improve exercise tolerance.\textsuperscript{218,219} Others have documented subnormal performance on objective exercise testing in patients who claim unrestricted activity with complete absence of symptoms. Nevertheless, subnormal performance represents a considerable improvement over preoperative status.\textsuperscript{219,220,221,222} Exercise capacity is severely restricted in Fontan patients at moderately high altitudes.\textsuperscript{215}

Somatic growth does not improve after the Fontan operation if the patient had previously undergone a bidirectional superior cavopulmonary shunt, mainly because catch-up growth has already occurred (somatic growth does improve after the bidirectional superior cavopulmonary shunt, demonstrating catch-up growth that was lost during the volume overloaded previous state).\textsuperscript{211}

\textbf{Hemodynamic Status}

Notwithstanding good functional status in most patients for at least several years after the Fontan operation, objectively studied hemodynamic state is usually subnormal.\textsuperscript{219,220,221,222} Peterson and colleagues, studying 16 patients (5 of whom had a valve used in the Fontan repair) with average follow-up of 25 months, found that resting and exercise cardiac indexes were not different from those of healthy children.\textsuperscript{219} The mechanism used by the patients to achieve high cardiac outputs during exercise was an increase in heart rate. However, ventricular ejection fraction was low, 0.45 ± 0.11 at rest and 0.51 ± 0.13 at peak exercise, and ventricular end-diastolic volumes were considerably greater than those of healthy children. Findings by Shachar and colleagues were similar, indicating reduced ejection fraction and increased left ventricular end-diastolic volume at rest and exercise.\textsuperscript{214}

An important aspect of the hemodynamic state after the Fontan operation is increase in Fontan pathway pressure during exercise.\textsuperscript{214,215} Its elevation can lead to reflux into caval and hepatic veins during atrial systole.\textsuperscript{220} Observant patients occasionally note that garments become tight around the waist during exercise, presumably because of increased Fontan pathway pressure and hepatic swelling. Qp is biphasic after the atroipulmonary Fontan operation, from both right atrial relaxation and contraction as well as left atrial emptying into the main ventricular chamber.\textsuperscript{212,214,215,219}

Not surprisingly, the respiratory cycle strongly affects Qp after certain types of Fontan operations, and perhaps after all types.\textsuperscript{119} Qp is increased with normal inspiration and is considerably augmented during strenuous inspiration. It is nearly stopped during the Valsalva maneuver.

Ventricular morphology influences hemodynamics. The presence of LV morphology results in better ejection fraction, AV valve function, and semilunar valve function compared with right or indeterminate ventricular morphology.\textsuperscript{214}

De Leval and colleagues have studied flow characteristics of the total cavopulmonary connection, finding that laminar flow is maintained to a greater extent when SVC and IVC pulmonary artery connections are offset, avoiding direct collision of the two bloodstreams, and when 90-degree angled configurations of the cavopulmonary connections are avoided.\textsuperscript{218} Experimental studies have shown that the extracardiac conduit connection provides superior hemodynamics when compared with either the atriopulmonary or lateral tunnel connection\textsuperscript{219}; clinical studies have not been performed. Using three-dimensional phased-contrast MRI in the clinical setting, altered flow patterns in the pulmonary arteries were found equally in atriopulmonary and lateral tunnel Fontans.\textsuperscript{219,220} Extracardiac conduit Fontans were not evaluated.

\textbf{Cardiac Rhythm}

Importance of sinus rhythm postoperatively remains arguable, primarily because of uncertainty about hemodynamic events after the Fontan operation. There is little doubt that sinus rhythm enhances performance of the main ventricular chamber, because of “atrial kick.” Dynamics of flow from cavae to pulmonary arteries are less firmly established. Acute animal experiments of Matsuda and colleagues and of Shemin and colleagues indicate that loss of sinus rhythm does not alter flow through an atriopulmonary conduit regardless of whether it contains a valve.\textsuperscript{220,211} However, using Doppler techniques, Bull and colleagues showed that in patients with an atriopulmonary connection, pulmonary flow accelerates during atrial systole.\textsuperscript{212} This was also observed by Ishikawa and colleagues using low-pressure contrast injection into the pulmonary artery.\textsuperscript{17}

Although sinus rhythm may not have a demonstrable direct effect on flow from right atrium to pulmonary arteries, it may influence this flow indirectly by permitting a lower PLa than otherwise would be the case. Also, because sinus rhythm seems to provide at least some pulsatility in the pulmonary arterial circulation, it may be advantageous in minimizing late changes in the pulmonary circulation. Loss of sinus rhythm and other supraventricular dysrhythmias, especially atrial flutter, are common after the atriopulmonary Fontan and increase with longer follow-up.\textsuperscript{15,19} Freedom from supraventricular tachydysrhythmias at 20 years after the atriopulmonary-type Fontan can be as low as 46%. Electrophysiologic ablation procedures are initially successful, but recurrence is common.\textsuperscript{219}

The lateral tunnel Fontan is also associated with a high prevalence of loss of sinus rhythm in some studies.\textsuperscript{210,213,216} In contrast, one study finds a greater loss of sinus rhythm in extracardiac conduit than in lateral tunnel Fontans; however, the follow-up period was almost twice as long in the extracardiac conduit group, putting the validity of this comparison into question.\textsuperscript{219} Experimental work in animal models suggests that the foreign body and suture line inherent in the lateral tunnel and hemi-Fontan techniques can induce supraventricular rhythm disturbance.\textsuperscript{22,26} Early and midterm follow-up studies indicate that loss of sinus rhythm and
other supraventricular dysrhythmias are markedly reduced following the extracardiac conduit Fontan compared historically with lateral tunnel and atrio pulmonary Fontan operations. It should be emphasized, however, that randomized and long-term follow-up studies are not available.

Loss of sinus rhythm and occurrence of supraventricular dysrhythmias may have complex etiologies and likely are not exclusively the result of the type of Fontan connection. Influence of previous operations, such as atrial septectomy or AV valve repair or replacement, myocardial ischemia from prior insults both intraoperatively and perioperatively, type of superior cavopulmonary connection (bidirectional superior cavopulmonary shunt vs. hemi-Fontan), and prior hemodynamic circumstances (chronic volume loads or obstructions) are all likely to affect atrial rhythm.

Sudden death has occurred in some patients late after operation (see Table 41-3). Multiform premature ventricular contractions appear to be present late postoperatively in about one third of patients and asymptomatic bradycardia in about 20%. These findings suggest that disturbances of cardiac rhythm may cause some late failures of the Fontan operation. Many of the factors mentioned in the previous paragraph may influence ventricular rhythm as well.

Complete heart block is rare after the Fontan operation.

Abnormalities of Pulmonary Circulation
Decrease in upper-to-lower lobe pulmonary blood flow perfusion ratio was observed by Cloutier and colleagues in most patients after the Fontan operation, similar to that seen in those who had undergone the classic Glenn operation (see “Classic Glenn Operation” under Special Situations and Controversies in Section 1). To date, however, pulmonary arteriovenous fistulas have been observed uncommonly after the Fontan operation.

A longer interval between operation and time of observation clearly increases prevalence of pulmonary arteriovenous fistulas after a classic Glenn operation. Thus, long follow-up is required to document the impression that this complication is uncommon.

Nevertheless, it is becoming increasingly clear that pulmonary arteriovenous fistulas are much less likely to form following Fontan completion. There is increasing anecdotal evidence that fistulas that form after a bidirectional superior cavopulmonary shunt regress following the Fontan. Pathophysiology of these fistulas remains elusive, and various etiologic factors have been suggested, including reduced Qp, nonpulsatile flow, cyanosis, and lack of splanchnic venous blood in the pulmonary circulation. Using contrast echocardiography, a sensitive method for identifying pulmonary arteriovenous fistulae, it has been shown that patients with single-ventricle physiology at any stage in their surgical reconstruction—that is, at the stage with completely mixed circulation with a systemic–pulmonary arterial shunt or at the stage with a bidirectional superior cavopulmonary shunt—were more likely to show evidence of fistulae than patients with isolated circulations. Echocardiographic evidence of fistulae, however, did not necessarily predict clinical cyanosis.

Protein-Losing Enteropathy
An important complication of the Fontan operation is protein-losing enteropathy. It is characterized by depressed serum albumin concentration with no obvious cause. It may be suggested by late postoperative onset of generalized edema and pleural or peritoneal fluid accumulations. Patients may or may not have diarrhea. Antitrypsin clearance is abnormally high, and because of low serum protein, total serum calcium is abnormally low. Special studies show excessive loss of serum proteins from the gastrointestinal tract; endoscopic investigations show prominent lymph vessels in the jejunal mucosa. This gastrointestinal protein loss occurs before clinical evidence of protein-losing enteropathy.

About 13% of patients develop evidence of protein-losing enteropathy by 10 years, and interval between operation and its appearance ranges widely, from 1 month to 16 years. Protein-losing enteropathy is associated with death, with near 50% mortality 5 years after diagnosis.

Protein-losing enteropathy is not limited to patients who have undergone the Fontan operation. It has been reported in almost all situations in which there is chronically elevated central venous pressure, including heart failure, chronic constrictive pericarditis, and atrial switch operations for transposition of the great arteries. It has also been observed in patients who have undergone SVC-RPA anastomosis and in patients with isolated SVC obstruction after an atrial switch operation. Presumably, the combination of increased lymph production from increased IVC pressure and impaired lymph drainage from increased SVC pressure contribute to this complication. Other potential influences are an elevated systemic inflammatory state and changes in mesenteric vascular resistance.

It may be relieved by reoperations that result in a lower right atrial pressure, such as when bidirectional superior cavopulmonary shunt or Fontan revisions are used to relieve systemic venous pathway obstruction. However, there is considerable early mortality after reoperation.

Correcting other hemodynamic abnormalities when right atrial pressure is low has resulted in regression. Creating a late fenestration has been reported to result in resolution of protein-losing enteropathy in three of five cases. Nonsurgical therapy, including use of steroids and heparin, has been associated with its resolution. Resolution has been reported after pacemaker placement in two patients with sinus node dysfunction, and in two patients following diaphragm pllication for phrenic nerve palsy. In a multicenter study, transplantation was found to effectively reverse protein-losing enteropathy.

Thromboembolic Complications
The cumulative occurrence of thrombotic complications ranges from 3% to 16%, and of embolic complications from 3% to 19%, according to a recent literature review. However, essentially all the primary reports reviewed involved patients predominantly receiving their operation prior to the modern era. Most of the studies indicate that these complications occur either early, within the first year after the Fontan, or late, beyond 10 years after surgery. Massive thrombi may form in the right atrium, particularly in atriopulmonary Fontan connections. Thus, in about half of the few cases reported, thrombi developed within a few weeks of operation; in the other half, they became evident a number of years later. Although infrequent, occurring early or over the intermediate term in about 10% of patients, this complication is of importance because a large thrombus or a piece of it may migrate from the right atrium and occlude the Fontan anastomosis or fill the RV or pulmonary arteries with sufficient thrombi to be fatal. Recently, a high prevalence of
thrombus has been documented in the Fontan pathway when this complication was sought by routine echocardiography in asymptomatic patients, and embolic complications have been reported as high as 29%.\textsuperscript{155} Presumably, slower-than-normal flow through the cavae and presence of foreign material predispose patients to thrombus formation and subsequent embolization. However, acquired abnormalities of the clotting system may be involved. In a study of this specific problem, the most common and most pronounced of these was a presumably acquired deficiency of protein C.\textsuperscript{156} Additional deficiencies in proteins and factor VII have been identified, which may relate in part to chronic impairment of liver function.\textsuperscript{157-159} The extracardiac conduit and lateral tunnel Fontan techniques currently favored by most centers may reduce thrombotic complications by maintaining laminar flow and reducing stasis. At mid-term follow-up, the risk of thrombosis is almost nonexistent in a large series of extracardiac conduit Fontans.\textsuperscript{160}

**Neurologic Complications**

Neurodevelopmental outcome is reported to be generally within the normal range.\textsuperscript{161-163} Thromboembolic cerebrovascular events have been reported, but their true prevalence is not known. Association of these events with ligated pulmonary artery segments and with fenestrations have been cited.\textsuperscript{164,165} Intracerebral venous thrombosis has been reported. Overall prevalence of stroke ranges from 3% to 9% over a 15-year period.\textsuperscript{166}

**Desaturation after Fontan**

Early and late systemic desaturation can occur from various systemic venous channels connecting to the pulmonary veins, coronary sinus, or left-sided atrial structures that may become manifest immediately or develop over time.\textsuperscript{167,168,169} Evaluation with cardiac catheterization is indicated to distinguish these entities from lung disease or intrapulmonary arteriovenous malformations, and to define specific morphology of the venous connections. Surgical or interventional closure of the connection is indicated.

**Reoperation**

**Takedown**

Reoperation for takedown of the Fontan operation has been necessary in a few patients in whom death has seemed otherwise inevitable. In earlier eras, risk of takedown (with substitution of a systemic–pulmonary arterial shunt) has been high, with 3 of 7 patients dying after the procedure in the combined University of Bordeaux–UB experience (43%; CL 20%-68%).\textsuperscript{170} Most of these patients were seriously ill when takedown was performed.

Mayer and colleagues also reported a high mortality (100%; CL 79%-100%) among 8 patients treated in this manner, but 2 survived and did well after takedown to a bidirectional superior cavopulmonary shunt (0%; CL 0%-61%).\textsuperscript{171} With this latter type of takedown, results in the future may be better (see “Takedown or Modification of Fontan Operation” earlier under Technique of Operation).

**Reoperation for Pathway Obstruction**

Reoperation for pathway obstruction has been the most common type of reoperation after the Fontan operation, and freedom from it has not been as high as desirable\textsuperscript{172} (Fig. 41-36). Furthermore, in this group of patients, instantaneous risk of requiring reoperation for pathway obstruction increased throughout follow-up, suggesting that with certain techniques of creating these pathways (see text that follows), nearly all patients will at some time require surgical revision of the pathway.\textsuperscript{173} Hospital mortality after reoperation has been high: 5 of 21 patients (24%; CL 14%-37%) in the University of Bordeaux–UAB experience.\textsuperscript{174} However, among hospital survivors, late survival and functional status have been as satisfactory as after the original Fontan operation. Need for reoperation for pathway obstruction has varied considerably, depending on the type of Fontan operation. Direct nonvalved connections between right atrium and either RV or pulmonary trunk have had a low prevalence of reoperations for pathway obstruction (Table 41-5), specifically, 4 instances among 200 patients (2%; CL 1%-3.6%). By contrast, 17 of 134 patients (13%; CL 9.6%-16%) receiving conduit connections, either valved or nonvalved, underwent reoperations for pathway obstruction.\textsuperscript{175} Pathway obstruction has not been evident following the extracardiac conduit and lateral tunnel Fontans, but follow-up has been shorter than for older procedures.\textsuperscript{176,177,178}

**Other Reoperations**

In about 5% of patients undergoing the atripulmonary Fontan operation for double inlet ventricle, closure of the right-sided AV valve dehisced and required reoperation.\textsuperscript{179} Likewise, re-repair of the ASD has been required in about 2% of patients. Cardiac transplantation was required late postoperatively in four patients in the combined University of Bordeaux–UAB experience for progressive myocardial failure.\textsuperscript{180} This final form of treatment may be required with increasing frequency in the future.
Table 41-5 Site and Type of Distal Right Atrial Connection in Fontan Operation and Prevalence of Reoperation for Pathway Obstruction

<table>
<thead>
<tr>
<th>Site and Type of Distal RA Connection</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ventricle</td>
<td>114</td>
<td>14</td>
<td>12</td>
<td>9-16</td>
</tr>
<tr>
<td>Conduit</td>
<td>69</td>
<td>12</td>
<td>17</td>
<td>13-23</td>
</tr>
<tr>
<td>Valved</td>
<td>20</td>
<td>2</td>
<td>10</td>
<td>3-22</td>
</tr>
<tr>
<td>Xenograft</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0-85</td>
</tr>
<tr>
<td>Allograft</td>
<td>19</td>
<td>2</td>
<td>11</td>
<td>4-23</td>
</tr>
<tr>
<td>Nonvalved</td>
<td>49</td>
<td>10</td>
<td>20</td>
<td>14-28</td>
</tr>
<tr>
<td>Direct</td>
<td>45</td>
<td>2</td>
<td>4</td>
<td>1-10</td>
</tr>
<tr>
<td>Simple</td>
<td>32</td>
<td>2</td>
<td>6</td>
<td>2-14</td>
</tr>
<tr>
<td>Roofed</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>0-14</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>220</td>
<td>7</td>
<td>3</td>
<td>2-5</td>
</tr>
<tr>
<td>Conduit</td>
<td>65</td>
<td>5</td>
<td>8</td>
<td>4-13</td>
</tr>
<tr>
<td>Valved</td>
<td>63</td>
<td>5</td>
<td>8</td>
<td>4-13</td>
</tr>
<tr>
<td>Xenograft</td>
<td>11</td>
<td>1</td>
<td>9</td>
<td>1-28</td>
</tr>
<tr>
<td>Allograft</td>
<td>52</td>
<td>4</td>
<td>8</td>
<td>4-14</td>
</tr>
<tr>
<td>Nonvalved</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0-61</td>
</tr>
<tr>
<td>Direct</td>
<td>155</td>
<td>2</td>
<td>1.3</td>
<td>0-4</td>
</tr>
<tr>
<td>Simple</td>
<td>118</td>
<td>2</td>
<td>2</td>
<td>0-6</td>
</tr>
<tr>
<td>Roofed</td>
<td>37</td>
<td>0</td>
<td>0</td>
<td>0-5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>334</td>
<td>21</td>
<td>6</td>
<td>5-8</td>
</tr>
</tbody>
</table>

Data from Fernandez and colleagues.15

Key: RA, Right atrial.

As the extracardiac conduit and lateral tunnel Fontan procedures have come into favor, they are being used with increasing frequency to revise atrio-pulmonary and AV Fontan connections. Indications include obstruction in the systemic venous Fontan pathway, thrombus formation in the right atrium, right pulmonary vein compression, and atrial dysrhythmias.18,42,46 Use of the maze procedure, its modifications (see “Maze III Procedure” and “Modified Maze Procedures” under Results in Section IV of Chapter 16), or intraoperative cryoablation may be indicated in a substantial portion of these patients.621 These Fontan revisions have achieved substantial improvement in almost all patients. Operative mortality is about 10%.411 It has been suggested from experimental studies that simply performing a bidirectional superior cavopulmonary shunt in patients with an atrio-pulmonary Fontan and dilated right atrial chamber and impaired hemodynamics may be beneficial, although there are no clinical data to support this.411

Fontan Operation with Deliberately Incomplete Atrial Partitioning

A number of operations have evolved that, despite their name, are not a Fontan operation. They have in common partial diversion of systemic venous blood to the pulmonary arteries and thus, an incomplete separation of pulmonary and systemic circulations. Some are intended as preliminary procedures to a Fontan operation, whereas others, such as the permanently “fenestrated Fontan,” replace the Fontan operation. Results of these operations have to be considered separately from those of a completed Fontan operation, although it is not yet known whether they are different.

The Fontan operation with deliberately incomplete atrial partitioning (fenestrated Fontan, Fontan with adjustable ASD) is difficult to evaluate because of the small number of patients in whom it has been performed and absence of risk-adjusted comparisons with other approaches. Early mortality has been 0% to 5%.29,31,34,38,52 Early closure of the residual aperture has been possible in at least 50% of patients, but this proportion, as well as the early and late results, varies according to characteristics of the patients being operated on and policies of the responsible physicians.29 Both techniques, the method of Laks and colleagues44 and that of percutaneous catheter closure,518 are well controlled and achieve secondary closure of the residual aperture (when this is elected) with low risk and good success. Late results of the specific subgroup of patients receiving permanently fenestrated Fontan operation have not yet been determined.

INDICATIONS FOR OPERATION

Fontan Operation

Most patients will have previously undergone palliative operations as newborns and again later in infancy, although a small group will have undergone one or no previous procedures. The Fontan procedure is rarely performed before age 1 year and typically not before age 18 to 24 months. Certain physiologic and morphologic criteria must be met for the Fontan to succeed. Currently, there are no clear indications for specifically performing either the extracardiac conduit Fontan or the lateral tunnel Fontan, although there is general consensus that these forms of total cavopulmonary Fontan are preferred over variations that include the right atrium.21,31,34,38,42 Despite lack of established superiority of one or the other of these, important differences between the two operations exist.39,713 These differences may ultimately be found to be important factors influencing outcome (see “Extracardiac Conduit versus Lateral Tunnel Fontan” in Special Situations and Controversies).

Many criteria, classically expounded by Choussat, Fontan, and colleagues, for performing a completed Fontan operation are arguable.21 However, Rp greater than about 4 units · m² seems a clear contraindication. Pathologic data from lung biopsy have not aided in making this decision.518 When Rp is 2 to 4 units · m², a bidirectional superior cavopulmonary shunt (or a hemi-Fontan procedure21) or a fenestrated Fontan operation rather than a completed Fontan operation may be indicated (see Section III). If subsequent evaluation confirms adequacy of the pulmonary vascular bed, the preliminary procedure can be converted to a total cavopulmonary connection. Evaluation of Qp and Rp should be performed shortly before the intended Fontan procedure, because they can be affected over time by factors such as chronic pulmonary microemboli.67

When branches of right and left pulmonary arteries are small, a Fontan operation will probably not succeed, although it can be argued that this should be the case only if they are small enough to cause elevation in Rp.513 For these cases, only
Because two thirds of all Fontans are extracardiac conduits, this indicates that many extracardiac conduit Fontans are also being fenestrated. It is not clear from the STS report whether it is primarily the extracardiac conduits performed using CPB that are receiving a fenestration, or whether particular institutions and surgeons are using the fenestration independent of CPB management. The lateral tunnel Fontan requires full CPB, hypothermia, and aortic clamping with administration of cardioplegia, and thus patients undergoing this procedure typically have perioperative perturbations in ventricular filling pressure and Rp. Most institutions that routinely perform the lateral tunnel Fontan use incomplete atrial partitioning, but some never do.

The argument remains whether a fenestrated Fontan operation should be done as a routine procedure or only in high-risk situations. In any event, use of some form of incomplete atrial partitioning seems advantageous in high-risk patients, especially when CPB is used to perform the procedure.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Definitive Palliation Other Than Fontan Operation**

Although the predominant view is that the Fontan is the best available definitive palliation for patients with single-ventricle physiology, few or no definitive data support this view. Some studies suggest that final palliation in the form of superior cavopulmonary shunt or aortopulmonary shunt provide long-term palliation that compares favorably with the Fontan.\(^7\)

**Conversion of Atriopulmonary Fontan to Cavopulmonary Fontan Operation**

Increasingly, patients who have previously undergone Fontan surgery with atriopulmonary connections of various kinds present with complications specifically related to them, including giant right atrium, right atrial thrombosis, compression of right pulmonary veins, atrial dysrhythmias, and obstruction at the atriopulmonary connection. They may present for Fontan revision, but only if ventricular function and Rp are adequate to sustain the Fontan circulation once the complications described previously are surgically addressed (if ventricular function is compromised and it is not due to a surgically correctable hemodynamic cause, or if the Rp is elevated, the only option is transplantation\(^11,18\)). The Fontan conversion operation entails removing the atriopulmonary connection and creating either an extracardiac conduit IVC–to–pulmonary artery connection or a lateral tunnel inferior cavopulmonary connection. Additionally, atrial reduction plasty, thrombus removal, and atrial dysrhythmia surgery, such as a formal maze procedure or one of its modifications (see “Interruption of Macro-reentrant Circuits” in Section IV of Chapter 16), may also be performed.\(^4,14,30,11,26\)

Another reason for Fontan conversion is to remove coronary sinus drainage from the high-pressure systemic venous compartment and place it in the low-pressure pulmonary venous compartment. It has been argued that elevated coronary sinus pressure reduces coronary perfusion pressure, which in theory may reduce coronary flow reserve; however,
Recent data suggest that the site of the coronary sinus drainage does not influence coronary flow reserve.\textsuperscript{3,4} Giardini and colleagues\textsuperscript{8} have documented that peak oxygen uptake improved and heart failure symptoms resolved when studied 6 months after conversion. Most conversions have been performed using the extracardiac conduit.\textsuperscript{4,6,17} However, Morales and colleagues\textsuperscript{14,22} provide evidence that lateral tunnel and extracardiac conduit revisions have equal outcomes.

In appropriately chosen candidates, early mortality is 0% to 5%.\textsuperscript{4,6,17,26,417} Outcomes will be optimized if appropriate preoperative medical management of the failing Fontan is undertaken.\textsuperscript{415}

**Routine Use of Fontan Operation with Deliberately Incomplete Atrial Partitioning**

Some institutions routinely fenestrate,\textsuperscript{12,34} and others rarely or never do.\textsuperscript{417,212} The advantages of fenestrating are reported to be improved hemodynamics, lower early mortality, and reduced pleural effusions. The need for routine fenestration has been supported\textsuperscript{35} and has been questioned.\textsuperscript{10,31,212}

Improvement in perioperative hemodynamics does occur in selected cases—specifically in those that have a systemic inflammatory response or temporary myocardial dysfunction as a result of the operation. These perturbations are more likely to occur when CPB is used and when cardiac arrest is used during CPB. Thus, fenestration is likely to be beneficial when the Fontan is performed using CPB, and of little or no benefit in most cases when CPB is not used.

The evidence that fenestration improves early mortality and reduces duration of effusions is not convincing. Table 41-6 shows that the majority of studies examining the effects of fenestration on effusions indicate that absence of a fenestration is not a risk factor for effusions, and Table 41-7 shows no difference in duration of effusions based on whether a fenestration is performed. Table 41-8 lists all studies examining the association between fenestration (or not) and early death. Four of the eight studies, and importantly the four most recent ones, show no association. Table 41-9 lists early mortality in studies that routinely use a fenestration, and in those that do not. Results are similar.

### Table 41-6 Single-Institution Studies Examining “Absence of Fenestration” as a Risk Factor for Effusions: Multivariable Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Risk of Effusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airan et al.\textsuperscript{45}</td>
<td>2000</td>
<td>•</td>
</tr>
<tr>
<td>Gaynor et al.\textsuperscript{49}</td>
<td>2002</td>
<td>•</td>
</tr>
<tr>
<td>Lemler et al.\textsuperscript{118}</td>
<td>2002</td>
<td>•</td>
</tr>
<tr>
<td>Fedderly et al.\textsuperscript{41}</td>
<td>2001</td>
<td>•</td>
</tr>
<tr>
<td>Atik et al.\textsuperscript{21}</td>
<td>2002</td>
<td>•</td>
</tr>
<tr>
<td>McGuirk et al.\textsuperscript{330}</td>
<td>2003</td>
<td>•</td>
</tr>
<tr>
<td>Gupta et al.\textsuperscript{228}</td>
<td>2004</td>
<td>•</td>
</tr>
<tr>
<td>Schreiber et al.\textsuperscript{58}</td>
<td>2006</td>
<td>•</td>
</tr>
<tr>
<td>Meyer et al.\textsuperscript{334}</td>
<td>2006</td>
<td>•</td>
</tr>
<tr>
<td>Hosein et al.\textsuperscript{116}</td>
<td>2007</td>
<td>•</td>
</tr>
<tr>
<td>Mascio et al.\textsuperscript{114}</td>
<td>2009</td>
<td>•</td>
</tr>
</tbody>
</table>

### Extracardiac Conduit versus Lateral Tunnel Fontan Operation

When usual morphologic variants are being considered, there remains considerable difference of opinion as to the best way to construct the Fontan physiology. Currently, extracardiac conduit or lateral tunnel cavopulmonary variants are preferred by most surgeons, largely because of the many long-term complications associated with the atriopulmonary connection. These complications include atrial dysrhythmia, loss of sinus node function, giant right atrium, atrial thrombus formation, compression of right pulmonary veins, and loss of laminar flow (see Clinical Features and Diagnostic Criteria earlier in this section). Any form of total cavopulmonary connection will address many of these complications, but controversy exists as to whether the lateral tunnel or the extracardiac conduit is better. According to the STS database, two thirds of all recent Fontans are extracardiac conduits, and one third are lateral tunnels.\textsuperscript{30} Some surgeons perform both operations, having specific indications for each, but most surgeons perform predominantly one or the other in the belief that they are choosing the operation that provides the least overall morbidity.

No definitive data support the superiority of either the lateral tunnel or extracardiac conduit Fontan. There are distinct differences between these two techniques, and it is a matter of speculation as to how these differences translate into patient benefit. The lateral tunnel procedure provides reasonable laminar flow and has the advantage of growth potential; however, it is an open cardiac procedure requiring CPB, hypothermia, and myocardial ischemia, which may have both immediate postoperative effects and long-term implications. The procedure also requires substantial manipulation of tissue in the region of the sinoatrial node and sinoatrial nodal artery, and atrial suture and foreign body load exposed to the systemic circulation is substantial. As a result, there are concerns regarding maintaining sinus rhythm and avoiding atrial dysrhythmias. The extracardiac conduit provides hemodynamics that most closely approximate laminar flow.\textsuperscript{110} It can be performed as a closed cardiac procedure without hypothermia, myocardial ischemia, or CPB, reducing the risks related to CPB, as well as the CPB-related systemic inflammatory response\textsuperscript{39} and the transient physiologic perturbations that increase the need for fenestration.\textsuperscript{212} Minimal or no manipulation of the right atrium is typical, and suture and foreign body load in the right atrium is eliminated, removing stimuli for dysrhythmia and systemic thromboembolic phenomena.\textsuperscript{212,213} The sinoatrial node and sinoatrial nodal artery regions are completely avoided. It can be argued, therefore, that the immediate postoperative and long-term ventricular mechanics, sinus node function, and atrial rhythm status are maximized. The extracardiac conduit, however, does not have growth potential and in general is performed in slightly older children to allow for a full-sized conduit. This delay until Fontan completion, and concern regarding long-term obstructive problems, have been cited as theoretical disadvantages.

Although there are no randomized trials comparing the two procedures, there exists a substantial body of data evaluating a wide spectrum of outcomes for each. Mahnke and colleagues noted a greater occurrence of cerebrovascular accidents in lateral tunnel than in extracardiac conduit Fontans, but follow-up was shorter in the latter group.\textsuperscript{33} Azakie,\textsuperscript{24}
Table 41-7  Single-Institution Studies Examining Duration of Effusions, Categorized by Use of Fenestration or Not

<table>
<thead>
<tr>
<th>Study</th>
<th>Fenestration</th>
<th>Year</th>
<th>Chest Tube Drainage (median days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azakie et al.</td>
<td>Yes</td>
<td>2001</td>
<td>8</td>
</tr>
<tr>
<td>Kumar et al.</td>
<td>Yes</td>
<td>2003</td>
<td>9</td>
</tr>
<tr>
<td>Woods et al.</td>
<td>Yes</td>
<td>2003</td>
<td>7</td>
</tr>
<tr>
<td>Meyer et al.</td>
<td>Yes</td>
<td>2006</td>
<td>2</td>
</tr>
<tr>
<td>Hosein et al.</td>
<td>Yes</td>
<td>2007</td>
<td>8</td>
</tr>
<tr>
<td>No Fenestration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hsu et al.</td>
<td>Yes</td>
<td>1997</td>
<td>5</td>
</tr>
<tr>
<td>Gupta et al.</td>
<td>Yes</td>
<td>2004</td>
<td>10</td>
</tr>
<tr>
<td>Petrossian et al.</td>
<td>Yes</td>
<td>2006</td>
<td>8</td>
</tr>
<tr>
<td>Schreiber et al.</td>
<td>Yes</td>
<td>2007</td>
<td>4</td>
</tr>
<tr>
<td>Hosein et al.</td>
<td>Yes</td>
<td>2007</td>
<td>8</td>
</tr>
<tr>
<td>Harada et al.</td>
<td>Yes</td>
<td>2009</td>
<td>11</td>
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</tbody>
</table>

Table 41-8  Single-Institution Studies Examining “Absence of Fenestration” as a Risk Factor for Death: Multivariable Analysis

<table>
<thead>
<tr>
<th>Study</th>
<th>Risk of Death</th>
<th>Year</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jacobs &amp; Norwood</td>
<td>Yes</td>
<td>1994</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gentles et al.</td>
<td>Yes</td>
<td>1997</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Airan et al.</td>
<td>Yes</td>
<td>2000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gaynor et al.</td>
<td>Yes</td>
<td>2002</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schreiber et al.</td>
<td>Yes</td>
<td>2004</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meyer et al.</td>
<td>Yes</td>
<td>2006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hosein et al.</td>
<td>Yes</td>
<td>2007</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kim et al.</td>
<td>Yes</td>
<td>2008</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Nurnberg et al., Lee, and Robbers-Visser and their colleagues all identified the lateral tunnel as an independent risk factor for both early and midterm atrial dysrhythmias, but Hakacova and colleagues did not. Fiore and colleagues showed that there was no difference in outcomes for the two operations with respect to early or late mortality, dysrhythmias, thromboembolic events, neurologic complications, or readmissions for effusions; however, they noted that the extracardiac conduit required fewer fenestrations but used a greater amount of resources. In contrast, Kumar and colleagues examined multiple outcome measures both early and midterm and found no differences between the groups, including resource utilization. None of these studies note an increased thrombosis risk for extracardiac conduit Fontans, and Petrossian and colleagues have documented a close to zero occurrence of thrombosis both early and up to 10 years after the extracardiac conduit operation.

Midterm follow-up of a large series of extracardiac conduit Fontan procedures indicates that performing the Fontan procedure at 3 to 4 years of age does not result in development of significant complications such as pulmonary arteriovenous malformations or acquired systemic to pulmonary artery collaterals. It is also well documented that the extracardiac conduit operation can be performed without aortic clamping and even without CPB, whereas the lateral tunnel operation requires both. Longer length of hospital stay has been linked to a greater need for perioperative fluid administration, which is secondarily linked to use of CPB. Avoiding CPB and reducing its length are associated with reduced effusions, providing indirect evidence supporting the advantages of the extracardiac conduit technique. There is no evidence to support the contention that the extracardiac conduit develops stenosis over time. Follow-up of up to 10 years reveals that the extracardiac conduit does not develop obstruction as the child grows, and formal measurement of the conduit by angiography at midterm follow-up indicates the conduit diameter shows little or no change from the diameter at insertion. In the Pediatric Heart Network multicenter study that retrospectively examined outcomes for the Fontan in 546 patients, the lateral tunnel Fontan was shown to have lower exercise performance than the extracardiac conduit Fontan.

Transplantation Following Fontan Operation

Patients with Fontan physiology may become candidates for transplantation for several reasons. One is that a critically important physiologic variable becomes abnormal, and as a result, the circulation can no longer be sustained. There are two such variables: ventricular function and Rp. If ventricular function decreases to the point that end-diastolic filling pressure becomes elevated, or if Rp becomes elevated, the Fontan circulation will fail, and transplantation is the only therapeutic option. Another reason is that intractable complications of the Fontan circulation develop, despite preserved ventricular function and low Rp. These complications include protein-losing enteropathy and plastic bronchitis. Patients who present for transplantation with preserved ventricular function and Fontan-related complications may have a particularly high mortality, implying that earlier transplantation may be necessary when these intractable complications develop. Protein-losing enteropathy will reverse after successful transplantation. Some studies report that survival after transplantation in Fontan patients is similar to that of patients undergoing transplantation for other causes, with 1-year survival of 72% and 5-year survival of 68%, whereas others report much higher early and late mortality. In a multicenter study assessing 98 patients, survival after transplantation in Fontan patients was slightly less than in other children with congenital heart disease and in those without congenital heart disease.

Hepatic Function in Fontan Patients

Hepatic dysfunction is universally recognized following the Fontan operation. Liver abnormalities correlate with older age and with time since the Fontan operation. Some studies correlate elevated systemic venous pressure and poor cardiac
function with liver abnormalities, and others do not. Liver abnormalities include fibrosis and cirrhosis, with their attendant consequences, and synthetic dysfunction, which particularly affects the coagulation system.

Use of Long-Term Anticoagulation

It is well recognized that the Fontan population is at high risk for thrombotic complications, second only to the nonbiological prosthetic valve population. Thus, anticoagulation therapy is an important consideration in this population. There are currently no prospective studies examining the efficacy of long-term anticoagulation following the Fontan operation; however, one study that recognized pulmonary emboli in 17% of Fontan patients also found that this complication did not occur if patients were on warfarin therapy. Another study showed no benefit for the use of warfarin. Nevertheless, practices vary widely. Some advocate no routine therapy but use varying pharmacologic regimens including aspirin, warfarin, or heparin for patients with risk factors for thrombosis. Others recommend aspirin routinely but no additional therapy. Still others recommend warfarin therapy, citing their experience that this approach reduces thrombosis when compared with no therapy or aspirin therapy.

Type of Operation for Tricuspid Atresia

When the cardiac malformation is tricuspid atresia and concordant ventriculoarterial connection, most patients will undergo either an extracardiac conduit or lateral tunnel Fontan; however, there is a possibility that the RV can become sufficiently functional to provide some benefit to the pulmonary circulation. Therefore, consideration can be given to performing an initial nonvalved right atrial–RV connection, generally at age 3 to 5 years. The RV enlarges considerably after this procedure, at least in some patients. If the ventricle becomes 30% or greater of normal size, the secondary insertion at age 8 to 10 years of an allograft valved conduit between right atrium and RV should provide a reasonably effective two-ventricle system. However, risk of conduit compression by the sternum must be overcome for this to be a generally useful alternative.

Bowman and colleagues were the first to demonstrate progressive RV enlargement when a valved right AV conduit was used. Pumping action of the enlarged ventricle can contribute to Qp and reduction of Fontan pathway pressure. Moreover, pulmonary artery systolic and pulse pressures can increase almost to normal. Fontan and colleagues also reported data from standardized exercise testing supporting the idea that an allograft valve in the connection between right atrium and RV provides a better late functional result than does a nonvalved connection. Del Toro and colleagues also noted less abnormality in both ejection fraction and hemodynamic response to exercise in patients with an AV connection than in those with an atrio-pulmonary connection. Magnitude of the hemodynamic advantages of a valved connection between right atrium and RV seem sufficient to affect functional status and survival late postoperatively, but this remains to be proven.

Valved Fontan Pathway

Studies suggest that a valve does not function when the RV is totally excluded, as in the Kreutzer modification of the Fontan procedure, even though the valve remains structurally perfect. Bull and colleagues also showed echocardiographically that the valve in a valved allograft conduit between right atrium and pulmonary artery closed momentarily or not at all. In similar circumstances, Sharratt and colleagues demonstrated delayed opening and slow closing of the conduit valve, suggesting that its presence in the pulmonary circuit may not contribute much to the hemodynamic state. Finally, in acute animal experiments, Shemin and colleagues showed that flow through a right atrial–to–pulmonary artery conduit was similar whether a valve was present or not.

Persistent Left Superior Vena Cava with Hemiazygos Extension of Inferior Vena Cava

As a part of the complex cardiac anatomy that usually coexists with atrial isomerism (see Morphology in Chapter 58) and sometimes in the absence of atrial isomerism, a persistent left SVC receiving IVC return via the hemiazygos vein may drain into the upper left corner of the left or common atrium. When the hepatic veins attach to the atrium well to the right, a slightly modified form of lateral tunnel total cavopulmonary connection can be used in which the left SVC is disconnected from the left atrium, the atrial opening oversewn, and the end of the left SVC anastomosed end to side to an incision in the left pulmonary artery. Occasionally, the left SVC lies virtually parallel to the left pulmonary artery, and then a side-to-side anastomosis without caval division permits a better fit of the two structures. In this case, the left SVC-atrial junction should be closed securely with a ligature and several

### Table 41-9 Single-Institution Studies Examining Early Mortality, Categorized by Use of Fenestration or Not

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
<th>Study</th>
<th>Year</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jacobs &amp; Norwood</td>
<td>1994</td>
<td>112</td>
<td>5</td>
<td>4.5</td>
<td>2.5-7.5</td>
<td>Jacobs &amp; Norwood</td>
<td>1994</td>
<td>88</td>
<td>11</td>
<td>12</td>
<td>8.8-17</td>
</tr>
<tr>
<td>Woods et al.</td>
<td>2003</td>
<td>54</td>
<td>3</td>
<td>5</td>
<td>2.5-11</td>
<td>Hsu et al.</td>
<td>1997</td>
<td>61</td>
<td>3</td>
<td>4.9</td>
<td>2.2-9.6</td>
</tr>
<tr>
<td>Meyer et al.</td>
<td>2006</td>
<td>144</td>
<td>2</td>
<td>1.4</td>
<td>0.5-3.3</td>
<td>Tokunaga et al.</td>
<td>2002</td>
<td>99</td>
<td>0</td>
<td>0</td>
<td>0-1.9</td>
</tr>
<tr>
<td>Petrossian</td>
<td>2006</td>
<td>49</td>
<td>0</td>
<td>0</td>
<td>0-3.8</td>
<td>Petrossian et al.</td>
<td>2006</td>
<td>236</td>
<td>4</td>
<td>1.7</td>
<td>0.9-3.1</td>
</tr>
<tr>
<td>Jacobs et al.</td>
<td>2008</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0-1.9</td>
<td>Schreiber et al.</td>
<td>2007</td>
<td>132</td>
<td>2</td>
<td>1.5</td>
<td>0.5-3.5</td>
</tr>
<tr>
<td>Schreiber et al.</td>
<td>2007</td>
<td>100</td>
<td>6</td>
<td>6</td>
<td>3.6-9.5</td>
<td>Ocello et al.</td>
<td>2007</td>
<td>100</td>
<td>6</td>
<td>6</td>
<td>3.6-9.5</td>
</tr>
<tr>
<td>Harada et al.</td>
<td>2009</td>
<td>72</td>
<td>0</td>
<td>0</td>
<td>0-2.6</td>
<td>Harada et al.</td>
<td>2009</td>
<td>72</td>
<td>0</td>
<td>0</td>
<td>0-2.6</td>
</tr>
</tbody>
</table>
pledged mattress transfusion sutures. The right-sided SVC is managed as usual in this variant of the lateral tunnel total cavopulmonary connection, but the intratrial tunnel brings only hepatic vein blood (not IVC blood) to the anastomosis of the cardiac end of the SVC to the RPA. Alternatively, the extracardiac conduit technique can be used, with the conduit connecting the hepatic venous confluence to the pulmonary artery system.119

In some hearts with these complex venous drainages, the hepatic veins enter a common atrium in the midline or to the left of it. This, and sometimes position of orifices of pulmonary veins, can make connection of hepatic veins to the cardiac end of the SVC possible only by a long and circuitous tunnel if the lateral tunnel technique is being considered. The extracardiac conduit Fontan does not present this limitation under these morphologic circumstances and can be used effectively. The conduit can be routed to either the left or right of the cardiac mass to reach the pulmonary arterial system. The total cavopulmonary shunt of Kawashima, which permanently leaves hepatic vein blood draining to the pulmonary venous atrium, has also been suggested as an option under these circumstances.120 After this operation, resting SaO2 has been between 87% and 92% but decreases with exercise.120 There is also the important concern of pulmonary arteriovenous malformations, which develop frequently following this procedure. As a result, the Kawashima variant is no longer recommended as a long-term solution.

Preoperative Cardiac Catheterization

Some have suggested that the Fontan operation can be performed without cardiac catheterization, but this approach is not widely accepted. Other studies suggest that catheterization should be performed using actual measurement of oxygen uptake rather than relying on predicted oxygen uptake in calculating cardiac output and pulmonary vascular resistance, because predicted values underestimate Rp.126

Several other studies indicate that pulmonary artery pressure can be accurately estimated by measuring pulmonary venous wedge pressure in single-ventricle patients, thus obviating the need to directly measure pulmonary artery pressure.125,128

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A


B

PART VII Congenital Heart Disease


E


F

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G


5. Hanley FL. The one and a half ventricle repair—we can do it, but should we do it? J Thorac Cardiovasc Surg 1999;117:659.


I

J

K
24. Kopf GS, Kleinman CS, Hijazi ZM, Fahey JT, Dewar ML, Hellenbrand WE. Fenerstrated Fontan operation with delayed


O


P


Chapter 41 Tricuspid Atresia and Single-Ventricle Physiology


U


V


W

Y

Z
Ebstein Anomaly

DEFINITION

Ebstein anomaly is a congenital defect of the tricuspid valve in which origins of the septal or posterior leaflets or both are displaced downward into the right ventricle, and the leaflets are variably deformed. Characteristically, the anterior leaflet is enlarged and “sail-like.” There is a wide spectrum of severity; in the mildest asymptomatic forms, the valve may appear normal at first sight, and classification as Ebstein anomaly may be debatable.57

This chapter discusses Ebstein anomaly in hearts with atrioventricular concordant connection and without other major cardiac anomalies. Ebstein-type tricuspid atresia and Ebstein anomaly associated with pulmonary atresia and with atrioventricular discordant connection are discussed elsewhere (see Chapters 40, 41, and 55). Details of Wolff-Parkinson-White syndrome, which is occasionally associated with Ebstein anomaly, are presented in Chapter 16.

HISTORICAL NOTE

Wilhelm Ebstein’s scholarly description of the tricuspid valve abnormality bearing his name was published in 1866.61 His report describes a single autopsy specimen and includes a hypothesis of pathophysiology based on correlation of the morphology with clinical notes on the deeply cyanosed patient supplied by a colleague (Ebstein did not apparently...
Table 42-1 Autopsy Findings in 16 Hearts with Ebstein Anomaly

<table>
<thead>
<tr>
<th>Tricuspid Leaflet</th>
<th>Totally Absent</th>
<th>Leafllet Origin</th>
<th>Leaflet Size</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Normal</td>
<td>Displaced</td>
</tr>
<tr>
<td>Septal</td>
<td>1</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Posterior</td>
<td>1</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Anterior</td>
<td>0</td>
<td>14</td>
<td>1</td>
</tr>
</tbody>
</table>

Data from GLH group.
1Obliteration of the functional ventricle was present in 15, of the atrialized chamber in 4, and of the tricuspid anulus in 12. There was an atrial communication in all specimens (small probe-patent foramen ovale in 2, an enlarged foramen ovale in 7, and fossa ovalis atrial septal defect in 7).
In two hearts, the whole cusp was adherent.
In three hearts, up to half the leaflet was missing.
In three hearts, the elongation was slight.

see the patient, Joseph Prescher, alive.) According to the historical review by Mann and Lie, the second case was not described until 20 years later, and the first description in the English literature was by MacCallum in 1900. The eponym Ebstein’s disease was first suggested by Arnstein in 1927 and was used by Yater and Shapiro in their 1937 review article that reported the sixteenth case and the first to be examined by both radiography and electrocardiography. These investigators commented that “it would appear impossible to make the diagnosis during life.” In 1950, Engle and colleagues as well as Reynolds suggested that the disease was associated with a clinical syndrome that should make diagnosis possible. In 1951, Van Lingen and colleagues and Soloff and colleagues made the diagnosis during life using cardiac catheterization and angiography, respectively. In 1955, Lev and colleagues described a patient with coexisting Wolff-Parkinson-White (WPW) syndrome and provided histologic details of the course of the conducting tissue in this anomaly.

Palliative surgery was attempted unsuccessfully using a Blalock-Taussig shunt in 1950. A superior vena cava–to–right pulmonary artery anastomosis (Glenn procedure) was used successfully by Gasul and colleagues in 1959 and subsequently by McCredie and colleagues and Scott and colleagues. Barnard and Schrire were the first to report the use of prosthetic valve replacement in 1962, followed by Cartwright and colleagues and Lillehei and colleagues. Hardy and colleagues reported the first successful valvuloplasty in 1964 based on the concepts of Hunter and Lillehei. A similar technique was used by Bahnsen in 1965.

MORPHOLOGY AND MORPHOGENESIS

Tricuspid Valve

Both the origin of the tricuspid valve from the atrioventricular (AV) ring and its chordal attachments within the right ventricle (RV) are malpositioned, and the leaflets are malformed. The leaflets are either enlarged or reduced in size and are frequently dysplastic (thickened and distorted). These deformities vary widely in severity (Table 42-1). In the mildest forms, the valve is functionally near normal; in the fully developed syndrome, function is severely compromised. Displacement of the origin of the leaflets from the AV ring is reasonably constant. The septal leaflet appears always to be affected, the posterior leaflet nearly always, and the anterior leaflet seldom (Fig. 42-1). As noted by Anderson and colleagues, when both the septal and posterior leaflets are displaced, the point of maximum displacement is usually at the commissure between them. Thus, the functional tricuspid anulus is rotated apically and anteriorly (Fig. 42-2). In the few cases in which the anterior leaflet is displaced, the commissural area between it and the septal leaflet, attached to the right trigone at the point of penetration of the bundle of His, remains in normal position (see Fig. 42-1). In many patients, the apparent displacement is due to adherence of the base of the leaflet to the RV wall (see Table 42-1 and Fig. 42-1). Adherence of leaflet tissue to the underlying myocardium is thought to represent a failure of delamination during development. This failure effectively moves the hinge points of the septal and posterior leaflets (the functional anulus) into the ventricular cavity. When adherence is incomplete, there is a potential or obvious pocket beneath the leaflet.

The septal or posterior leaflet may be partially absent, in which case the belly of the leaflet is small or absent (see Fig. 42-1). The posterior leaflet is more often elongated than reduced in size (see Table 42-1), due in part to lack of a commissure between the posterior and anterior cusps. This was the case in 8 of 15 hearts examined at autopsy at GLH. The septal–posterior leafllet commissure may also occasionally be absent. Leaflet enlargement and elongation are characteristic of the anterior leaflet, which has been described as sail-like. The leaflet is usually diffusely thickened or ridged and occasionally consists partly of muscle. All the leaflets are frequently dysplastic, and isolated accessory leaflets may occur.

Distal leaflet attachments are variable and usually abnormal. Displaced and dysplastic posterior and septal leaflets frequently have multiple short chordae connecting to multiple small papillary muscles (see Fig. 42-1). The sail-like anterior leaflet may also have multiple short chordae arising around most of its free edge, binding it relatively closely to the septum and occasionally to the free wall, or the leaflet edge may be directly adherent to the anterior papillary muscle and moderator band or the posterior edge of the septal band. Presence of a free anterior leaflet is an important morphologic detail, because it greatly increases the likelihood of a successful repair. Leafllet fenestrations are common, with the opening typically guarded by a single papillary muscle, which gives rise to chords that attach to the periphery of the fenestration.

If the entire free margin of the leaflets is adherent and imperforate, one variety of tricuspid atresia is produced (see Chapter 41). When the adherence is partial, the large
Figure 42-1 Autopsy specimens of Ebstein anomaly with varying degrees of tricuspid valve deformity. Right atrium and right ventricle have been opened. A, Site of true atrioventricular ring is marked by dashed line between arrows. All three leaflets are enlarged and elongated (anterior leaflet is poorly displayed). Septal leaflet is completely adherent to ventricular septal surface and has abnormal distal chordal attachments, as does posterior leaflet. Note normal leaflet origin at right trigone (anteroseptal commissure). B, Septal leaflet origin is displaced well downward into ventricle, and leaflet tissue is diminutive and dysplastic. Posterior leaflet is adherent from the ring to point marked with large asterisk. Anterior leaflet origin is normal, its belly is mildly elongated and cleft, and there are multiple short chordal attachments.

Continued

anterior leaflet produces a variable degree of stenosis between the portion of ventricle proximal to it (atrialized ventricle) and that distal to it (functional or ventricularized ventricle), because blood can pass only between openings that remain between the leaflet margin and ventricular wall (or through the commissures when these are present) (Fig. 42-3). Stiffness of the anterior leaflet contributes to stenosis.

Although important stenosis is uncommon, most Ebstein valves are regurgitant, often severely so (Fig. 42-4). This is contributed to by marked dilatation of the true tricuspid anulus and the RV, as by well as by morphologic abnormalities of the tricuspid valve.

The functional tricuspid orifice is determined by the hinge points of the valve leaflets, which rotate around the aortic root. The resultant functional valve orifice resides at the junction of the inlet and apical trabecular portions of the RV. We emphasize Anderson’s focus on this rotational understanding of Ebstein anomaly to differentiate it from
tricuspid valve dysplasia, which is often mistaken for Ebstein anomaly.

Right Ventricle
Rotational displacement of the valve divides the RV into proximal (atrialized) and distal (ventricularized) portions. The proximal portion lies between the true tricuspid anulus and the valve attachment and comprises a variable portion of the posterior and inferior (diaphragmatic) aspects of the ventricular cavity (see Figs. 42-3 and 42-4). The right coronary artery denotes location of the true tricuspid anulus.

The proximal portion is atrialized in about one fourth of hearts in which the posterior and septal leaflets are severely displaced (Fig. 42-5). This atrIALIZED portion of ventricular wall is dilated. Uncommonly, it is so thin as to seem aneurysmal, in which case it is largely fibrous tissue, and the endocardium is smooth. When very thin, it moves paradoxically during ventricular systole and may also expand during atrial systole. Its electrical potentials are ventricular, but its

Figure 42-1, cont’d  C, Septal leaflet is absent except for a strand of fibrous tissue. Anterior leaflet origin is downwardly displaced (except at right trigone), as is the posterior leaflet origin. Darkened, bruised portion of ventricular wall is thinned, atrialized ventricle. D, Elongated anterior and posterior leaflets originating normally from ring (arrow) but with poor commissural development. Central part of distal anterior leaflet edge is completely fused to a broad muscle group on the right ventricular free wall; adjacent to this are thickened, short chordae. Septal leaflet is not visible. Key: A, Anterior tricuspid valve leaflet; At, atrialized ventricle; CoS, coronary sinus; P, posterior tricuspid valve leaflet; S, septal tricuspid valve leaflet.
ventricle is usually thinner walled than normal and contains few muscle fibers. Anderson and Lie suggested there may be a congenital paucity of myocardial cells in the RV, such that dilatation of both portions of the ventricle is part of the developmental anomaly rather than entirely its hemodynamic consequence.

In 1988, Carpentier proposed a classification system based on size of the functional RV and adequacy of the anterior leaflet for repair:\cite{55}

- **Type A**: volume of true RV is adequate.
- **Type B**: a large atrialized component of RV is present, and anterior leaflet of tricuspid valve moves freely.

The functional ventricularized portion of the RV lies distal (downstream) to the displaced valve and is therefore smaller than the normal RV. However, this feature is modified by RV dilatation, which is an almost constant finding. The functional portion consists of the infundibulum (conus), trabeculated apex, and that portion of the ventricle beneath the large anterior cusp (anterolateral recess)\cite{44} (Figs. 42-6 and 42-7).

Ebstein anomaly is more than a valve abnormality, in that the RV has an underlying myopathy. The dilated functional ventricle is usually thinner walled than normal and contains fewer muscle fibers. Anderson and Lie suggested there may be a congenital paucity of myocardial cells in the RV, such that dilatation of both portions of the ventricle is part of the developmental anomaly rather than entirely its hemodynamic consequence.\cite{45}

In 1988, Carpentier proposed a classification system based on size of the functional RV and adequacy of the anterior leaflet for repair:\cite{46,47,48}:

- **Type A**: volume of true RV is adequate.
- **Type B**: a large atrialized component of RV is present, and anterior leaflet of tricuspid valve moves freely.

Figure 42-2 Functional tricuspid valve annulus in Ebstein anomaly. A, Normal proximal tricuspid attachments at atrioventricular junction (circular dotted line) and direction of hinge line (square dotted line). Displacement of valve orifice is rotational (flat arrow). B, Location of functional orifice of the abnormal valve (black ovals) as observed in the series of hearts examined by Schreiber and colleagues.\cite{55} Key: ARV, Atrialized right ventricle; CS, coronary sinus; IVC, inferior vena cava; RA, right atrium; SVC, superior vena cava; TRV, true right ventricle.

Figure 42-3 Cineangiogram in right anterior oblique projection of Ebstein anomaly. Injection is into a large atrIALIZED right ventricle, demonstrating dome formed by the fused leaflets. Free reflux is present into right atrium (RA) through atrioventricular ring (arrows). Relatively small functional (ventricularized) ventricle is poorly outlined because displaced valve is stenotic (virtual tricuspid atresia). Key: A, Atrialized portion of right ventricle; F, functional portion of right ventricle.

Figure 42-4 Cineangiogram in right anterior oblique projection of neonate with pulmonary atresia and Ebstein anomaly. Injection was into right ventricle, but catheter has recoiled into right atrium. Curved margin (black arrowheads) represents a dome formed by abnormally tethered distal edge of tricuspid leaflets. This margin separates atrialized ventricle from functional ventricle. There is severe tricuspid regurgitation. Normally positioned atrioventricular ring is readily identified (white arrow). Key: A, Atrialized portion of right ventricle; F, functional portion of right ventricle.
Type C: movement of anterior leaflet is severely restricted and may cause obstruction of RV outflow tract.

Type D: RV is nearly completely atrialized, except for a small infundibular component.

Right Atrium

The right atrium is enormously dilated in advanced cases. There is usually an interatrial communication (60% of autopsy specimens, 42% at catheterization, and 21 of 22 surgical cases in Watson’s collective review), most commonly a patent foramen ovale, although an atrial septal defect (ASD) of any type may be present.81 Interatrial communication was present in 94% of patients at operation in the series reported by Danielson and colleagues.84 Rarely, an ostium primum AV septal defect coexists.

The bundle of His and AV node lie in their usual locations, although the right bundle and node may be compressed by thickened endocardium (a possible explanation of the frequent right bundle branch block pattern in the electrocardiogram).87,15,12,13 WPW syndrome is present in about 14% of persons with Ebstein anomaly.84,75

Left Ventricle

Monibi and colleagues and Ng and colleagues report that abnormal left ventricular contraction and contour and mitral valve prolapse are frequently present.91,95 Marked dilatation of the RV produces leftward septal shift and compression and posterior displacement of the left ventricle. Daliento and colleagues studied nine autopsied hearts and found the ventricular septum normal in six and thin in three, which could account for the exaggerated leftward diastolic movement observed by angiography in 24 of 26 patients.81 Severe leftward displacement produced a “banana” appearance of the left ventricle. Regional left ventricular wall motion abnormality was observed in 67% of patients. In a Mayo Clinic experience of over 500 surgical patients with Ebstein anomaly, 9% had moderate or severe LV dysfunction.94 When mitral valve prolapse is present, the valve is frequently nodular and thickened.91,81,12,82 A Mayo Clinic study of 106 patients identified left ventricular abnormalities in 39%, of whom 18% had left ventricular dysplasia resembling noncompaction.81

Lungs

In severe Ebstein anomaly associated with fetal and neonatal distress or death, both lungs are usually hypoplastic but otherwise normal. The hypoplasia is secondary to gross cardiomegaly from severe tricuspid regurgitation.11
left-sided valves are regurgitant, this is frequently due to Ebstein anomaly. \(^5,\!^6,\!^6\) This Ebstein anomaly differs from the usual right-sided form in that dilatation of the AV ring and separation of the morphologic RV into atrialized and ventricularized portions are uncommon. The anterior leaflet is also less prominent and may be cleft (see Chapter 55).

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

**Mechanisms Underlying Clinical Presentation and Natural History**

Three primary pathophysiologic features predominate in patients with Ebstein anomaly:

- RV abnormalities
- Tricuspid valve abnormalities
- Accessory conduction pathways (WPW syndrome)

Their severity determines secondary pathophysiologic features, clinical presentation, and natural history.

**Right Ventricular Abnormalities**

Severity of RV abnormality is partly related to the extent to which the number of muscle fibers in the ventricular wall is reduced. \(^6,\!^7\) Nearly all patients have at least mild RV cavity enlargement and wall thinning. In the most severe cases, the RV cavity is greatly enlarged and free wall extremely thin. \(^6,\!^7\) The ventricular septum is often abnormal as well, with leftward bulging and consequent reduction in cavity size of the left ventricle, impairing left ventricular function. \(^6,\!^6,\!^1\) In the most advanced examples, the RV free wall is paper thin, a condition referred to as Uhl disease.

Extensiveness of the atrialized portion of the RV, which exhibits systolic expansion rather than contraction, importantly affects RV performance. RV dysfunction, along with tricuspid valve regurgitation, is responsible for right atrial enlargement and its wall thickening, which are at times extreme.

In aggregate, these abnormalities of RV structure and function underlie the variable cardiomegaly exhibited by patients with Ebstein anomaly: hepatomegaly, ascites, and fluid retention that may be advanced; cyanosis that is occasionally extreme, resulting from right-to-left shunting across a patent foramen ovale or ASD; and paroxysms of supraventricular and occasionally ventricular tachyarrhythmias that can cause advanced disability and sometimes sudden death.

**Tricuspid Valve Abnormalities**

Tricuspid regurgitation, usually present to some degree, exacerbates the abnormalities of RV structure and function. Degree of regurgitation is determined by the valve’s morphologic anomalies. Those valves in which the anterior leaflet is tightly tethered and adherent to the underlying RV free wall and septum and, to a lesser extent, those in which the posterior leaflet is displaced and immobilized, are more likely to be regurgitant. \(^6,\!^7\)

Pulmonary hypoplasia, a feature that contributes to neonatal death, is correlated with the degree of tricuspid regurgitation, occurring in association with severe regurgitation and gross cardiomegaly. If these features are corrected, the lungs presumably grow normally. \(^1\)

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**Figure 42-7** Right anterior oblique cineangiographic frames of Ebstein anomaly. Injection was into right ventricular apex. **A**, Early frame showing reflux through displaced leaflets into atrialized ventricle. Deep notch (arrow) represents attachment of a dysplastic posterior leaflet to inferior wall. **B**, Later frame showing more extensive filling of atrialized ventricle and right atrium (RA). X marks position of true atrioventricular ring. Key: A, Atrialized right ventricle.
**Wolff-Parkinson-White Syndrome**  
Arrhythmic features of WPW syndrome, present in about 14% of patients, may dominate the clinical picture in patients whose tricuspid valve and RV anomalies are mild (see Section III in Chapter 16).

**Associated Anomalies**  
In general, coexisting cardiac anomalies have little impact on the clinical features and course of patients with Ebstein anomaly. Exceptions are congenital pulmonary stenosis or atresia; when these coexist with Ebstein anomaly, death in utero or soon after birth is common. A patent foramen ovale or ASD, present in many patients, is necessary for right-to-left shunting and for the occasional paradoxical embolus or cerebral abscess that develops, but otherwise usually plays little role in the etiology of signs and symptoms. However, in the uncommon circumstance of only mild RV and tricuspid abnormalities, important left-to-right shunting may occur across an ASD.

**Symptoms and Signs**  
Breathlessness in association with cyanosis, severe cardiomegaly, and often heart failure may appear during the first week of life. However, many patients have milder symptoms and do not present until later in life. Nonetheless, objective exercise testing shows that their functional capacity is less than normal. Oxygen saturation at rest is a major predictor of exercise tolerance. Mild dyspnea and fatigue may become evident in childhood or early adult life, or more severe symptoms and signs of various types may develop. If heart failure develops, the patient becomes severely limited by breathlessness and fatigue.

Cyanosis is a common sign of Ebstein anomaly, occurring in more than half of patients and severe in about one third. It may appear at birth, but in most patients, onset is in infancy or early childhood.

Palpitations caused by various types of arrhythmia are also common. Severe arrhythmic symptoms are frequent in patients of all ages and may be disabling. WPW syndrome is the best known type of arrhythmia, but less specific types of supraventricular tachycardias are more common. Numerous electrophysiologic abnormalities have been identified, which no doubt account for the frequent occurrence and persistence of arrhythmic symptoms even after operation. Symptoms are more severe when there are important associated cardiac anomalies.

A malar flush, similar to the so-called mitral facies, was noted by Ebstein’s colleague and occurs in about one third of patients. It is unrelated to cyanosis or polycythemia or to cardiac output.

The left anterior chest is often prominent in association with marked cardiomegaly, and there may be a systolic thrill along the left sternal edge originating from the tricuspid valve. Characteristically, the precordium and apex remain quiet despite marked cardiomegaly. Jugular venous pressure is generally unremarkable and rarely suggests tricuspid regurgitation or stenosis, even though free tricuspid regurgitation is revealed by imaging studies. This is related to the large size and compliance of both the right atrium and atrialized RV, as well as the low RV and pulmonary artery pressure.

**Chest Radiography**  
In classic Ebstein anomaly, the chest radiograph shows marked cardiomegaly with a rounded or boxlike cardiac contour beneath a narrow pedicle. In the posteroanterior view, the whole of the silhouette is formed by the right atrium and RV, and because of their minimal excursion and the normal or oligemic lung fields, the silhouette has a peculiarly sharp edge. However, as with other features of the disease, there is wide variation in heart size. In a few cases, it remains normal; in most, it is only moderately enlarged.

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*Figure 42-8* Chest radiograph of a 12-year-old girl with classic Ebstein anomaly.
Electrocardiography

A right bundle branch pattern together with a relatively low-amplitude R wave in right-sided chest leads and right atrial hypertrophy are characteristic of the anomaly. According to Kumar and colleagues, height of the P wave varies inversely with arterial oxygen saturation ($r = .82$, $P < .001$).\textsuperscript{11} In addition, the taller the P wave, the shorter the survival time ($P < .001$). RV hypertrophy does not occur in uncomplicated Ebstein anomaly, and inverted T waves in leads V\textsubscript{1} to V\textsubscript{4} are fairly common. Using intraluminal electrode catheters, Kastor and colleagues demonstrated prolonged intra–right atrial and infranodal conduction in patients with a large right atrium and well-defined atrialized ventricle.\textsuperscript{2}

In approximately 14% of patients, the electrocardiogram shows type B (right-sided) WPW syndrome. In any cyanotic patient with this type of preexcitation, Ebstein anomaly should be considered. Supraventricular arrhythmias occur in more than half of patients, and they may be paroxysmal and recurrent. Paroxysmal atrial tachycardia, atrial fibrillation, and nodal rhythm can all occur, as can first-degree heart block. Serious ventricular arrhythmias resulting from RV dilatation may also occur.\textsuperscript{10}

Cardiac Catheterization and Cineangiography

Currently, cardiac catheterization and cineangiography are required only when specific hemodynamic details need to be identified,\textsuperscript{3} or in patients about aged 40, when the coronary tree should be examined.

In the past, cardiac catheterization showed that the mean right atrial pressure is often modestly elevated, and the pressure pulse may have either a dominant $a$ or $v$ wave. These correlate poorly with degree of tricuspid regurgitation or stenosis. An additional $s$ wave preceding the $v$ wave and interrupting the $e$ wave is said to indicate tricuspid regurgitation.\textsuperscript{5,11,53} The right atrial waveform is also recorded in the atrialized portion of the RV so that the tricuspid valve is noted to be displaced well toward the left of the spine. An electrocatheter may define the position and size of the atrialized RV chamber.\textsuperscript{49,53} RV systolic pressure is normal or low, and RV end-diastolic pressure is frequently elevated, more so when there is the syndrome of chronic heart failure. It is uncommon to record an important gradient across the tricuspid valve, although Takayasu and colleagues noted this in 8 of 26 cases and considered that stenosis could still be important in its absence.\textsuperscript{11,51}

When there is an interatrial communication, the shunt through it is usually right to left in association with systemic arterial desaturation and a reduced pulmonary blood flow ($Q_p$). The right-to-left shunt can be quantified by indicator dilution. The shunt may occasionally be left to right, and the resultant increase in $Q_p$ may be associated with heart failure.\textsuperscript{38} Direction of shunting is no doubt influenced by RV compliance.

In the newborn with Ebstein anomaly, a functional pulmonary outflow obstruction can occur.\textsuperscript{4} Thus, a normal pulmonary valve may fail to open following a right-sided injection of contrast media because of the combination of massive tricuspid regurgitation, poor RV contraction, and a high neonatal pulmonary vascular resistance with or without a large shunt at ductal level. High-quality imaging is therefore necessary to distinguish this situation from true pulmonary atresia.

Cineangiography (see Figs. 42-3 to 42-7) is usually diagnostic as long as there is important displacement and dysplasia of the septal or posterior leaflets.\textsuperscript{11} In the right anterior oblique projection, the conjoined posterior and anterior leaflets, and therefore the distal limit of the atrialized ventricle, can frequently be identified. Contrast media trapped beneath the posterior leaflet can indicate the degree of its adherence to, and level of its origin from, the diaphragmatic border of the RV, which may be notched at this point.\textsuperscript{317} The site of the true anulus is also visible more proximally. An injection into the functional RV enables tricuspid regurgitation to be assessed together with size and behavior of the functional ventricle. Angiography in left anterior oblique projection also permits visualization of the right-to-left shunt at atrial level, and any ventricular septal defects can be localized by left ventriculography.

**Figure 42-9** Two-dimensional echocardiogram of Ebstein anomaly. There is characteristic displacement of hinge point of septal leaflet below natural tricuspid anulus and adherence to septal wall. Anterior leaflet is elongated.
with more frequency in babies of mothers who are on lithium medication during pregnancy.\textsuperscript{15,81}

The natural history is determined primarily by the three primary pathophysiologic features described in Clinical Features and Diagnostic Criteria earlier in this chapter. Extent and severity of these relate to age at presentation; thus, age at presentation tends to correlate with prognosis. The presentation takes two general forms: symptomatic neonatal and infant presentation, and presentation in older children and adults.


date from Celermajer and colleagues.\textsuperscript{64}

Key: \textit{ARV}, Atrialized right ventricle; \textit{LA}, left atrium; \textit{LV}, left ventricle; \textit{RA}, right atrium; \textit{RV}, right ventricle.

The outlook is generally poor for patients with Ebstein anomaly who survive after presentation early in life have a good chance of long-term survival.\textsuperscript{53}

Many studies have probably underestimated the incidence and severity of this entity in neonates. The review by Vacca and colleagues of 108 clinical or autopsy cases reported between 1866 and 1957 recorded only two patients younger than 1 month.\textsuperscript{61} In Watson’s collective review of 505 cases, only 35 (7%) were younger than 1 year (half were younger than 1 month).\textsuperscript{51} In Bialostozky and colleagues’ review of 65 patients, neonates were not included.\textsuperscript{69} In a Mayo Clinic series, only 10 of 67 patients were diagnosed in infancy.\textsuperscript{65} In a Boston Children’s Hospital series, 12 of their 55 patients (22%) were seen during the first week of life, and 34 (64%) were younger than 2 years.\textsuperscript{11} Eleven of the 34 died early. These series must have been in some way selective and therefore are not useful in assessing natural history. In contrast, Schiebler and colleagues’ earlier study from the Mayo Clinic found that 12 of 23 patients presented during the neonatal period, and of these, 5 died.\textsuperscript{33} Roberson and Silverman reported that among 16 consecutive patients diagnosed in utero or presenting during the first 3 days of life, 7 died before age 3 months; all had severe RV and tricuspid morphologic abnormalities.\textsuperscript{87} In the 40-institution administrative registry of the Pediatric Health Information System (PHIS), of 464 neonates diagnosed with Ebstein anomaly from January 2003 to January 2008, 415 with complete data, mortality during initial hospitalization among 257 (62%) managed medically was 22% (56/257; CL 19%-25%).\textsuperscript{67}

Presentation during First Week of Life

Ebstein anomaly is a recognized cause of death in utero.\textsuperscript{64,34,13} When severe tricuspid regurgitation accompanies Ebstein anomaly at birth, the elevated newborn pulmonary vascular resistance worsens it, \( Q_p \) may be ductal dependent. The resultant severe hypoxemia (right-to-left shunting through an ASD), coupled with marked right-sided heart failure, may also be accompanied by low cardiac output if the ASD is restrictive. This is because maintenance of normal cardiac output requires shunting at the atrial level through a nonrestrictive ASD. Low cardiac output may also result from abnormal ventricular interactions caused by paradoxical septal bowing and flattening of the left ventricle. The hypoxemia may be aggravated by pulmonary dysfunction secondary to lung compression by marked cardiomegaly. Although lung hypoplasia has been suggested\textsuperscript{68,11} pathologic studies indicate that the lungs are rarely hypoplastic in surviving newborns, but are instead compressed by the enlarged heart.\textsuperscript{12}

Celermajer and colleagues from Great Ormond Street identified neonates with good and poor outcomes based on a score (Celermajer Score or Great Ormond Street Ratio)\textsuperscript{69,63} derived from echocardiographic measurements of the right atrium, RV, left atrium, and left ventricle.\textsuperscript{66} The score is calculated from a four-chamber echocardiographic view in which the combined area of the anatomic right atrium plus atrialized RV is divided by the sum of the areas of the functional (nonatrialized) RV, left atrium, and left ventricle (Table 42.2). The outlook is generally dismal for patients with Celermajer grades 3 or 4\textsuperscript{64,62} (severe Ebstein anomaly; Fig. 42.10).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{celermajer.png}
\caption{Changes in tricuspid anular dimension with progression of rotational tricuspid valve displacement from normal (left panel) to moderate (middle panel) to severe (right panel). Dotted line indicates functional tricuspid placement with increasing severity of Ebstein anomaly. (From Malhotra and colleagues.\textsuperscript{65})}
\end{figure}

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|}
\hline
Grade & Ratio (RA+ARV): (RV+LA+LV) & Risk of Death (%) \\
\hline
1 & <0.5 & 0 \\
2 & 0.5 to 0.99 & 10 \\
3 & 1 to 1.49 & 44 to 100 \\
4 & ≥1.50 & 100 \\
\hline
\end{tabular}
\caption{Celermajer Scale for Neonatal Ebstein Anomaly}
\end{table}
Presentation in Infancy

Presentation in infancy is associated with less risk of death and milder symptoms than occur with neonatal presentation (Fig. 42-11), although some studies suggest an increased mortality until presentation is beyond about 6 months. Beyond this age, Watson’s series indicates a prognosis similar to that of older children. He states that “whereas 72% of those under 1 year were in heart failure, 71% of the children and adolescents had little or no disability.”

Presentation in Childhood and Adult Life

Patients presenting after infancy often have mild symptoms. Prognosis is generally good, consistent with less severe RV and tricuspid valve pathophysiology. Patients presenting in adult life are often acyanotic and have a normal-sized heart. However, even these patients, who report few symptoms, have clearly definable abnormalities. Without preexcitation, nearly half have episodic supraventricular tachyarrhythmias, although these usually produce few symptoms. Exercise tolerance measured by objective testing is often reduced. The degree of tricuspid regurgitation does not correlate with symptoms, but as time passes, left ventricular dysfunction often appears as symptoms develop.

Death in this group of patients is often due to paroxysmal embolization or paradoxical supraventricular tachycardia, with heart failure appearing either much later or not at all. An atrial level communication increases the risk of paradoxical embolism, brain abscess, and sudden death.

Modes of Death

Heart failure is the mode of death in somewhat less than half of patients who die of causes related to their heart disease after the neonatal period. Sudden death, presumably caused for the most part by arrhythmias other than those associated with WPW, occurs in about 60% (CL 43%-77%) of these patients. Sudden death correlates with marked cardiomegaly, rather than with New York Heart Association (NYHA) status. Cerebral abscess and paradoxical emboli account for most of the remaining deaths, particularly in patients older than about 50 years. Infective endocarditis is rare.

TECHNIQUE OF OPERATION

Repair of Tricuspid Valve and Atrial Septal Defect Closure

The usual preparations are made for operation, anesthetic management (see Chapter 4), and cardiopulmonary bypass (CPB) (see Chapter 2). Before commencing CPB, the atrialized portion of the RV is assessed, noting particularly whether it moves paradoxically.

CPB is established using two venous cannulae, and the patient’s body temperature is lowered to about 25°C. The aorta is occluded and tourniquets secured around the venae cavae and cannulae. Cold cardioplegia may be administered directly into the aortic root or into the coronary sinus after the atrium is opened (see “Technique of Retrograde Infusion” in Chapter 3). The right atrium is incised parallel to the AV groove. A sump-sucker is placed across the atrial septum into the left atrium.

The atrial septum and tricuspid valve are examined (Fig. 42-12). The anterior leaflet of the tricuspid valve is studied with particular care, because successful repair of a regurgitant tricuspid valve relies on it. The anterior leaflet is rarely displaced into the RV, but if it is, the tricuspid valve may require replacement (see “Replacement of Tricuspid Valve” in text that follows). However, if the displacement is limited to that portion near the commissure, repair may be possible. Extreme thickening of the anterior leaflet, and particularly the dense attachment of its free edge to the underlying RV endocardium, makes successful repair unlikely and therefore contraindicates it.

Tricuspid valve repair with ASD closure is the preferred operation. Most repairs are designed to convert the tricuspid valve into a monoleaflet valve using the anterior leaflet to establish valve competence. The most important features that predict successful repair are a mobile, free leading edge of the anterior leaflet and attachment of more than 50% of it at the anatomic tricuspid anulus. A variety of maneuvers have been used to mobilize and extend this leading edge, with or without plication of the atrialized portion of the RV.

The method devised by Danielson and colleagues is the best tested. It plicates the atrialized portion of the ventricle, narrows the tricuspid orifice in a selective manner, and results in a monoleaflet valve that is usually competent or nearly so. A modification of the Danielson method in which the tricuspid valve anulus is remodeled by an anuloplasty ring is shown in Fig. Dearani and colleagues have also recommended moving the anterior leaflet closer to the ventricular septum by displacing the major papillary muscles supporting the anterior leaflet to a position closer to the septum. This is accomplished by placing pledgeted mattress sutures from the papillary muscle to the ventricular septum. An alternative is the Carpentier repair, in which the anterior leaflet is mobilized and detached from the anulus. The atrialized ventricle is plicated vertically, at right angles to the direction used by Danielson. This is accomplished by placing pledgeted mattress sutures from the papillary muscle to the ventricular septum.
Figure 42-12  Morphology of interior of right atrium in Ebstein anomaly at operation. Septal and posterior leaflets of tricuspid valve are adhered to septum and right ventricular (RV) wall. Downward displacement of tricuspid valve divides RV into a proximal atrialized portion and a distal ventricularized portion. Anterior leaflet is enlarged and elongated, described as sail-like. There is a foramen ovale type of atrial septal defect. Coronary sinus, atrioventricular node, and bundle of His are in their usual locations.
Figure 42-13  Repair of regurgitant tricuspid valve in Ebstein anomaly using a modification of the Danielson method.\textsuperscript{D3,D6,D14}  
\textbf{A}, A series of pledget-reinforced mattress sutures are placed at base of the septal and posterior leaflets of tricuspid valve. Stitches are continued to plicate atrialized portion of right ventricle (RV) up to the natural location of the valve anulus. Stitches are passed through a Carpentier anuloplasty ring. Atrial septal defect is closed by pericardial patch.  
\textbf{B}, Plication sutures are tied over anuloplasty ring to remodel the anulus and obliterate atrialized portion of the RV to complete the repair. Large anterior leaflet occludes the atroventricular orifice.
Figure 42-14  Diagram of modified Mayo Clinic method of tricuspid valve repair technique used for Ebstein anomaly. A, Two papillary muscles arise from free wall of right ventricle, with short chordal attachments to leading edge of anterior leaflet. Septal leaflet is diminutive and only a ridge of tissue. Posterior leaflet is not well formed and is adherent to underlying endocardium. A small patent foramen ovale is present. B-C, Base of each papillary muscle is moved toward ventricular septum at the appropriate level with horizontal mattress sutures backed with felt pledgets. Patent foramen ovale is closed by direct suture. D, Posterior angle of tricuspid orifice is closed by bringing right side of anterior leaflet down to the septum and plicating the nonfunctional posterior leaflet in the process. E, A posterior anuloplasty is performed to narrow diameter of tricuspid anulus; the coronary sinus marks posterior and leftward extent of anuloplasty. F, An anterior purse-string anuloplasty is performed to further narrow tricuspid anulus. This anuloplasty stitch is tied down over a 25-mm valve sizer in an adult to prevent tricuspid stenosis. G, Completed repair that allows anterior leaflet to function as a monoleaflet valve. (From Dearani and colleagues. Used with permission of Mayo Foundation for Medical Education and Research.)
Figure 42-15  Repair of regurgitant tricuspid valve in Ebstein anomaly using the Carpentier method. A, Three fourths of the enlarged anterior leaflet and as much as possible of the posterior leaflet are detached from the anulus. Incision is continued to the point at which valve begins to be displaced on ventricular wall at atrialized portion of right ventricle (RV). B, Detached leaflet is everted to expose support mechanism. There is usually chordal fusion, which may be marked in some cases. Fenestrations are made in the support mechanism to lengthen chordae and relieve obstruction below leaflets. C, Unique aspect of repair is placing pledget-reinforced plication stitches in atrialized portion of RV to create a vertical plication. Plication stitches are continued from base of leaflet attachment to ventricle to true anulus. Anulus is narrowed by this technique. A few stitches are placed in floor of right atrium. Plication stitches may be woven across atrialized portion for better obliteration of this portion of ventricle.
Others have used autologous or bovine pericardium to augment the anterior leaflet or septal leaflet (Fig. 42-18) to increase the area of leaflet coaptation. Midterm follow-up on a small number of patients has indicated good valve function.

Use of a bidirectional cavopulmonary shunt as an adjunctive procedure to create a one-and-a-half ventricle repair is an important surgical option to consider in valve reconstruction procedures. A protocolized approach to application of a one-and-a-half ventricle strategy (see Special Situations and Controversies) may increase the frequency of successful valve repair with aggressive anuloplasty techniques that may create some degree of tricuspid valve stenosis in order to eliminate regurgitation.

Replacement of Tricuspid Valve

In about 20% to 30% of patients, immobility or morphology of the tricuspid valve prevents repair and valve replacement is required. For this, the leaflet tissue is excised (Fig. 42-19, A), leaving a more generous portion of the base of the anterior and septal leaflets where they attach to the membranous septum and right trigone at the point of penetration of the bundle of His. The general suture technique for inserting the valve prosthesis is described in Chapters 11 and 14. When the septal and posterior leaflets are displaced into the RV, or the septal leaflet is absent, sutures may be passed through the usual location of the tricuspid ring. Alternatively, the suture line in this area can be placed well posterior to the AV node area and coronary sinus, as described by Barnard and Schrire. The replacement valve is usually a large mechanical prosthesis (Fig. 42-19, B) or stent-mounted xenograft. A pulmonary allograft mounted in a short polyester sleeve has been used. A mitral allograft could also be considered.

Figure 42-15, cont’d  D, Detached portion of tricuspid leaflet is rotated clockwise to cover tricuspid orifice beyond plication and as far toward septum as it will reach comfortably. Leaflet is reattached to anulus by continuous suture. E, Repair is supported by a Carpentier anuloplasty ring, which also remodels shape of anulus. It is attached to tricuspid anulus by a series of mattress sutures placed at perimeter of anulus. These stitches are most easily placed before anterior leaflet is reattached. A gap in the anuloplasty ring protects conduction system from injury.
Figure 42-16  Operative steps for Ebstein anomaly repair with cone procedure. A, Opened right atrium showing displacement of tricuspid valve. B, Detached part of anterior and posterior leaflet forming a single piece. C, Clockwise rotation of posterior leaflet edge to be sutured to anterior leaflet septal edge and plication of true tricuspid anulus (TTA). D, Completed valve attachment to true tricuspid anulus and valved closure of atrial septal defect (ASD). Key: CS, Coronary sinus. (From da Silva and colleagues.)

Figure 42-17  “Play it where it lies” approach to repair of Ebstein anomaly. Operation involves limited plication of tricuspid valve. Points A and B are approximated with one or two mattress sutures at the level of the native valve, not to the level of the true tricuspid anulus. This results in approximating apical aspects of septal and anterior leaflets, effectively creating a bicuspid valve. (From Malhotra and colleagues.)

Figure 42-18  Leaflet augmentation procedure for Ebstein anomaly. Patch of polytetrafluoroethylene is tailored to form a new septal anulus, attached to the atrium remote from the area of the atrioventricular node. Accommodation for coronary sinus is made by placing a notch in the patch. Tailored patch in place, defining a new septal anulus and an armature, onto which leaflet advancement is performed, attached at the plane of the reconstructed anulus. All suture material is remote from the atrioventricular node and bundle of His. (From Bichell and colleagues.)
Figure 42-19 Replacement of tricuspid valve in Ebstein anomaly. A, Valve is excised. B, Valve is replaced with a mechanical prosthesis or stent-mounted xenograft. Device is attached to anulus by pledget-reinforced mattress sutures. Atrialized portion of the right ventricle may be plicated by sutures used to attach the prosthesis. (From Doty and colleagues.)

When the atrialized ventricle is thin walled and fibrous and moves paradoxically, it is plicated by passing sutures used to position the valve first through tissue that forms the margin of the atrialized ventricle (corresponding to attachment of the displaced septal and posterior leaflets) and then through the true tricuspid ring. The valve is seated and sutures tied and cut. If the atrialized ventricle has been plicated, this portion may be further obliterated by a running polypropylene suture placed from outside the heart, taking care not to compromise the arterial supply of the remainder of the RV.
by occluding large coronary arteries. Plication is probably unnecessary in most cases when valve replacement is performed.\textsuperscript{[62]}

The interatrial communication is closed. In many instances, the septal tissue is stretched and the fossa ovalis tissue thinned. A patch must then be used (pericardium is ideal); it is positioned without tension using a continuous 4-0 polypropylene suture (see Fig. 42-13, A). Direct suture is avoided unless the tissues are strong and the defect small, which is uncommon. The left atrium is deliberately not emptied of blood, and the patch suture line is completed at the highest point (superiorly) to avoid air entrapment on the left side of the septum.

The right atriotomy is closed. When the atrium is very large, its size may be reduced by excising an ellipse from the lateral wall. The procedure is completed in the usual fashion, including placement of atrial and ventricular pacing wires and left and right atrial pressure catheters (see Chapter 2).

Simple Atrial Septal Defect Closure

Simple ASD closure may be done as described for closure in conjunction with valve replacement. However, this procedure is rarely indicated in patients with Ebstein anomaly.

Ventricular Exclusion in Critically Ill Neonates (Starnes Operation)

The Starnes operation is designed to abolish the detrimental tricuspid regurgitation by patch closing the tricuspid valve, creating a widely opened and nonrestrictive ASD, and establishing controlled pulmonary blood flow through a systemic-to-pulmonary artery shunt. A single ventricle palliation strategy is then pursued.\textsuperscript{[518]} CPB is established. Bicaval cannulation may be used (see “Venous Cannulation” in Section III of Chapter 2) and the operation performed during hypothermic CPB. Alternatively, a single venous cannula may be used and the intraatrial portion of the operation performed during hypothermic circulatory arrest. Cold cardioplegia is used (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). The right atrium is opened obliquely. The ASD is enlarged by excising all remnants of the septum primum (floor of the fossa ovalis). The tricuspid valve is closed by sewing into place an appropriately sized pericardial patch, sewn at the anatomic level of the tricuspid anulus. The coronary sinus is maintained on the atrial side of the patch. The patch is fenestrated with a 4-mm punch (Fig. 42-20). The right atrium is reduced in size by removing a segment of the right atrial free wall, and then is closed. If this portion of the procedure is done during hypothermic circulatory arrest, CPB is reestablished. If pulmonary regurgitation is present, the proximal main pulmonary trunk is closed.

A systemic-pulmonary shunt is created. Starnes and colleagues prefer a central shunt of 4-mm polytetrafluoroethylene (PTFE) tube interposed between the ascending aorta and pulmonary trunk.\textsuperscript{[518]} Alternatively, a 3.5- or 4-mm PTFE tube may be interposed between the brachiocephalic–right carotid artery junction and the medial aspect of the right pulmonary artery (see “Reconstructive Surgery” in Chapter 49), or between the right lateral aspect of the ascending aorta and anterior aspect of the right pulmonary artery. After rewarming has been accomplished, the remainder of the operation is completed in the usual manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). The sternum is generally left open and the skin closed with a patch of bovine pericardium. The sternum can usually be closed in the intensive care unit 48 to 72 hours later.

Treatment of Arrhythmias

Dearani and colleagues at the Mayo Clinic\textsuperscript{[69]} recommend routine electrophysiologic evaluation in children and adults undergoing Ebstein repair. If arrhythmic substrate is identified (e.g., WPW syndrome is present), and there is a history of life-threatening paroxysmal arrhythmia, the accessory conduction pathways are divided at the same operation, after proper electrophysiologic study.\textsuperscript{[512,588]} (see Technique of Intervention in Section III of Chapter 16). This is generally done before valve repair or replacement. Alternatively, these pathways may be obliterated preoperatively in the electrophysiology laboratory.\textsuperscript{[62]}

Supraventricular arrhythmia such as atrial flutter and fibrillation may occur paroxysmally or chronically as the right atrium enlarges. A right-sided maze procedure may be done at the time of operation.\textsuperscript{[519,74]}

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**Figure 42-20** Fenestrated patch closure of tricuspid valve in Starnes procedure. A, Glutaraldehyde-fixed autologous pericardial patch is sewn at anatomic level of tricuspid valve anulus. B, A 4-mm coronary punch is used to create a fenestration in the patch. Coronary sinus remains on right atrial side of patch. Key: ASD, Atrial septal defect. (From Reemtsen and colleagues.\textsuperscript{[44]})
SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is as usual after repair or replacement of the tricuspid valve for Ebstein anomaly (see Chapter 5). Convalescence is generally rapid and normal.

Critically ill neonates undergoing the Starnes operation, however, require the type of care accorded all neonates in whom pulmonary blood flow originates exclusively from the systemic circulation (see “General Care of Neonates and Infants” in Chapter 5). Additionally, pulmonary artery vasodilatation is encouraged by nitric oxide administration (see Chapter 5). Lowering pulmonary vascular resistance decreases the tendency to RV distention (see Special Situations and Controversies). Further operations and procedures follow the Fontan pathway strategies (see Indications for Operation and Special Situations and Controversies in Section IV of Chapter 41).

RESULTS AFTER REPAIR

Survival

Mortality after Surgery in the Neonatal Period

Historically, hospital mortality has been high (>50%) for critically ill neonates who undergo emergency or urgent operation. However, with current techniques of intensive neonatal medical management and surgical and percutaneous therapy as needed, survival has importantly improved. Thus, in the 40-institution report of the PHIS, overall hospital mortality of neonates initially managed by percutaneous procedures with or without surgery was 22% (9/40; CL 15%-31%), for those managed by systemic-to–pulmonary shunting 27%, for those undergoing tricuspid valve repair 31%, and for those receiving a transplant 0% (Table 42-3). Notably, half the neonates were medically managed, and 15% were managed by placement of a systemic-to–pulmonary system shunt, 9.6% by a percutaneous procedure, 8.7% by single ventricle palliation, and 3.9% by tricuspid valve repair.

Among 16 neonates undergoing surgical intervention between 1992 and 2005, Starnes and colleagues reported a hospital mortality of 31% with a variety of surgical procedures (Reemtsan 2006). The best survival occurred in the 10 patients (80% hospital survival; CL 59%-93%) who underwent patch fenestration as part of a RV exclusion procedure (Starnes operation). No late deaths were reported, all had undergone a subsequent bidirectional Glenn, and three had a completed Fontan.

Knott-Craig and colleagues have pursued tricuspid valve repair and two-ventricle physiology, creating a competent monolateral valve based on the anterior leaflet, partially closing the ASD, and performing a reduction atriotomy. Hospital survival among neonates exceeded 65%, but mortality was 55% (6/11; CL 35%-73%) among patients with anatomic pulmonary atresia.

An experience with surgical intervention in 24 neonates with Ebstein anomaly reported by Shinkawa and colleagues supports a policy of shunt only in the presence of refractory cyanosis without severe tricuspid regurgitation. In the presence of severe regurgitation and refractory heart failure, RV exclusion provided possibly superior hospital (73%, 8/11; CL 53%-87%) and late survival (63%) compared with tricuspid valve repair (25%, 1/4; CL 4.0%-62% for hospital and late survival).

Early (Hospital) Death in Children and Adults

Thirty-day mortality in the Mayo Clinic series of 539 patients (1972-2006) was 6.1% (33 deaths; CL 5.0%-7.4%), but 2.7% after 2001, which is representative of what can be accomplished in these often ill patients. Augustin and colleagues reported two hospital deaths among 60 patients (3.3%; CL 1.1%-7.7%) (1974-1995). These results are improved over those obtained in an earlier era. A multicenter study from the European Congenital Heart Surgeons Association reported a hospital mortality of 8.3% (CL 5.4%-12%) among 96 patients undergoing tricuspid valve repair or replacement between 1992 and 2005. In patients operated on from September 1993 to September 2008, Malhotra and colleagues report no early (0%; CL 0%-3.3%) or late mortality in a group of 57 non-neonatal patients (median age 8 years, range 7 months to 40 years), among whom 95% had valve repairs and 54% had concomitant cavopulmonary shunts. Using near routine excision of atrialized RV, detachment and repair of the tricuspid valve leaflets, and anulus plication, Wu and colleagues reported no early mortality (0%; CL 0%-2.3%) among 83 patients operated on between 1997 and 2006. Among 52 children aged 5 months to 12 years undergoing repair of Ebstein anomaly at the Mayo Clinic between 1974 and 2003, early mortality was 5.8% (3/52; CL 2.6%-11%), with no deaths since 1984 (0/31; CL 0%-5.9%). da Silva and colleagues reported a 2.5% hospital mortality (1/40; CL 0.4%-8.2%) among 40 patients undergoing the cone procedure between 1993 and 2005.

Mode of death is usually acute cardiac failure, probably related to preoperative RV enlargement and dysfunction. Improved methods of myocardial management, increasing prevalence and success of tricuspid valve repair rather than replacement, and possibly selective use of bidirectional cavopulmonary shunts have contributed to reduced early mortality.

Time-Related Survival

The seriousness of Ebstein anomaly is well demonstrated in a long-term follow-up study of a heterogeneous group of patients without major associated cardiac anomalies, 18 of whom (n = 48) underwent 22 operations. Median survival for the overall group was 47 years. Survival was similar in

<table>
<thead>
<tr>
<th>Table 42-3 Hospital Mortality According to Management Strategy Among 415 Neonates with Ebstein Anomaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strategy</td>
</tr>
<tr>
<td>Medical management</td>
</tr>
<tr>
<td>Percutaneous procedure</td>
</tr>
<tr>
<td>Percutaneous procedure and surgery</td>
</tr>
<tr>
<td>Systemic-to-pulmonary shunt</td>
</tr>
<tr>
<td>Tricuspid valve repair</td>
</tr>
<tr>
<td>Single-ventricle palliation</td>
</tr>
<tr>
<td>Transplantation</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

patients who presented during the first 3 days of life but survived to 6 months of age, and those who presented after 3 months of age. All four patients in whom permanent atrial fibrillation developed died within 5 years.

Late deaths are uncommon after tricuspid valve repair (or replacement) and ASD closure, with about 80% of patients surviving long term. However, among 52 children undergoing repair, 15-year survival was 90%. Deaths are often sudden and attributable to rhythm disturbances. Although it seems that late survival and freedom from reoperation would be better after successful valve repair than replacement, the Mayo Clinic analysis indicates no difference in late reoperation-free survival between patients receiving tricuspid valve repair vs. replacement among patients 12 years of age or older. However, among patients under age 12, reoperation-free survival is superior for those undergoing valve repair.

Preoperative risk factors for late mortality include higher hematocrit (worse cyanosis), severe mitral valve regurgitation, prior cardiac operations, and moderate to severe reduction in RV systolic function. Left ventricular dysfunction is also a risk factor for early and late mortality, despite the finding of improved left ventricular systolic function in most such patients following Ebstein anomaly repair.

**Right Ventricular Function**

Little is known about the long-term fate of RV function after neonatal surgery for Ebstein anomaly. However, Reemtsen and colleagues compared echocardiographic findings at 6 to 204 months (median 30 months) with those immediately prior to the Starnes procedure performed in the neonatal period. The Great Ormond Street ratio (see Table 42.2) and RV size decreased prior to the bidirectional Glenn, indicating RV regression. Left ventricular septal impingement on left ventricular cavity dimensions decreased an average of 38%, with normalization of left ventricular morphology and systolic function. These findings have important implications in predicting favorable outcomes after the Fontan operation if a single-ventricle strategy is selected in the neonatal period.

**Functional Status**

Most patients (about 85%) achieve good functional status (NYHA class I or II) and improved performance during objective exercise testing postoperatively, although many are severely limited preoperatively. Residual symptoms, when present, are usually related to troublesome, non-WPW supraventricular arrhythmias. Failure to eliminate the atrialized portion of the RV has not been shown to decrease the probability of a good functional result. The effect of a bidirectional cavopulmonary shunt on late functional status has been incompletely studied, but favorable midterm functional status has been reported.

**Tricuspid Valve Function after Repair and Freedom from Reoperation**

Although many reports indicate absent or mild tricuspid regurgitation early and midterm after repair, concerns remain about the important occurrence of late tricuspid valve replacement. Several areas of controversy relate to the optimal methods to prevent late, progressive tricuspid regurgitation. The Danielson and Carpentier techniques (see Technique of Operation) rely on creating essentially a monoleaflet valve that coapts against the RV septum in the area of the septal leaflet. This area has been observed as the site of recurrent tricuspid regurgitation, which theoretically may be obviated by direct leaflet coaptation in the septal area, as is achieved with the cone procedure (see Technique of Operation).

da Silva and colleagues reported no reoperations for tricuspid valve replacement, but one for re-repair and a 9% occurrence of moderately severe early tricuspid regurgitation among 40 patients who underwent the cone procedure. Freedom from further tricuspid regurgitation has been maintained in the intermediate term. Whether this technique and repair principles provide an important improvement in late valve function will require further long-term studies.

**Postrepair Rhythm Disturbances**

Complete heart block is uncommon after repair, despite the distorted morphology in the region of the bundle of His. WPW has mostly been cured by concomitant sectioning of the accessory pathways (see Chapter 16), which can be accomplished without increasing operative risk. However, episodic non-WPW supraventricular tachycardia continues late postoperatively in about 20% of patients. Uncommonly, even after successful surgical relief of WPW syndrome, late sudden death occurs. The substrate for atrial arrhythmias is enhanced by the large right atrium, RV dysfunction, and tricuspid regurgitation that frequently accompany Ebstein anomaly late after operation. Stulak and colleagues at the Mayo Clinic reported greater than 90% freedom from late recurrence of atrial fibrillation or flutter with a right-sided maze procedure plus isthmus ablation. An ongoing area of controversy relates to the possible benefit of a prophylactic right-sided maze procedure at the time of Ebstein anomaly repair.

**RESULTS OF OTHER PROCEDURES**

Repair of Atrial Septal Defect Alone

The risk associated with simple ASD closure is low in properly selected patients. In the combined UAB-GLH experience, nine patients with either left-to-right or right-to-left shunts and competent but abnormal tricuspid valves underwent simple ASD closure, with no hospital deaths (CL 0%-19%; Table 42.4). It is surprising that closure of the ASD was well tolerated in the face of preoperative right-to-left shunting, but this was also the experience at the Mayo Clinic and has been the case in pulmonary stenosis with intact ventricular septum (see Chapter 39).

When a left-to-right shunt is present preoperatively, late results are good (see Table 42.4). Thus, in the combined UAB-GLH experience, three patients in this category were hospital survivors; two had excellent long-term results, and one had WPW syndrome with episodic arrhythmias.

If the indication is appropriate, late results of simple ASD closure are also good in patients with right-to-left shunting preoperatively and important cyanosis. At late postoperative...
Table 42-4  Late Results of Atrial Septal Defect Closure without Tricuspid Valve Repair or Replacement*

<table>
<thead>
<tr>
<th>Age at Operation (Years)</th>
<th>Shunt</th>
<th>Preop NYHA Class</th>
<th>Length of Follow-Up (Years)</th>
<th>Postop NYHA Class</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2</td>
<td>L → R</td>
<td>IV</td>
<td>6</td>
<td>I</td>
<td>Moderate-sized VSD also closed</td>
</tr>
<tr>
<td>8</td>
<td>L → R</td>
<td>II</td>
<td>3.2</td>
<td>I</td>
<td>Kent bundle cut; pulmonary valvotomy performed; SV tachycardia PO</td>
</tr>
<tr>
<td>11</td>
<td>L → R</td>
<td>II</td>
<td>18</td>
<td>II</td>
<td>WPW, with episodic dysrhythmia PO</td>
</tr>
<tr>
<td>13</td>
<td>R → L</td>
<td>III</td>
<td>10</td>
<td>I</td>
<td>Episodic SV tachycardia PO</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>I</td>
<td>4</td>
<td>I</td>
<td>Operation for suspected RA myxoma</td>
</tr>
<tr>
<td>17</td>
<td>R → L</td>
<td>I</td>
<td>3</td>
<td>I</td>
<td>Operation for peripheral embolism; episodic SV tachycardia PO</td>
</tr>
<tr>
<td>20</td>
<td>R → L</td>
<td>II</td>
<td>14</td>
<td>II</td>
<td>Episodic severe dysrhythmia PO</td>
</tr>
<tr>
<td>26</td>
<td>L → R</td>
<td>III</td>
<td>6</td>
<td>II</td>
<td>Kent bundle cut; severe dysrhythmias PO</td>
</tr>
<tr>
<td>32</td>
<td>R → L</td>
<td>IV</td>
<td>3</td>
<td>I</td>
<td>Late death at operation for TVR</td>
</tr>
<tr>
<td>40</td>
<td>R → L</td>
<td>III</td>
<td>12</td>
<td>I</td>
<td>Episodic severe SV tachycardia PO</td>
</tr>
<tr>
<td>59</td>
<td>L → R</td>
<td>I</td>
<td>1</td>
<td>I</td>
<td></td>
</tr>
</tbody>
</table>

Data from combined UAB-GLH experience.

*ASD repair alone was performed in eight; ASD and VSD repair in one; ASD repair and pulmonary valvotomy in one; ASD repair in patient with suspected myxoma in one. One patient with ASD repair and tricuspid valvotomy, not included in this table, died 2 weeks after hospital discharge.

†Bidirectional, but dominantly R → L.

Key: ASD, Atrial septal defect; L → R, left to right; NYHA, New York Heart Association; postop, postoperative; preop, preoperative; R → L, right to left; RA, right atrial; SV, supraventricular; TVR, tricuspid valve replacement; VSD, ventricular septal defect; WPW, Wolff-Parkinson-White syndrome.

follow-up, four of five such patients in the UAB-GLH experience were alive and acyanotic, but all had episodic arrhythmias, severe in three cases. Two patients considered themselves functionally normal (NYHA class I), whereas two were in NYHA class II (see Table 42-4). One patient had an initially good result, and then cyanosis and severe disability recurred. Three years after his initial operation, he died after reoperation for reclosure of the septal defect and tricuspid valve replacement.

Tricuspid Valvotomy

The rare occurrence of tricuspid stenosis invites tricuspid valvotomy, but severe regurgitation may result. If the Carpenter technique of fenestration to restore or substitute for interchordal spaces is not satisfactory, valve replacement is indicated.

Pulmonary Valvotomy

Pulmonary valvotomy can have low hospital mortality in patients with Ebstein anomaly when indications are appropriate. This procedure may be life saving in neonates, because it decreases the degree of tricuspid regurgitation.

**INDICATIONS FOR OPERATION**

Neonates presenting in extremis, usually in the first week of life, are immediately intubated and begun on prostaglandin E₁, appropriate catecholamine support, aggressive treatment of metabolic acidosis, and other intensive therapy (see Special Situations and Controversies). Once stabilized, a Starnes procedure is performed, particularly if the patient has a Celermajer grade of 3 or 4 (see Special Situations and Controversies). If the patient’s condition does not stabilize, operation is performed at an exceptionally high risk.

Extracorporeal membrane oxygenation (ECMO) should be considered in such circumstances, either before or following emergency operation.

In the absence of severe cyanosis or symptoms of heart failure, medical management is advisable. Surgical intervention should be considered with the development of heart failure symptoms, worsening cyanosis, progressive increase in heart size, reduction in ventricular systolic function, or the appearance of atrial or ventricular tachyarrhythmias. The presence of severe tricuspid regurgitation and moderate cyanosis secondary to right-to-left shunting through the ASD should prompt earlier surgical intervention. Severe limitations and severe hypoxia are not contraindications to repair, although increased hospital mortality in patients in functional NYHA class IV argues strongly in favor of advising operation before disability is this advanced. The correlation between sudden death and cardiomegaly argues for operation when the cardiothoracic ratio reaches 0.60 or greater, regardless of symptoms.

Among patients under about 12 to 14 years of age, valve repair is greatly preferable to replacement. In older teenagers and adults, tricuspid valve replacement is a suitable option if repair appears unlikely to succeed.

Simple repair of the ASD is indicated when there is a large left-to-right shunt (Qp/Qs > 2), with or without symptoms of heart failure, and little or no tricuspid regurgitation. Simple repair of the ASD, without repair (or replacement if needed) of the tricuspid valve, is otherwise rarely advisable.

In patients with WPW syndrome that is producing life-threatening arrhythmia, the accessory conduction pathways should be divided or ablated, and the valve defect should be treated concomitantly on its merits. Atrial communications should be closed at the time of accessory pathways division. Other arrhythmias are not an indication for operation, because their occurrence is not altered by correction of the valve defect. However, they are undoubtedly less well tolerated in the presence of severe tricuspid regurgitation,
cardiomegaly, and cyanosis, and can then be an added indication for operation on the valve.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Morphology**

Confusion as to morphologic classification has arisen in some infants who have pulmonary atresia and minor downward displacement (or adherence) of the septal tricuspid leaflet origin (see Chapter 40). When this is the only Ebstein-like leaflet abnormality present, the defect is not classified or treated as Ebstein anomaly. In a number of infants with pulmonary atresia, however, the tricuspid valve shows additional typical and often florid features of Ebstein anomaly in association with severe regurgitation. Such patients form one variety of complex Ebstein anomaly.

**Management of Critically Ill Neonates with Ebstein Anomaly**

When neonates with Ebstein anomaly present with severe cyanosis, prostaglandin infusion is initiated to maintain or restore ductal patency. Urgent echocardiographic evaluation is performed to establish the diagnosis and evaluate the RV outflow tract. If antegrade flow through the pulmonary valve is absent, the pulmonary atresia may be functional (elevated pulmonary vascular resistance coupled with severe tricuspid regurgitation and RV dysfunction) or anatomic. A trial of inhaled nitric oxide is warranted to lower pulmonary vascular resistance and promote antegrade flow through the pulmonary valve if it is patent. If nitric oxide is helpful in bridging a marginal patient through the neonatal period, the addition of oral sildenafil may be useful. Other standard measures for critical ill neonates with Ebstein anomaly include placement of umbilical arterial and venous catheters and mechanical ventilation with the minimum effective airway pressure and tidal volumes of 10 to 15 mL · kg⁻¹ to recruit areas of atelectasis. If the RV outflow tract is functional, a trial of prostaglandin weaning is indicated. If SaO₂ is maintained at 70% or greater without heart failure, surgical intervention may not be necessary.

If prostaglandin weaning is not successful, two situations may occur. If the circulation is stable without evidence of heart failure and the only problem is unacceptable cyanosis, a systemic-to-pulmonary shunt may be the only necessary procedure. However, if heart failure and circulatory compromise persist, the tricuspid valve itself must be addressed, either through the Starnes procedure or valve reconstruction (see Technique of Operation).

In planning for continued medical therapy vs. the likelihood of needing surgical intervention, calculation of the Celerier score is useful in predicting risk of death (see Table 42-2).

**Type of Prosthesis for Tricuspid Valve Replacement**

A stent-mounted glutaraldehyde-preserved porcine bioprosthesis or bovine pericardial bioprosthesis may be considered optimal in most patients with Ebstein anomaly, but both are subject to the usual problems of a bioprosthesis. Mechanical prostheses may also be used to achieve long-term durability, but anticoagulant therapy is required. An analysis of the Mayo Clinic experience identified use of a bioprosthetic valve (vs. mechanical prosthetic valve) as an independent predictor of long-term survival. An allograft, either a stent-mounted pulmonary or aortic valve, or a directly attached mitral allograft supported by an anuloplasty ring, could also be considered.

**Indications for Plication (or Resection) of Atrialized Ventricle**

Indications for plication of an atrialized ventricle at the time of tricuspid valve replacement are controversial. Potential advantages of plication (or resection) include (1) reducing the size of the nonfunctional RV, potentially increasing transit of blood by improved systolic function; (2) improving left ventricular function by alleviating left ventricular compression and septal bowing; (3) moving the anterior leaflet closer to the septum by elevating the papillary muscles; and (4) providing more space for lung expansion, especially in neonates. The major potential disadvantage relates to possible distortion of or injury to the right coronary artery and its branches, which could worsen RV function and contribute to ventricular arrhythmias. Some suggest that omitting routine plication compromises RV function postoperatively; others believe that plication is indicated only when the atrialized portion of the RV is very thin walled and aneurysmal (probably about 10% to 15% of cases). Excision or plication of the atrialized portion of the repair, without need to plicate the remainder of the atrialized portion.

**Excision or Plication of Right Atrial Wall**

Excision or plication of the right atrial wall was suggested by Timmis and colleagues, who considered it important “to promote atrial emptying and lessen the likelihood of clot formation” when a mechanical prosthesis was used. Danielson and colleagues incorporate excision of the right atrial wall in their repair. The simplicity of this maneuver during valve replacement or repair makes it an attractive step when the right atrium is markedly enlarged.

**Role of Bidirectional Cavopulmonary Shunt and One-and-a-Half Ventricle Repair**

The vast majority of patients with Ebstein anomaly can undergo successful biventricular repair. However, creating a “one-and-a-half” ventricle repair can be an effective strategy if reducing the tricuspid anulus to a z value of less than −2 (or about 2.5 cm in the adult) is necessary to eliminate important tricuspid regurgitation in an infant or child with normal pulmonary vascular resistance. In this instance, functional tricuspid stenosis is managed by constructing a bidirectional cavopulmonary shunt with division of the superior vena cava at its junction with the right atrium (see Chapter 41). This strategy may also be useful when the RV is severely dysfunctional, as long as the left atrial and
pulmonary artery pressures are low. By reducing the RV stroke volume required to maintain effective cardiac output, RV work requirement is reduced and preload of the left ventricle optimized. Furthermore, the adverse effect on left ventricular function by a massively enlarged RV can be ameliorated. Bidirectional cavopulmonary shunt may also reduce residual tricuspid regurgitation. Dearani and colleagues have recommended the following criteria for constructing a bidirectional cavopulmonary shunt: left ventricular end-diastolic pressure less than 15 mmHg, transpulmonary gradient less than 10 mmHg, and mean pulmonary artery pressure less than 18 to 20 mmHg. Malhotra and colleagues recommend performing a bidirectional cavopulmonary shunt if, at the end of the repair, right atrial pressure is more than 1.5 times left atrial pressure.

The potential disadvantages of this approach include possible facial suffusion secondary to elevated jugular venous pressure and pulsations in the head and neck veins, development of collateral veins and pulmonary arteriovenous fistulas, and compromise of access for pacemaker leads.

Malhotra and colleagues reported an experience of valve repair in 54 of 57 patients with Ebstein anomaly, of whom 55% received a bidirectional cavopulmonary shunt (half of these in adults). Freedom from subsequent valve replacement was 92% at 4 years, with 95% of patients in NYHA class I. Van Arsdell and colleagues reported 90% 10-year survival following one-and-a-half ventricle repair.

**Indications for Single-Ventricle Pathway**

The potential advantages of RV exclusion (Starnes procedure) for severely ill neonates with Ebstein anomaly are discussed under “Survival” in Results after Repair. Such patients, if they survive the initial neonatal procedure, have a high likelihood of survival through the bidirectional Glenn stage.

A particularly high-risk morphologic subset of Ebstein anomaly is hearts with the combination of severe tricuspid regurgitation and anatomic pulmonary atresia. Symptomatic infants and children with this combination are likely best treated with a single-ventricle strategy. Polimenakos and colleagues have also applied this strategy successfully in an adult Ebstein’s treated with a single-ventricle strategy. Polimenakos and colleagues have recommended the following criteria for constructing a bidirectional cavopulmonary shunt: left ventricular end-diastolic pressure less than 15 mmHg, transpulmonary gradient less than 10 mmHg, and mean pulmonary artery pressure less than 18 to 20 mmHg.

Malhotra and colleagues reported an experience of valve repair in 54 of 57 patients with Ebstein anomaly, of whom 55% received a bidirectional cavopulmonary shunt (half of these in adults). Freedom from subsequent valve replacement was 92% at 4 years, with 95% of patients in NYHA class I. Van Arsdell and colleagues reported 90% 10-year survival following one-and-a-half ventricle repair.

**REFERENCES**

A


B


C


D

E

F

G
PART VII Congenital Heart Disease

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Truncus arteriosus (persistent truncus arteriosus, truncus arteriosus communis, common aorticopulmonary trunk) is a congenital cardiovascular malformation in which one great artery arising from the base of the heart by way of a single semilunar (truncal) valve gives origin to the coronary, systemic, and one or two pulmonary arteries proximal to the origin of the brachiocephalic branches. It is one of several diagnoses within the phylum of common ventriculoatrial junction (see http://www.ipcc.net/). A ventricular septal defect (VSD) is almost always present beneath the truncal valve.

This definition excludes those hearts in which there are no true pulmonary arteries and in which the lungs are supplied only by large aortopulmonary arteries (Collett and Edwards type IV), characteristic of tetralogy of Fallot and pulmonary atresia with absence of the pulmonary trunk and the central and hilar portions of the right and left pulmonary arteries (see “Morphology” under Tetralogy of Fallot with Pulmonary Atresia in Section II of Chapter 38). Excluded also from discussion in this chapter are hearts with a common arterial trunk but an intact ventricular septum. Whether hearts in which there is a VSD but no interventricular communication during diastole (because the semilunar cusps close against the crest of the ventricular septum) should be considered to have an intact septum is controversial.

HISTORICAL NOTE

The first well-documented case of truncus arteriosus was reported by Wilson in 1798, and existence of the entity was confirmed by accurate clinical and autopsy reports of a 6-month-old infant by Buchanan in 1864. In the early literature, there was frequent confusion with a single arterial trunk and, although Vievordt clarified this aspect in 1898...
(quoted by Victoria and colleagues\textsuperscript{17,23}), confusion existed as late as 1930 when Shapiro\textsuperscript{55} distinguished it from hearts with aortic and pulmonary atresia. Lev and Saphir proposed the basic morphologic criteria defining the anomaly in 1942,\textsuperscript{1,5} and in 1949 Collett and Edwards\textsuperscript{17} reviewed previously published cases and proposed a classification. An alternative classification was suggested by the Van Praagh in 1965.\textsuperscript{12}

Surgical treatment was initially confined to banding of one or both pulmonary arteries.\textsuperscript{19,16,89} Intracardiac repair was first successfully accomplished in 1962 at the University of Michigan using a nonvalved polytetrafluoroethylene (PTFE) conduit; the patient was alive and well 11 years later.\textsuperscript{23} Experimental work using ascending aortic allografts including the aortic valve was reported from Japan by Arai and colleagues in 1965,\textsuperscript{88} and by Rastelli and colleagues at the Mayo Clinic in 1967.\textsuperscript{2,34} Before this, in 1966, Ross and Somerville had successfully used an ascending aortic allograft in reconstructing tetralogy of Fallot with pulmonary atresia.\textsuperscript{83}

McGoon and colleagues were the first to successfully repair truncus arteriosus using an ascending aortic allograft and valve conduit (cylinder) in September 1967.\textsuperscript{89,90} Weldon and Cameron reported a successful repair in 1967.\textsuperscript{92} Binet used a xenograft valve incorporated within a polyester cylinder in 1971 (see discussion of paper by Moore and colleagues\textsuperscript{1415}), and Bowman and colleagues reported use of a glutaraldehyde-treated porcine aortic valve in a polyester cylinder in 1973.\textsuperscript{88}

The first successful conduit repair in infancy was carried out in a 6-week-old infant by Barratt-Boyes in 1971, as reported by Girinath.\textsuperscript{83}

**MORPHOGENESIS AND MORPHOLOGY**

**Morphogenesis**

Deletion of chromosome 22q11 is present in a substantial number of patients with conotruncal abnormalities. About one third of subjects with truncus arteriosus have been found to have 22q11 deletion,\textsuperscript{84,112} and many of these have additional characteristic features of DiGeorge syndrome, velocardiofacial syndrome, or conotruncal face syndrome. As such, their natural history and also their course following operation may be complicated by hypocalcemia, palatal abnormalities, learning disability, and other noncardiac problems.

**Morphology**

Truncus arteriosus is classified based on origins of the pulmonary arteries from the truncal artery (Collett and Edwards\textsuperscript{17}) and also on degree of development of the ascending aorta and ductus arteriosus in cases with a single pulmonary artery (Van Praagh and Van Praagh\textsuperscript{12}).

**Truncal Artery**

The arterial trunk (truncal artery) is larger than a normal aorta and is the only vessel arising from the base of the heart. It originates in part from both ventricles, but usually is more over the right than left ventricle.\textsuperscript{85,88,12} In an autopsy series of 56 cases, the trunk was equally balanced over both ventricles in 50%. In the remainder, it was either exclusively or predominantly over the right ventricle in 40% and over the left ventricle in 10%.\textsuperscript{41} In the unbalanced cases, the VSD was much more likely to be smaller (both shallower and narrower). From the truncal artery arise the coronary arteries and one or both pulmonary arteries.

**Pulmonary Arteries**

The pulmonary arteries usually originate just downstream from the truncal valve on the left posterolateral aspect of the truncus artery, although their origin may lie truly laterally, truly posteriorly,\textsuperscript{60} or (rarely) anterolaterally (Table 43-1).\textsuperscript{83} There is frequently a single orifice leading into a short pulmonary trunk (type I of Collett and Edwards), which then divides into left and right pulmonary arteries that follow a normal course (Figs. 43-1 and 43-2). Alternatively and less commonly, the orifice is double, the left and right branches arising separately side by side (Fig. 43-3) or occasionally with the orifice of the left pulmonary artery superior (anterior) to the right rather than to the left of it (type II of Collett and Edwards). Types I and II merge into each other and are best considered together. They comprise the majority of cases\textsuperscript{85,17,7,18} (89% of the Toronto surgical series).\textsuperscript{83}

Rarely, ostia of left and right pulmonary arteries may be widely separated and arise from opposite lateral walls of the truncal artery at either the same or different levels above the valve (type III of Collett and Edwards). This arrangement poses special problems for repair.\textsuperscript{841}

Occasionally, only one pulmonary artery originates from the truncal artery. The arterial vascular supply to the opposite lung arises either from a patent ductus arteriosus as a complete branch pulmonary artery or from large aortopulmonary collateral arteries, as in tetralogy of Fallot with pulmonary atresia.\textsuperscript{88,12} When the left pulmonary artery is the one that does not originate from the truncus (or is absent), the right often continues to arise from the left posterolateral surface of the proximal truncal artery.\textsuperscript{17,12} The term hemitrunicus has been used to describe the condition of the common arterial trunk giving rise to only one branch pulmonary artery,\textsuperscript{87} but the term is more commonly used to describe the slightly more common “origin of right (or left) pulmonary artery from the aorta.” In the latter, of course, there are two separate semilunar valves (see Chapter 45).

Stenosis of the origin of one or both branch pulmonary arteries is more frequent than absence of the origin; it is probably underestimated in autopsy compared with cineangiographic studies. It was noted in five clinical cases (10%) in one series.\textsuperscript{17}
Figure 43-1  Autopsy specimen from 12-day-old neonate with type I truncus arteriosus. A distinct short pulmonary trunk arises from the left lateral aspect of truncal artery. Right ventricle (RV) has been opened, revealing its thick wall. Ventricular septal defect (VSD) lies immediately beneath truncal valve. Note that defect's lower margin is separated from the tricuspid valve (TV) by a prominent right posterior division of the septal band (trabecula septomarginalis). Infundibular septum is absent. Key: LPA, Left pulmonary artery; RPA, right pulmonary artery; RPD, right posterior division of septal band; TrV, truncal valve.

Figure 43-2  Autopsy specimen from 6-week-old infant with type I truncus arteriosus viewed from opened right ventricle and truncal artery. Truncal valve has three cusps of normal appearance. Orifice of pulmonary trunk arises from truncal artery close to the commissure between right and left cusps of truncal valve. There is lack of continuity between the right posterior division of septal band (trabecula septomarginalis) and ventriculoinfundibular fold, allowing tricuspid–truncal valve fibrous continuity at posteroinferior margin of ventricular septal defect (VSD). Bundle of His therefore lies along this edge of VSD. Key: L, Left cusp of truncal valve; LAD, left anterior division of septal band; PA, pulmonary artery; R, right cusp of truncal valve; RPD, right posterior division of septal band; S, septal band; TV, tricuspid valve; VIF, ventriculoinfundibular fold.

Figure 43-3  Autopsy specimen from a 4-week-old infant with type II truncus arteriosus. Proximal carina between left and right pulmonary arteries is well seen lying flush with posterolateral wall of widely opened truncal artery. Truncal valve (TrV) is quadricuspid with moderately abnormal leaflets, which clinically were considered to be both stenotic and regurgitant. Key: LPA, Left pulmonary artery; RPA, right pulmonary artery.
Chapter 43  Truncus Arteriosus

“Types” under Morphology in Section II of Chapter 48), or there is severe coarctation including tubular hypoplasia of the aortic isthmus and arch (see Fig. 43-4). This arrangement (Van Praagh type A4) was present in 12% of the cases of Van Praagh and colleagues and 14% (28 of 303) of the Toronto surgical series.

Coronary Arteries

Orifices of the coronary arteries have a variable relationship to the sinuses of Valsalva above the truncal cusps (Fig. 43-5). A minority (≈20%) arise centrally (more or less normally) within the sinuses; about 80% (whether the usual two or a single orifice) are at the margin of the sinus or at the upper margin of a commissure. In at least a third of cases, one coronary orifice (usually the left) is displaced cephalad above the sinutubular ridge and must be differentiated from the pulmonary artery orifices at the time of repair. In about two thirds of cases, the left coronary artery arises from the left posterior aspect of the truncal artery, and the right coronary artery from the right anterior aspect in a position similar to normal. Deviations from this pattern occur in the remainder of cases and include a single ostium (found in 18% of hearts reported by de la Cruz and colleagues), closely approximated right and left ostia, and small, slitlike, or stenotic and kinked proximal left coronary artery.

Rarely, a coronary artery may arise from a pulmonary artery rather than the truncal artery; Daskalopoulos and colleagues report the circumflex artery’s origin from the right pulmonary artery in a patient in whom pulmonary artery banding was not tolerated. The proximal part of the left anterior descending coronary artery is frequently displaced to the left of the interventricular sulcus and does not reach it until about halfway down the front of the heart. It tends to be small. Larger-than-normal diagonal branches from the

Ascending Aorta and Ductus Arteriosus

In truncus arteriosus, there is reciprocal development between ascending and transverse aortic arches (arising from fourth aortic arch) and ductus arteriosus (arising from sixth aortic arch). Thus, in the majority of cases the ascending aorta is a direct continuation of the truncus artery and of about the same diameter (see Fig. 43-1), whereas the ductus arteriosus is usually entirely absent. Rarely a ductus is present with a well-developed arch.

By contrast, when the ductus arteriosus is present, the transverse arch is usually absent (interrupted aortic arch) and the ascending aorta is underdeveloped. The ductus is a direct continuation of the truncus artery, arching leftward to join the descending aorta (Fig. 43-4). In this situation, left and right pulmonary artery branches usually arise separately from superior and inferior (leftward and rightward) walls of the truncal artery (type III of Collett and Edwards). The ascending aorta now arises from the superior rightward aspect of the truncus artery as the relatively smaller branch. Usually the transverse aorta is interrupted beyond the origin of the left common carotid artery (type B interrupted aortic arch; see

Figure 43-4  Autopsy specimen from 7-day-old neonate with truncus arteriosus (Van Praagh type 4). A large patent ductus arteriosus is similar in diameter to the descending aorta. There is also severe coarctation of the aorta consisting of a short, nearly atretic segment and a hypoplastic arch between left common carotid (LCC) and left subclavian (LSC) arteries. Truncal artery (opened anteriorly) is wider than usual with this arrangement. Origins of left and right pulmonary arteries (not visible in photograph) are widely separated. Key: AsA, Ascending aorta; Brach, brachiocephalic artery; D, patent ductus arteriosus; Desc Ao, descending aorta; LPA, left pulmonary artery; RPA, right pulmonary artery; Tr, truncal artery.

Figure 43-5  A volume-rendered image from a computed tomography angiogram of a 2-week-old neonate with truncus arteriosus, type II of Collette and Edwards. It shows that left and right branch pulmonary arteries (arrow) arise separately from the truncus arteriosus. Aorta is normal in appearance. Key: Ao, Aorta; LPA, left pulmonary artery; T, truncus.
right coronary artery cross the anterior right ventricle inferior to conal branches, contributing to the blood supply of the upper interventricular septum and occasionally part of the left ventricle. In autopsy material, obvious severe myxomatous thickening of the cusps is present in a third of cases and is much more common in those dying as neonates (Fig. 43-7). Less severe myxomatous changes are present in two thirds of older infants (Fig. 43-8), and microscopic increase in thickness of the distal portions of the cusps is apparent in many more. Rarely stenosis is contributed to right coronary artery cross the anterior right ventricle inferior to conal branches, contributing to the blood supply of the upper interventricular septum and occasionally part of the left ventricle. In autopsy material, obvious severe myxomatous thickening of the cusps is present in a third of cases and is much more common in those dying as neonates (Fig. 43-7). 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by commissural fusion. A redundant truncal valve leaflet may obstruct the pulmonary trunk ostium during ventricular ejection when the ostium is proximally placed.

Ventricular Septal Defect
The VSD is high, anterior, usually large, and juxatruncal in position. It is typically stated that the truncal valve forms its superior margin (see Figs. 43-2 and 43-6). Consistent with this observation is the fact that the infundibular septum is absent in truncus arteriosus, so there is no infundibular structure to form the superior margin of the VSD, leaving the superior margin to be formed by the valve itself. Another way to characterize the VSD is to describe it as U shaped—that is, with no superior margin. This perspective can be best appreciated if one examines a specimen with the truncal valve leaflets opened to the position they occupy during systole. Inferiorly and anteriorly, the VSD is bounded by the two divisions of the septal band (trabecula septomarginalis [TSM]) and posteriorly by the free wall muscle band that separates the semilunar from the tricuspid valve (the ventriculo-infundibular fold) (see Fig. 43-2).

Usually the junction of the right posterior division of the TSM and ventriculo-infundibular fold forms a muscle bridge that separates the defect from the tricuspid valve and right trigone (see Fig. 43-1) and therefore from the bundle of His. Occasionally, this muscle bridge is absent (see Fig. 43-2) or poorly formed (see Fig. 43-8); the lower margin of the defect then approaches the tricuspid anulus, or the VSD becomes juxatruncal in position, in which case the His bundle is at risk of damage during repair. In these hearts, there may be fibrous truncal-tricuspid-mitral valve continuity. Part of the membranous ventricular septum may still be present at the postero-inferior margin of the VSD.

Right Ventricle
The infundibular (conal) septum is absent from the right ventricular outflow tract. Contrariwise, it has been asserted that the infundibular septum can be recognized fused to the distal anterior (free) right ventricular wall; rarely, there is a persistent blind right ventricular outflow pouch in front of it. The right ventricle is nearly always hypotrophied and enlarged.

Left Ventricle
In contrast to the right ventricular outflow tract, the left ventricular outflow tract is relatively normal in hearts with truncus arteriosus (see Fig. 43-6), and flow from this chamber into the truncal artery is restricted only in the unusual situation when the truncal artery originates mainly from the right ventricle and the VSD is small. A pressure gradient demonstrable on catheter withdrawal from left ventricle to aorta in such rare instances will lie at the VSD level rather than at the truncal valve. Although a moderate-sized VSD is not restrictive before surgical repair, it may prove so afterward and thus may need to be enlarged at operation (see Technique of Operation later).

Associated Anomalies
The most common associated cardiac and noncardiac anomalies are shown in Tables 43-2 and 43-3. About 10% to 20% of patients with truncus arteriosus have coexisting interrupted aortic arch or coarctation with patency of the ductus arteriosus. Truncus arteriosus is rarely associated with atrioventricular discordant connection, situs inversus, asplenia or polysplenia, or dextrocardia. Double inlet ventricle is also rare, although mitral stenosis or atresia with left ventricular hypoplasia occurs.

Frequent total absence of the ductus arteriosus has already been mentioned together with association of a widely patent ductus arteriosus in patients in whom there is also aortic arch interruption or, less often, aortic coarctation or atresia. When hearts with aortic arch interruption are excluded, right aortic arch is as common in truncus arteriosus as in tetralogy of Fallot (25%-35%). Anomalous aortic branch origins occur frequently, usually of the subclavian arteries (10%). A persistent left superior vena cava drains to the coronary sinus in about 10% of patients, and occasionally there is partial anomalous pulmonary venous connection. Patent foramen ovale is
### Table 43-2 Associated Congenital Anomalies in Truncus Arteriosus Communis Patients

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>No. of Patients</th>
<th>Percent</th>
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<tbody>
<tr>
<td><strong>Cardiac</strong></td>
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<tr>
<td>VSD</td>
<td>29</td>
<td>100</td>
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<tr>
<td>Truncal valve, regurgitation</td>
<td>15 (9/5)</td>
<td>51.7</td>
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<tr>
<td>Truncal valve, stenosis</td>
<td>8 (6/2)</td>
<td>27.6</td>
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<tr>
<td>(mild/moderate)</td>
<td></td>
<td></td>
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<tr>
<td>Secundum ASD/PFO</td>
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<td>37.9</td>
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<tr>
<td>Right aortic arch</td>
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<td>24.1</td>
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<tr>
<td>Coronary anomalies</td>
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<td>13.8</td>
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<td>Persistent L SVC</td>
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<tr>
<td>IAA:</td>
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<tr>
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<td></td>
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<td>PDA</td>
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<tr>
<td><strong>Noncardiac</strong></td>
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<td></td>
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<tr>
<td>DiGeorge syndrome</td>
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<tr>
<td>Hypocalcemia</td>
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<td>von Willebrand disease</td>
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<td>Anovestibular fistula</td>
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<tr>
<td>Other</td>
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<td>13.8</td>
</tr>
</tbody>
</table>

Adapted from Kalavrouziotis and colleagues.¹¹

^ The two patients with IAA are excluded.

ASD, Atrial septal defect; IAA, interrupted aortic arch; L SVC, left superior vena cava; PDA, patent ductus arteriosus; PFO, patent foramen ovale; VSD, ventricular septal defect.

### Table 43-3 Associated Congenital Cardiovascular Anomalies

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>Patients</th>
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<tbody>
<tr>
<td></td>
<td>Number</td>
</tr>
<tr>
<td><strong>Major</strong></td>
<td></td>
</tr>
<tr>
<td>Truncal stenosis/regurgitation (severe)</td>
<td>7</td>
</tr>
<tr>
<td>IAA</td>
<td>6</td>
</tr>
<tr>
<td>Non-confluent pulmonary arteries</td>
<td>4</td>
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<tr>
<td>TAPVR</td>
<td>1</td>
</tr>
<tr>
<td><strong>Minor</strong></td>
<td></td>
</tr>
<tr>
<td>Secundum ASD/PFO</td>
<td>15</td>
</tr>
<tr>
<td>Other (right aortic arch, coarctation, anomalous systemic-venous connection, DiGeorge syndrome)</td>
<td>13</td>
</tr>
<tr>
<td>Other than three truncal leaflets</td>
<td>15</td>
</tr>
<tr>
<td>Coronary anomaly</td>
<td>6</td>
</tr>
</tbody>
</table>

From Brown and colleagues.¹¹²

Key: ASD, Atrial septal defect; IAA, interrupted aortic arch; PFO, patent foramen ovale; TAPVR, total anomalous pulmonary venous return.

common, and atrial septal defect of moderate or large size is found in about 10% of patients. Mitral valve anomalies of various types are present with similar frequency. Other rare lesions include atroventricular septal defect, double aortic arch, and according to Bharati and colleagues, tricuspid stenosis and (rarely) atresia.

Extracardiac congenital defects are not uncommon and may occasionally contribute to death. DiGeorge syndrome (thymic and parathyroid aplasia or hypoplasia) is known to be associated with truncus arteriosus.²²

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

#### Symptoms

Presenting symptoms are almost always tachypnea, tachycardia, irritability, and unwillingness to take either breast or bottle feedings during the early weeks of life, all manifestations of heart failure.⁴ Rarely, respiratory distress is aggravated by compression of the left upper lobe bronchus between an anteriorly placed left pulmonary artery and the posterior aortic arch.⁵ Even more rarely, an aneurysmal truncal valve associated with interrupted aortic arch may severely compress the right main bronchus and produce total right lung collapse. Mild cyanosis accompanies these symptoms in about one third of cases but rarely is the presenting feature. By contrast, in those infants who survive for longer periods, recurrent respiratory infections, dyspnea, and failure to thrive are usually present, and cyanosis is more apparent secondary to rising pulmonary vascular resistance. Older children may occasionally present with increasing cyanosis (Eisenmenger syndrome) and fail to give a history of heart failure in infancy.

#### Physical Examination

On examination, signs of heart failure are accompanied by a jerky to collapsing arterial pulse produced by rapid runoff from the truncal artery into the pulmonary arteries. The heart is overactive, and a prominent left parasternal systolic ejection murmur and thrill are appreciated. There is frequently an ejection click coinciding with full opening of the truncal valve, and an apical gallop rhythm may be present, although it is surprisingly rare in neonates. An aortic early diastolic murmur (from truncal valve regurgitation) is highly suggestive of truncus arteriosus, particularly when it is accompanied by pulmonary plethora on chest radiograph and right aortic arch. The second heart sound is usually single but split in about one third of cases. A continuous murmur is noted occasionally and is most often due to stenosis at the origin of one or both pulmonary arteries. Important truncal valve stenosis is a confusing feature and usually results in diminished peripheral pulses accompanied by a harsh ejection systolic murmur and thrill, maximal in the right upper intercostal spaces.

#### Chest Radiography

Chest radiography shows marked cardiomegaly as well as plethoric lung fields in neonates and infants. The pulmonary trunk segment is deficient (as in transposition), but a high origin or arching of the left pulmonary artery may be evident in older children as a “comma” sign on the left upper mediastinal border. A solitary right pulmonary artery arising from the left side of the truncus artery may give a similar appearance. The hemithorax may be smaller and vascularity
less on the side of the “absent” branch pulmonary artery (when this lung is supplied by bronchial collaterals or by a relatively small patent ductus arteriosus). In truncus arteriosus with aortic arch interruption, the descending aorta is often prominent in the chest radiograph. In those few infants who survive without treatment, pulmonary plethora subsides, as does cardiomegaly, from increasing pulmonary vascular disease.

**Electrocardiography**

Electrocardiography (ECG) usually shows combined ventricular hypertrophy and a normal or slightly rightward axis, although left ventricular hypertrophy is usually dominant in the tracing (occasionally it is absent). 

**Echocardiography**

Two-dimensional echocardiography can be diagnostic and is usually definitive, with infrequent occurrence of only minor errors. It demonstrates a single vessel overriding the ventricular septum and reveals abnormalities in the truncal valve cusps. In addition, origins of pulmonary arteries can be predicted with some accuracy, and presence of major associated abnormalities, particularly interrupted aortic arch, can be determined.

**Cardiac Catheterization and Angiography**

Cardiac catheterization and angiography may still be performed in the occasional neonate or young infant to define the pulmonary arteries, and hemodynamic state when there is an atypical physiologic presentation, such as severe cyanosis, or when there is suspicion on echocardiography that the pulmonary artery morphology is complex (e.g., unilateral aortopulmonary collaterals). Magnetic resonance imaging (MRI) and computed tomography (CT) compete with traditional angiography when structural details and some physiologic details require definition (see "Computed Tomography Angiography and Magnetic Resonance Imaging" later). There is an absolute indication for catheterization in patients who present after 6 months of life to define the status of the pulmonary microvasculature.

In neonates and young infants with typical physiology, there is left-to-right shunting at the ventricular level with a high pulmonary-to-systemic blood flow ratio (Qp/Qs) and systemic pressures in the right ventricle and pulmonary artery. The high pulmonary blood flow keeps aortic oxygen saturation at 85% or more. Pulmonary vascular resistance is mildly raised (2-4 units · m²). Atypical physiology may occur. Rarely, when the VSD is restrictive and the truncal origin is mainly from the right ventricle, left ventricular pressure may exceed that in the right. When there is truncal valve stenosis, there is a withdrawal gradient across it. The site of stenosis may be difficult to identify preoperatively. Pulmonary artery pressure is often slightly below systemic pressure, but it is importantly reduced when there is stenosis at the origin of one or the other artery.

The progressive rise in pulmonary vascular resistance that occurs in virtually all children who survive infancy is associated with a fall in arterial oxygen saturation. Arterial oxygen saturations less than 80% are usually an indication that pulmonary vascular resistance is beyond the operable range.

Cineangiography with contrast injections into both ventricles and ascending aorta demonstrates the exact site of origin of the pulmonary arteries and differentiates this lesion from patent ductus arteriosus. Special views are required to demonstrate the origin of right and left pulmonary artery branches to assess any proximal stenosis. Should one pulmonary artery fail to outline after routine contrast injections, the origin and distribution of the blood supply to the other lung must be identified. This is usually possible by injections into the upper descending thoracic aorta and its branches, defining either a ductus or large collaterals. In addition, a pulmonary vein wedge injection can be used to retrogradely fill true pulmonary arteries that fill either inadequately or not at all from an aortic injection.

These studies also provide information on alignment of the truncal artery and truncal valve with the two ventricles, truncal valve cusp thickening, and truncal valve stenosis or regurgitation. A bicuspid or quadricuspid valve may show doming in systole without stenosis being present. Site of the VSD is demonstrated, as are the two ventricles.

**Computed Tomography Angiography and Magnetic Resonance Imaging**

CT angiography (CTA) and MRI are not routinely indicated, but these imaging modalities may be indicated in specific circumstances in both neonates and older children. CTA provides excellent spatial resolution (Fig. 43-10). When echocardiography suggests complex pulmonary artery problems such as stenosis or discontinuity, but there is no concern about pulmonary vascular resistance, CTA can...
define the morphologic details, and cardiac catheterization can be avoided (Fig. 43-11). MRI can quantify the regurgitant fraction of an abnormal truncal valve, providing objective data for longitudinal follow-up and decision making (Fig. 43-12).

NATURAL HISTORY

Truncus arteriosus is rare, occurring in 2.8% of cases of congenital heart disease in the cardiac registry report by Calder and colleagues and in 1.7% of the autopsy series of Tandon and colleagues. The natural history of patients with truncus arteriosus is unfavorable. No series follow a cohort of patients from birth, so exact data are not available. However, several studies when taken in aggregate provide an accurate estimate of survival without surgical treatment. Marcelletti and colleagues report on 23 cases prior to the era of intervention. Ten patients presented in the neonatal or infancy period (Table 43-4). Additional reports of autopsy cases by Calder and the Van Praaghes, Collett, Edwards, and colleagues, and Bharati, Lev, and colleagues imply similar mortality to the Marcelletti report. In two reports, the median age of death was 5 weeks, and in another, two thirds were dead before reaching age 6 months. Similar statistics are available from the review of 357 cases by Fontana and Edwards. Bharati and colleagues report a
Figure 43-12  Parasternal long-axis echocardiographic view showing important morphologic characteristics of truncus arteriosus. Small arrows show thickened truncal valve overriding crest of intraventricular septum (s), with the ventricular septal defect evident above septal crest and below truncal valve. Left pulmonary artery (LPA) is seen exiting from left and posterior aspect of common trunk (TR). Large arrows identify arch branches. Coronary arteries are not well visualized in this view. Right pulmonary artery is out of the plane of this view. Key: A Ao, Ascending aorta; ARCH, aortic arch; LA, left atrium; LV, left ventricle; RV, right ventricle.

Table 43-4  Natural History of Truncus Arteriosus for Patients Presenting before Age 1 Year

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex, Age at Diagnosis</th>
<th>Symptoms</th>
<th>Systemic O₂ Sat., %</th>
<th>Systemic Pressure, mm Hg</th>
<th>Rp, U/m²</th>
<th>Associated Defects</th>
<th>Time after 1st Exam</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F, 8 days</td>
<td>HF, C</td>
<td>89</td>
<td>—</td>
<td>*</td>
<td>—</td>
<td>10 days</td>
<td>HF</td>
</tr>
<tr>
<td>2</td>
<td>F, 2 mo</td>
<td>HF</td>
<td>90</td>
<td>85</td>
<td>*</td>
<td>—</td>
<td>Few days</td>
<td>HF</td>
</tr>
<tr>
<td>3</td>
<td>F, 2 mo</td>
<td>HF</td>
<td>—</td>
<td>—</td>
<td>*</td>
<td>—</td>
<td>Few days</td>
<td>HF</td>
</tr>
<tr>
<td>4</td>
<td>F, 3 mo</td>
<td>HF</td>
<td>—</td>
<td>—</td>
<td>*</td>
<td>—</td>
<td>Few days</td>
<td>HF</td>
</tr>
<tr>
<td>5</td>
<td>F, 5 mo</td>
<td>HF</td>
<td>80</td>
<td>80</td>
<td>*</td>
<td>Mild TVR</td>
<td>1 1/2 yr</td>
<td>HF</td>
</tr>
<tr>
<td>6</td>
<td>F, 6 mo</td>
<td>HF</td>
<td>82</td>
<td>84</td>
<td>*</td>
<td>—</td>
<td>8 1/2 yr</td>
<td>HF</td>
</tr>
<tr>
<td>7</td>
<td>F, 6 mo</td>
<td>HF</td>
<td>92</td>
<td>73</td>
<td>1.4</td>
<td>PDA, ASD</td>
<td>2 mo</td>
<td>Ventricular⁷ &amp; tachyarrhythmias</td>
</tr>
<tr>
<td>8</td>
<td>M, 8 mo</td>
<td>HF</td>
<td>90</td>
<td>—</td>
<td>*</td>
<td>—</td>
<td>Few days</td>
<td>HF</td>
</tr>
<tr>
<td>9</td>
<td>F, 1 yr</td>
<td>HF, C</td>
<td>86</td>
<td>80</td>
<td>*</td>
<td>PDA, tricuspid regurg., LPA absent</td>
<td>1 mo</td>
<td>HF</td>
</tr>
<tr>
<td>10</td>
<td>M, 1 yr</td>
<td>Asymp.</td>
<td>91</td>
<td>88</td>
<td>7.0</td>
<td>—</td>
<td>12 yr</td>
<td>ARI</td>
</tr>
</tbody>
</table>

Adapted from Marcelletti and colleagues. M3

*Where no value is given, the pulmonary artery pressure was unknown.

†Autopsy performed at Mayo Clinic; specimen available.

Key: ARI, Acute respiratory infection; ASD, atrial septal defect; Asymp., asymptomatic; C, cyanosis; HF, heart failure; LPA, left pulmonary artery; PDA, patent ductus arteriosus; Rp, pulmonary resistance; Sat., saturation; TVR, truncal valve regurgitation.
mean age of death of 6 months in 177 cases. Other isolated case reports confirm that some subjects, perhaps 10%, survive into adolescence or young adult life, but usually with severe pulmonary vascular disease.

Based on all these reports, about 50% of those born with this condition survive beyond the first month of life, 30% beyond 3 months, 15% beyond 6 months, and 10% beyond 1 year. There is little further mortality beyond this age until pulmonary vascular disease becomes severe and death occurs with Eisenmenger syndrome in about the third decade of life. Death in infancy is invariably due to heart failure, and when it occurs in the neonatal period, severe truncal valve regurgitation and large left-to-right shunt play contributing roles. The situation may be compounded by severe respiratory infection, as in other malformations with large left-to-right shunts in early life.

Longer-term survivors may occasionally succumb from infective endocarditis or cerebral abscess, but most eventually die from consequences of severe pulmonary vascular disease (see “Pulmonary Vascular Disease” under Natural History in Section I of Chapter 35). When pulmonary vascular disease develops during the first year of life or later (and it typically develops more rapidly than in patients with isolated VSD), the patient has a good chance of surviving at least into the teens, as is usually the case with Eisenmenger syndrome. Thus 7 of 10 Mayo Clinic patients with pulmonary vascular resistance greater than 8 units · m⁻² at diagnosis before 1 year of age were alive (without treatment) 1 to 15 years (average 8.3 years) later.

Rather remarkably, a few patients survive infancy and early childhood without developing severe pulmonary vascular disease despite large left-to-right shunts. These patients probably represent less than half of those surviving beyond 1 year of age and less than 5% of all those born with truncus arteriosus.

Survival is adversely affected by severe truncal valve regurgitation, as noted earlier, or by truncal valve stenosis. Even in older patients, truncal valve regurgitation is present in 60% to 70% of cases. Regurgitation may be predominantly into the right ventricle. Survival is also adversely affected by coexisting interrupted aortic arch or coarctation. Survival is also less favorable when there are other associated severe lesions such as left ventricular hypoplasia and a small or atretic mitral valve, complete atrioventricular septal defect, or serious extracardiac anomalies.

Survival is favorably affected by pulmonary stenosis (narrowing at the origins of the pulmonary trunk or right or left pulmonary arteries). Four of the first 28 (14%) truncus patients repaired beyond infancy at the Mayo Clinic had naturally occurring pulmonary artery stenosis.

The TECHNIQUE OF OPERATION

Repair by whatever technique chosen is usually performed during mildly to moderately hypothermic cardiopulmonary bypass (CPB) using a distally placed aortic cannula, one right atrial or two vena caval cannulae, and a left-sided vent placed through the right upper pulmonary vein. Although there is no technical reason to use deep hypothermia with either lowflow CPB or circulatory arrest, some surgeons prefer it. The branch pulmonary arteries are exposed and temporarily occluded with either nontraumatic microvascular clips or snares immediately after CPB is established.

Ideally, myocardial management is accomplished with cold blood cardioplegia using antegrade cardioplegia infused directly into the truncal root (also while the branch pulmonary arteries are occluded). When moderate or severe truncal regurgitation is present, the patient is cooled on CPB to the target temperature (or until ventricular fibrillation occurs spontaneously), the truncal root is clamped and opened, and cardioplegia is delivered directly into the coronary ostia (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3). However, surgeon preference and morphologic findings may dictate other combinations.

Repair with Allograft Aortic or Pulmonary Valved Conduit

Following primary median sternotomy, a piece of pericardium may be taken and laid aside in a moist sponge. The proper-sized allograft aortic or pulmonary valved conduit (10-12 mm for a neonate, 12-14 mm for an infant) is selected, and its processing for insertion is begun (see Appendix 12A in Chapter 12 and Technique of Repair in Section II of Chapter 38).

Left and right pulmonary arteries are dissected in preparation for immediate temporary occlusion at the institution of CPB, as described earlier. The usual purse-string sutures are placed (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2), positioning the one for aortic cannulation as far downstream as possible so that the aortic clamp (placed proximal, or upstream, to the cannula) will be as far distal as possible on the ascending aorta.

Once CPB has been established and the pulmonary arteries controlled, cooling to the target core temperature is accomplished. The aorta is clamped and cardioplegia delivered. Snare on the pulmonary arteries are released, and repair is begun. The pulmonary trunk origin is detached from the truncal artery (Fig. 43-13, A-B); in truncus type II, an appropriate ellipse of truncal wall is included in the excision. The incision for detachment is begun on the left side, typically only several millimeters distal to the sinutubular junction of the truncal valve. The incision is initially made only large enough so that the interior of the truncal artery and valve, ostia of the coronary arteries, and orifices of right and left pulmonary arteries can be directly visualized. High origin of the left coronary artery should be distinguished from a pulmonary artery orifice. Detachment is then completed while viewing all these structures from within. The resulting orifice in the truncal root is closed with two rows of continuous 4-0 or 5-0 polypropylene sutures, using the second row to bring adventitia over the first row. This is done carefully to avoid distorting the coronary arteries or the truncal valve; a patch is often used for closure if direct repair risks distortion.

Alternatively, in some cases of truncus type I, the main pulmonary trunk may have enough length before it bifurcates into the two pulmonary branches such that it can be controlled directly rather than controlling the two branch pulmonary arteries individually. When this is possible, a vascular clamp can be placed across the base of the pulmonary trunk flush against the truncal root immediately upon the institution of CPB. When this is possible, the pulmonary trunk can then be separated from the truncal root, and the truncal root sutured at the clamp while the core cooling is taking place.
place prior to aortic clamping and cardioplegia. Thus, the subsequent period of aortic clamping can be substantially shortened.

When the pulmonary trunk or separately arising (but closely related) left and right pulmonary arteries arise from the posterior aspect of the truncal artery, they are excised as part of a large button of truncal wall. The opening into the truncus is closed with a patch. The distal end of the allograft valve cylinder is then anastomosed to the large button. Similarly, when widely separated right and left pulmonary arteries come off the lateral truncal walls at the same level above the truncal valve, they are excised along with a strip of posterior truncal wall or with the entire circumference of that part of the truncal artery. Excised origins of the pulmonary arteries and adjacent aortic wall are converted into a tube, to which the distal end of the allograft valve cylinder is anastomosed.\textsuperscript{[50,51]} The transected truncal root is reconstituted by end-to-end anastomosis.

Complete mobilization of the distal portion of the ascending aorta, arch, and brachiocephalic arteries should nearly always

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure43-13.png}
\caption{Repair of truncus arteriosus I, II with allograft valve cylinder. A, After establishing cardiopulmonary bypass and clamping the aorta, pulmonary arteries are temporarily occluded while cardioplegic solution is infused, and incision for separation of pulmonary trunk from truncus artery is begun. After looking through the incision and determining the precise origin of coronary and pulmonary arteries, excision of pulmonary trunk is completed. Dashed line represents proposed vertical right ventriculotomy. B, Pulmonary trunk has been cut away from truncal artery, and suture line in the latter is near completion. Distal end of pulmonary trunk is prepared for conduit. Longitudinal ventriculotomy has been made. Ventricular septal defect (VSD) illustrated is typical, with a band of muscle (see Fig. 43-1) separating it from tricuspid anulus. C, VSD is closed by suturing patch to edges of VSD, the atrioventricular node and bundle of His being away from this edge. Key: IVC, inferior vena cava; LPA, left pulmonary artery; RPA, right pulmonary artery; RV, right ventricle; SVC, superior vena cava.}
\end{figure}
allow direct anastomosis. The alternative of interposing a short segment of polyester graft is undesirable.

When widely spaced left and right pulmonary arteries arise from the lateral truncal wall at different levels above the truncal valve, pulmonary arteries are removed separately from the truncal root, each with a segment of surrounding truncal tissue. The branch pulmonary arteries are sewn together behind the truncal root to create continuity, using the extra truncal tissue to create a short tunnel that will be used to accept the distal aspect of the right ventricle to pulmonary conduit. The two separate defects in the truncal root are repaired with patches. A longitudinal right ventriculotomy is made just proximal to the truncal valve, essentially parallel to and to the right of the left anterior coronary artery; stay sutures may be placed for exposure. Alternatively, the opening may be enlarged to an oval shape by excising muscle from the anterior wall, leaving adequate tissue along the right and left sides so that neither the left anterior descending nor right coronary arteries will be compromised during subsequent suturing.

The VSD is repaired through the right ventriculotomy as described for tetralogy of Fallot (see “Repair of Uncomplicated Tetralogy of Fallot with Pulmonary Stenosis via Right Ventricle” under Technique of Operation in Section I of Chapter 38). However, in most cases of truncus arteriosus, there is a rim of muscle between the VSD and tricuspid anulus (ventriculoinfundibular fold; see Morphology earlier); this facilitates repair of the VSD, because sutures may be placed in this muscular rim postero-inferiorly without producing heart block or tethering the septal leaflet of the tricuspid valve (Fig. 43-13, C). If the VSD extends far posteriorly and is juxtratricuspid as well as juxtatruncal, the appropriate suture technique must be used (away from the rim of the VSD) (see Technique of Operation in Section I of Chapters 35 and 38). As in repair of tetralogy of Fallot with pulmonary atresia (see Section II of Chapter 38), the superior sutures may pass into the anterior right ventricular wall where it forms the distal margin of the circular VSD opening. If the lower margin of the VSD lies so close to the truncal valve that the left ventricular outflow tract would be narrowed following patch closure, the VSD is enlarged by excising a wedge of muscle from its anteroinferior margin. The defect is then closed with a polyester, PTFE, or pericardial patch in a manner similar to that used in repair of double-outlet right ventricle (see Fig. 53-13 in Chapter 53).
While the heart is still under cardioplegic arrest, the atrial septum is addressed if necessary. In most circumstances when a valved right ventricular outflow tract conduit is used, both secundum atrial septal defects and patent foramen ovales should be closed. If two caval cannulae are used for CPB, the cavae are snared at this point. If a single right atrial cannula is used, it is positioned into the inferior vena cava at this point. A right atriotomy is made. In the case of a single right atrial cannula, a cardiotomy suction device is positioned into the superior vena cava orifice. The atrial defect is then closed either primarily or with an autologous pericardial patch, as appropriate, using a continuous 5-0 or 6-0 polypropylene suture. The atriotomy incision is then closed.

Before placing the right ventricular outflow tract conduit, the aortic clamp is removed and core rewarming started. The allograft valve cylinder is then trimmed to an appropriate length. A conduit that is too long tends to kink the pulmonary trunk bifurcation or the back wall of the conduit itself. Either an aortic or pulmonary allograft valved conduit can be used; however, pulmonary is preferred in those requiring augmentation of the native pulmonary trunk bifurcation or stenotic pulmonary artery orifice.  

If there is narrowing at the origins of the right or left pulmonary artery, the offending artery is opened longitudinally across the stenosis, and a tongue of allograft is left on the distal end of the conduit, widening this point. The distal conduit–to–pulmonary artery end-to-end anastomosis is constructed with continuous 6-0 or 7-0 polypropylene. The proximal end of the conduit may be anastomosed directly to the right ventriculotomy (Fig. 43-13, D). The posterior portion of the conduit suture line may also pick up adjacent edges of the VSD patch and right ventricular wall. A hood of pericardial or allograft arterial wall patch is usually needed to complete the anterior portion of the proximal attachment of the allograft to the ventriculotomy (Fig. 43-13, E). To avoid conduit valve compression or distortion and valvar regurgitation, the valve should be placed distal to its usual anatomic position, away from the back of the closed sternum. As this anastomosis is being made, rewarming is accomplished, and the remainder of the operation is completed in the usual manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

In neonates with typical preoperative physiology and in whom a post-CPB transesophageal echocardiogram shows normal left ventricular and right ventricular function, a right atrial volume and pressure monitoring polyvinyl catheter should be placed if one has not been placed preoperatively by the anesthesiology team. Pulmonary artery and left atrial catheters are not needed.

In older patients in whom pulmonary hypertensive episodes can be expected with a high likelihood, in patients with atypical preoperative physiology, and in those with reduced ventricular function by echocardiography post-CPB, a very important step is placing fine polyvinyl catheters in the left atrium, right atrium, and pulmonary artery by way of the right ventricle so that postoperative care may be rational, with particular regard for paroxysmal pulmonary hypertensive crisis. As for other repairs using right ventricular–to–pulmonary artery conduits, conduit reoperation may be expected in the future. Therefore, some form of pericardial closure should be considered, usually using PTFE pericardial membrane to protect the anteriorly placed conduit from injury during resternotomy.

Repair of Truncus I, II with Autologous Tissue for Right Ventricular Outflow Tract

Preliminary steps in the operation are the same as those already described, and mildly or moderately hypothermic CPB is established in a similar fashion. The snares previously placed around left and right pulmonary arteries are snugged down, cooling of the patient is begun, the aorta is clamped and cold cardioplegia given, the left side of the heart is vented via the right upper pulmonary vein, and the snares are removed.

A longitudinal incision is made into the anterosuperior aspect of the left pulmonary artery and extended inferiorly into the truncal root toward the left sinus of Valsalva (Fig. 43-14, A). The interior of the truncal root is inspected through the incision, and orifices of left and right pulmonary arteries, coronary ostia (particularly that of the left coronary artery), and truncal valve cusps are identified. A woven polyester, PTFE, or pericardial patch (with or without immersion in glutaraldehyde) is then sewn into place to partition the truncal root into aortic and pulmonary trunks (Fig. 43-14, B).

A vertical incision is made into the right ventricle, extending it nearly to the truncal wall over the left-sided sinus of Valsalva. The VSD is repaired. The posterior wall of the right ventricular–pulmonary trunk pathway is created by suturing the inferior flap of the initial left pulmonary artery/trunkal root incision to the superior aspect of the right ventricular borders of the ventriculotomy (Fig. 43-14, C). The anterior wall is created by suturing into place a patch of autologous or bovine pericardium or synthetic material (Fig. 43-14, D). Barbero-Marical, the innovator of this method, uses a bovine pericardial patch, to the undersurface of which has been attached a bovine pericardial monocuspid valve. The remainder of operation is completed in the usual manner.

When the pulmonary trunk or separate but closely related left and right pulmonary arteries arise from the posterior aspect of the truncal artery, excision is as described in the previous section. A modification of the technique may then be necessary because of the distance between the opening into the pulmonary arteries and right ventriculotomy. In this modification, the left atrial appendage is interposed to create the posterior wall of the right ventricular–pulmonary arterial pathway (Fig. 43-15).

Repair of Truncus with Single Branch Pulmonary Artery Arising from Truncal Root

Morphology of this lesion is highly variable, and experience with each type is limited. If the lung that does not have an arterial connection to the truncal root is supplied by a true branch pulmonary artery connected to a ductus arteriosus, single-stage neonatal repair is recommended. The technique of creating pulmonary artery continuity is similar to that described previously for widely separated branch pulmonary arteries that arise at different levels above the truncal valve. Care must be taken to eliminate the ductal tissue from the anastomosis.

If the lung that does not have an arterial connection to the truncal root is supplied by aortopulmonary collaterals, several options are available. If the collaterals are few and
At a second-stage procedure through a median sternotomy—which can be performed days to weeks later—vascular continuity of the two lungs is created and intracardiac repair performed. After taking down the previously created shunt and removing the pulmonary artery from the truncal root, the right and left pulmonary arteries are made confluent with each other behind the truncal artery, either by direct anastomosis or with interposition of an autologous pericardial tube. After the VSD has been repaired, a valved conduit is interposed between the confluent pulmonary and right ventriculotomy.

Figure 43-14  Repair of truncus arteriosus I, II with autologous tissue (Barbero-Marcial and colleagues). A, Incision is made into pulmonary trunk and adjacent portion of truncal artery. Proposed right ventriculotomy (dashed line) begins just beneath left side of sinuses of Valsalva and extends downward and slightly leftward, avoiding (inasmuch as possible) large diagonal branches of right coronary artery. Usually the incision opens widely after stay sutures are placed, but if it does not, some free right ventricular wall may be excised. B, Patch is placed to separate completely neoaorta from neopulmonary trunk. Illustration shows that the patch is placed clearly on the pulmonary trunk side of cusps of neoaortic valve and coronary ostia (i.e., anteriorly). After separating neopulmonary artery from truncus (now neoaorta) the ventricular septal defect (VSD) is closed with a patch. C, Inferior aspect of original “truncal” incision is attached to upper portion of right ventriculotomy using fine polypropylene suture. D, A roof is placed on the opening with essentially the same technique and materials used for inserting a transanular patch in repair of tetralogy of Fallot (see “Decision and Technique for Transanular Patching” under Technique of Operation in Section I of Chapter 38). Note: Barbero-Marcial places a monocusp valve in the outflow patch that closes against the posterior suture line between pulmonary trunk and right ventricle.

large, unifocalization and complete repair in one stage is preferred. The technique of unifocalization is similar to that described for single-stage unifocalization using a median sternotomy (see Chapter 38). The unifocalized lung arterial supply is then made continuous with the “normal” pulmonary artery from the opposite lung, and intracardiac repair is accomplished. If the collaterals are multiple and complex, an initial thoracotomy is performed to unifocalize the arterial supply and create a vascular hilar confluence in the affected lung. The unifocalized vessel is then connected to a systemic-to-pulmonary artery shunt.
Repair of Truncus Arteriosus with Interrupted Arch

One-stage repair from the anterior approach is the preferred procedure.\cite{33,57,33,55,31,53,55} We recommend using extracorporeal circulatory management without circulatory arrest. After standard exposure through a median sternotomy, the thymus gland is subtotally resected and the pericardium opened. The great vessels are dissected above the brachiocephalic vein into the base of the neck, providing full exposure of the brachiocephalic artery. A purse-string suture is placed in the midportion of the brachiocephalic artery in preparation for arterial cannulation (Fig. 43-16, A-B). Purse-string sutures are placed in the superior and inferior venae cavae for venous cannulation and in the right upper pulmonary vein in preparation for left-sided venting. Depending on patient size, either a 6F or 8F arterial cannula is used to perfuse the systemic circulation through the brachiocephalic artery. Bivacal cannulation with appropriately sized right-angled venous cannulae is also performed.

Once CPB is initiated, the two branch pulmonary arteries are temporarily occluded with either snares or vascular clamps, allowing perfusion of the lower body through the ductus arteriosus. After a core body temperature of 25°C is achieved, the ductus arteriosus is ligated and divided just distal to the left branch pulmonary artery origin, and perfusion flow is reduced to 30 to 40 mL · kg⁻¹ · min⁻¹, effectively establishing antegrade selective cerebral perfusion. The aorta is clamped and cardioplegia introduced into the aortic root. Cavai snares are tightened to provide occlusive venous return, and a vent is placed through the right upper pulmonary vein purse string, across the mitral valve, and into the left ventricle.

The distal ductus arteriosus and proximal descending aorta are dissected to the second set of intercostal vessels, and a curved vascular clamp is placed on the descending aorta to prevent backbleeding. All ductal tissue is resected from the descending aorta. The aortic clamp is then adjusted by moving it superiorly to allow arterial perfusion to the brachiocephalic and left carotid arteries while leaving the ascending aorta available for aortic arch reconstruction. This is achieved by placing the aortic clamp in a slightly oblique position as shown in Fig. 43-16, C.

Arch reconstruction as shown in Fig. 43-16, C and D is performed, using the left subclavian artery to establish arch continuity. The pulmonary trunk confluence is removed from the side of the common trunk in standard fashion. The ascending aorta is then incised from the opening in the truncal root that resulted from removing the pulmonary arteries, up to the arch. The ascending aorta, arch, and proximal descending aorta are augmented with a patch similar in length and shape to the patch used in stage-one reconstruction for patients with hypoplastic left heart physiology (see Chapter 49).

Alternatively, a direct descending-to-ascending aortic anastomosis can be performed. In this case, an appropriately sized incision is made in the left posterolateral aspect of the ascending aorta to accommodate the diameter of the descending aorta. A primary end-to-side anastomosis of the descending aorta to the ascending aorta is done (Fig. 43-16, F) using a nonabsorbable monofilament suture.

Once the arch repair is completed, the aortic clamp is repositioned at the mid–ascending aorta, reestablishing total body perfusion, and perfusion flow rate is increased appropriately. Additional doses of cardioplegia are given through the aortic root as appropriate every 20 to 25 minutes.

The cardiac portion of the repair is performed in standard fashion through a right ventriculotomy infundibular incision, with patch closure of the VSD, assessment of the atrial septum with maintenance of a competent foramen ovale, and placement of a right ventricle–to–pulmonary trunk valved allograft conduit (Fig. 43-16, E). Rewarming and separation from CPB are performed in standard fashion (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

An alternative approach is to use hypothermic circulatory arrest. The aortic cannula is placed distally into the ascending aorta, and a single venous cannula is placed into the right atrium at its junction with the inferior vena cava. Two periods of hypothermic circulatory arrest are used: to reconstruct the aortic arch and again to close the VSD (although the second period of arrest is not uniformly necessary).

Using either technique just described, it is imperative to achieve adequate resection of ductal tissue so that later anastomotic stenosis in the arch does not occur. When primary descending-to-ascending aortic anastomosis is used, the connection is made as distally on the arch as possible to prevent compression of the left bronchus.
Figure 43-16  Repair of truncus arteriosus with interrupted aortic arch. A, The malformation characteristically has a vertically oriented ascending aorta originating from a broad truncus. Proposed incisions to isolate the pulmonary artery branches and bifurcation are indicated by dashed line. Incision to open ascending aorta is indicated by dot-dashed line. B, Two venous cannulae are positioned, and arterial return is via brachiocephalic artery, which has been fully mobilized to accommodate anticipated leftward displacement of ascending aorta. Pulmonary artery branches are temporarily occluded while delivering cold cardioplegia. C, Diminutive aortic arch and descending aorta are thoroughly mobilized and all ductal tissue resected (see Technique of Operation in Section II of Chapter 48). Transection of left subclavian artery enhances mobilizing the ascending aorta, which has been opened in preparation for augmentation. Augmentation is by a segment of cryopreserved pulmonary allograft fashioned by confluence of donor pulmonary trunk and left pulmonary artery (LPA) to produce a curvilinear gusset, and amplified by spatulation of proximal left subclavian artery. Key: LAA, Left atrial appendage; SVC, superior vena cava.
Figure 43-16, cont’d  D, Descending aorta has been attached to ascending aorta and neoaorta augmented by the allograft gusset.  
E, Operation is completed as usual for truncus arteriosus by closing ventricular septal defect through a right ventriculotomy and connecting the isolated pulmonary trunk to the right ventricle using a valved allograft conduit.  
F, Alternative traditional repair. Ascending and descending aortae are fully mobilized. All ductal tissue is resected. Pulmonary trunk is isolated from truncus arteriosus and the latter closed with a small patch. Descending aorta is anastomosed directly to low ascending aorta. After closure of ventricular septal defect, right ventricle is connected to pulmonary trunk with a valved conduit.
If bronchial compression is still of concern, alternative arch reconstructive techniques, such as that shown in Fig. 43-16, A to E or the technique described by McKay and colleagues, can be used. The McKay technique involves placing the distal aortic segment beneath (posterior to) the pulmonary arteries and anastomosing it to the defect left in the truncal artery by excision of the pulmonary trunk. The ascending aortic valved allograft from the right ventricle to pulmonary trunk is placed anterior to the reconstructed aortic pathway.

Other techniques are described for bringing the pulmonary arteries anterior to the aorta. It has also been reported that success has been achieved by leaving the duc tus arteriosus open to serve as a permanent pathway to the descending aorta and performing the usual operation for truncus arteriosus. However, in most patients who are under consideration for surgery in the neonatal period, the ductus is not a reliable long-term pathway, because it will narrow and close.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Neonates and infants who have undergone repair of truncus arteriosus require the same standard intensive care required for all patients undergoing complex cardiac repair. If repair is undertaken after 12 weeks of age, a right ventricular or pulmonary artery pressure catheter is required because these patients are particularly susceptible to pulmonary hypertensive crises, the prevention and management of which are described under “General Care of Neonates and Infants” in Section IV of Chapter 5.

RESULTS

Survival

Early (Hospital) Death

Non–risk-adjusted hospital mortality of 17% (CL 12%-24%) was reported by Hanley and colleagues in 63 neonates and infants operated on between 1986 and 1991. Patients included those with interrupted aortic arch, severe coronary anomalies, and severe truncal valve regurgitation. In patients without these risk factors, there was no early mortality. Similarly, hospital mortality of 11% (CL 7%-17%) was reported in 46 neonates and infants operated on during the same period by Bove and colleagues. Kalavrouziotis and colleagues reported a 3.4% early mortality in 29 patients operated on between 1992 and 2005, and Thompson and colleagues reported a 5% mortality in 65 consecutive neonates operated on between 1992 and 1999. These studies are representative of what can be accomplished in the current era in institutions properly experienced to perform this type of surgery in neonates and young infants.

With the exception of the 1984 study by Ebert and colleagues that reported a mortality of 11%, most earlier studies reported much higher early mortality. No deaths (0%; CL 0%-24%) were reported by Sano and colleagues among 7 neonates and infants undergoing repair of truncus arteriosus and interrupted aortic arch, and Tlaskal and colleagues reported 1 death (12%) in 8 patients. In marked contrast to these single-institution studies, the multinstitutional Congenital Heart Surgeons Society report of 50 patients with truncus arteriosus with interrupted aortic arch operated on from 1987 to 1997 showed an early mortality of about 50%.

Incremental Risk Factors for Premature Death after Repair

Hanley and colleagues performed a multivariable analysis of 63 patients; interrupted aortic arch, severe truncal valve regurgitation, severe coronary artery abnormalities, and age older than 100 days at operation were identified as risk factors for early death. The multivariable analysis by Brown and colleagues indicated that earlier year of operation and coexisting interrupted aortic arch were risk factors. More recent studies, not surprisingly, suggest that morphologic factors such as interrupted aortic arch and truncal valve regurgitation may no longer be risk factors. Thompson and colleagues, however, show that some of these previously identified risk factors continue to be of clinical concern but fall just short of reaching statistical significance as risk factors (Table 43-5). Other variables have not been clearly identified as risk factors, but they have not been rigorously studied. They are discussed briefly in the text that follows.
Table 43-5  Results of Cox Regression Analysis for Factors Associated with Poorer Survival Over Time

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>Odds Ratioa,b</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic Variables</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≤1 week</td>
<td>4.2 (0.7-15)</td>
<td>.12</td>
</tr>
<tr>
<td>Weight ≤2.5 kg</td>
<td>10.2 (1.7-61)</td>
<td>.01</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.0 (0.2-6.2)</td>
<td>.98</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Associated Anomalies</th>
<th>Odds Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate or severe truncal valve regurgitation</td>
<td>4.6 (0.8-27)</td>
<td>.09</td>
</tr>
<tr>
<td>Interruption of aortic arch</td>
<td>5.2 (0.9-31)</td>
<td>.07</td>
</tr>
<tr>
<td>Coronary artery anomalies</td>
<td>1.0 (0.1-8.0)</td>
<td>.99</td>
</tr>
<tr>
<td>Nonconfluent pulmonary arteries</td>
<td>0.1 (0.0-8300)</td>
<td>.72</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Surgical Variables</th>
<th>Odds Ratio</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of cardiopulmonary bypass</td>
<td>0.98 (0.96-1.0)</td>
<td>.16</td>
</tr>
<tr>
<td>Duration of cardioplegic arrest</td>
<td>0.99 (0.96-1.0)</td>
<td>.13</td>
</tr>
<tr>
<td>Truncal valve procedure (repair or replacement)</td>
<td>4.4 (0.9-22)</td>
<td>.07</td>
</tr>
<tr>
<td>Truncal valve replacement</td>
<td>11.0 (1.8-66)</td>
<td>.009</td>
</tr>
</tbody>
</table>

From Thompson and colleagues.74

*Numbers in parentheses are 95% confidence intervals.

*An odds ratio >1 indicates shorter freedom from reintervention.

*Repair of interrupted aortic arch is not listed, because all patients with an interrupted arch underwent concurrent repair, and the odds ratio and P value were identical.

Age at Repair
Young age has been neutralized in institutions properly prepared for neonatal cardiac surgery, where risk after neonatal repair has been reduced to about 10%,87,144 In fact, many recent series involve only neonates.74 Older age at may be a risk factor for premature death after repair, both early and late. However, age is probably a surrogate for severity of pulmonary vascular disease144 (see later).

Low Birth Weight
Low birth weight has been identified as a risk factor for early death in two single-institution studies, one of 65 consecutive neonatal repairs and the other of 61 patients younger than 6 months of age at repair.13,74

Type of Truncus Arteriosus
Types I and II truncus arteriosus are so similar that no difference in risk of death after operation has been identified.56 Relatively few patients with truncus arteriosus type III have undergone repair, but increased complexity of operation is expected to increase risk of death to some extent.

Size of Ventricular Septal Defect
Closure of relatively small VSDs may result in some degree of left ventricular outflow obstruction; surgical enlargement of such defects risks interference with septal coronary arteries. Thus, small size of the VSD may be a risk factor.

Predominance of Origin of the Truncal Artery
The more the truncal artery lies over the right ventricle, the greater the probability that VSD closure will narrow the left ventricular outflow tract (particularly when the VSD is small and has not been surgically enlarged), potentially increasing the risk of death early after operation. Possibly this risk factor and that of small VSD size can be neutralized by appropriate VSD enlargement and proper contouring of the VSD patch.

Small Size of Right and Left Pulmonary Arteries
Small branch pulmonary arteries may present risk, especially if proximal obstruction is not addressed at surgical reconstruction.

Truncal Valve Abnormalities
Narrowing of the truncal valve may be difficult to identify and evaluate because flow through it, comprising both systemic and pulmonary flow, is large. Preoperative evaluation typically indicates obstruction across the truncal valve because of the high flow; however, true stenosis is rare and has not been specifically identified as a risk factor. Severe truncal valve regurgitation itself is a well-identified risk factor for death after repair.82,36 This is probably related to both its unfavorable effect postoperatively and its interference with myocardial management intraoperatively.35 Treatment of truncal valve regurgitation, either by valvuloplasty or by using an allograft valve conduit placed by the “mini” root-replacement technique (see “Allograft Aortic Valve Cylinder” under Technique of Operation in Chapter 12) is the most important modification of the operation for neutralizing incremental risk of truncal regurgitation (see Appendix 6C in Chapter 6).87

Truncus with Only One Branch Pulmonary Artery Connected to the Truncal Root
Neonates and infants undergoing repair of truncus with only one branch pulmonary artery connected to the truncal root undergo a complex single- or two-stage operation, increasing risk. Nonetheless, repair has been accomplished in 10 infants by Mee, with a 20% (CL 7%-41%) hospital mortality and no post-discharge deaths in a follow-up of nearly 5 years.88

In patients who do not undergo repair during the first 6 months of life, pulmonary vascular disease develops rapidly in the lung supplied from the truncus arteriosus, increasing both early and late risks of repair.541

Major Associated Cardiac Anomalies
Major associated cardiac anomalies increase overall risks. Repair of truncus arteriosus and interrupted arch has been associated with risk of early death in up to 50% of patients58,314 but more recent studies bring this association into question.13

Pulmonary Vascular Disease
Irreversible pulmonary vascular disease is rarely an issue when repair is performed during the first 3 months of life. The likelihood of postoperative pulmonary hypertensive episodes, however, increases in infants who are repaired after the first 3 weeks of age.144 These episodes are a manifestation of a damaged pulmonary vasculature, but the vasculature can remodel and become normal when hemodynamics are normalized with early repair. Progressive damage to the pulmonary vasculature may play an important role in the increased risk of death observed in patients operated on later than 3 months of age.144
Progressing Truncal Valve Regurgitation

Rajasinghe and colleagues show that pre-repair truncal valve regurgitation portends only a 20% freedom from eventual truncal valve replacement, and also that a few valves with no pre-repair truncal regurgitation will have to be replaced (Fig. 43-18).\textsuperscript{M4,R1} Henaine and colleagues showed the same associations.\textsuperscript{H7} Most patients have mild regurgitation 1 to 2 years after repair, and occasionally moderate regurgitation is observed at that time. Mortality for truncal valve replacement can be high when performed in children early after initial truncus repair, but mortality for late truncal valve replacement is low.\textsuperscript{M4}

Conduit Replacement

Conduit replacement or revision is almost inevitable (Fig. 43-19). Mean time to conduit replacement was 5.5 years in the study by Rajasinghe and colleagues.\textsuperscript{R1} The only factor associated with shorter time to replacement is smaller conduit size at initial repair.\textsuperscript{C3,R1} Type of conduit (aortic allograft, pulmonary allograft, or xenograft) does not seem to affect the interval between initial repair and need for reoperation.\textsuperscript{C3,R1} Avoidance of a conduit and use of the direct right ventricle-pulmonary artery connection at the initial operation may reduce the need for reoperation on the right ventricular outflow tract,\textsuperscript{C3} but the need for catheter-based intervention for obstruction is higher using the direct connection. Thus, the requirement for intervention of any kind (surgical and catheter-based combined) is the same for both conduit and direct connection techniques.\textsuperscript{C3} In the series by Honjo and colleagues, freedom from intervention for right ventricular outflow tract obstruction was only 50% at 5 years.\textsuperscript{H10} The jugular venous valved conduit has been evaluated in a prospective multicentered study and appears to be equivalent to allograft conduits in most respects.\textsuperscript{H9} Time to conduit replacement was similar, and both right ventricular outflow tract gradient and valve regurgitation showed similar progression in the two conduit types. Progression of stenosis after catheter intervention for stenosis was significantly slower in the jugular vein conduit.

INDICATIONS FOR OPERATION

Diagnosis of truncus arteriosus is an indication for repair. Because about 50% of surgically untreated patients die during the first month of life, repair should be recommended as early as possible, rather than deferring it to some predetermined age.\textsuperscript{A7,B6,B7,S12} This is true whether or not important cardiac anomalies coexist. In children older than 6 months at presentation, operation may be complicated, or even contraindicated, by presence of important elevation of pulmonary vascular resistance. Cardiac catheterization with assessment of pulmonary vascular resistance will determine operability. Criteria for inoperability are the same as for patients with VSD (see Indications for Operation in Section I of Chapter 35).

SPECIAL SITUATIONS AND CONTROVERSIES

Importance of a Valve in Repair

An unsettled matter is the importance of a right ventricular outflow valve. Several groups have reported success with use of valveless conduits.\textsuperscript{B5,B7,S10} Although there are no randomized trials comparing the valveless direct connection technique and the valved conduit technique, two studies that use both techniques retrospectively evaluated outcomes.\textsuperscript{C3,D1} Fewer total reinterventions were needed in the direct connection patients in one study\textsuperscript{D1} but not in the other.\textsuperscript{C3} Early mortality did not differ in one study.\textsuperscript{C3} In the other,\textsuperscript{D1} it was significantly higher in the direct connection group (22% vs. 8%) by univariable analysis; however, multivariable analysis did not confirm the univariable finding. The study authors believe that the validity of the multivariable analysis may be questionable because of the small number of patients and events. To further confuse matters, biases may exist in these retrospective studies that make inferences difficult. For example, in the study by Danton and colleagues,\textsuperscript{D3} neonates
and young infants (patients not likely to have pulmonary hypertension) predominantly received the valveless direct connection, and older patients (with higher risk for pulmonary hypertension) received valved conduits. These biases may affect timing and prevalence of right ventricular outflow tract reintervention and mortality.

REFERENCES

A

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Aortopulmonary window (APW) is a round, oval, or sometimes spiral opening between the ascending aorta and pulmonary trunk, occurring as a congenital anomaly in hearts with separate aortic and pulmonary valves. This malformation has also been termed aortic septal defect; aortopulmonary fistula, fenestration, or septal defect; and aortopulmonary window, fistula, fenestration, or septal defect.\(^{\text{R1}}\)

**HISTORICAL NOTE**

The first report of an APW was by Elliotson in 1830, and in the American literature by Cotton about 70 years later.\(^{\text{C6,R1}}\)

The first reported correct clinical diagnose are attributed to Dodds and Hoyle in 1949 and to Gasul and colleagues in 1951.\(^{\text{D5,G2}}\)

In 1952, Gross reported successful ligation of an APW using a closed technique.\(^{\text{G1}}\) Scott and Sabiston in 1953 and Fletcher and colleagues in 1954 reported successful division of an APW by a closed technique.\(^{\text{F2,F3}}\) The operation was difficult and hazardous, however.

The advent of open operation with cardiopulmonary bypass (CPB) in 1954 to 1955 made it easier to correct this malformation. Division of the connection between aorta and pulmonary trunk was used in early cases at the Mayo Clinic. In 1957, Cooley and colleagues reported the transaortic approach, but with polyester patch closure.\(^{\text{C9}}\)

In 1958, Gross reported successful ligation of an APW using a vascular clip in an infant weighing 758 g.\(^{\text{K1}}\)

**DEFINITION**

An APW is usually a large defect between the aorta and pulmonary trunk, although in about 10% of patients the defect is small. The pulmonary arteries are normally related to the pulmonary trunk. As the term window implies, there is little or no length to the communication in most patients. It is nearly always a single orifice, although it may be fenestrated.

Several classifications have been proposed to describe the location of the anomalous “window” on the ascending aorta and its relationship to the branch pulmonary arteries. Mori and colleagues proposed the terms proximal, distal, and total to describe the location within the ascending aorta.\(^{\text{M5}}\) Richardson and colleagues used the term type I to describe proximal defects and type II to indicate defects in the distal ascending aorta.\(^{\text{R1}}\) Ho and colleagues added the term intermediate to describe defects with upper and lower edges suitable for percutaneous closure.\(^{\text{H2}}\) Jacobs and colleagues from the Society of Thoracic Surgeons' Congenital Heart Surgery Database Committee recommended the terms type I–proximal defect, type II–distal defect, type III–total defect, and intermediate defect (Fig. 44-1).

Proximal (type I) APWs are located in the proximal ascending aorta (see Fig. 44-1). The window is in the left lateral wall of the ascending aorta, usually close to the orifice of the left coronary artery, and in the contiguous right wall of the pulmonary trunk inferior to the origin of the right pulmonary artery.\(^{\text{N1}}\) It is not surprising, therefore, that occasionally the right coronary artery, and rarely the left, may be transposed onto the pulmonary trunk close to the edge of the defect.\(^{\text{B4,B7,D6,D7,L2}}\) This must always be considered in the surgical treatment of APW.\(^{\text{K4}}\) When viewed from within the pulmonary trunk, the APW can be confused with the orifice of the right pulmonary artery. The proximal type occurs in about 90% of APW cases.\(^{\text{B6,F3,T4}}\)
APW is accompanied by other cardiac anomalies in about 50% of cases\textsuperscript{53,54}, of which interrupted aortic arch (IAA) (about 90% of which are type A and the rest type B) is the most frequently observed major associated lesion\textsuperscript{54,55} (although this combination is rare among all patients with congenital heart disease). Other major associated lesions include ventricular septal defect (VSD), tetralogy of Fallot, transposition of the great arteries (Vannini V: personal communication, 1980), anomalous origin of a coronary artery, aortic isthmic hypoplasia, and subaortic stenosis\textsuperscript{51,53,54,56,72}

Rarely, there is a complex syndrome of the APW, usually in the downstream portion of the ascending aorta, with aortic origin of the right pulmonary artery, intact ventricular septum, patent ductus arteriosus, and interrupted aortic arch or severe coarctation (Berry syndrome).\textsuperscript{A1,B2,F2,D1,T1} This is a particularly lethal combination; most affected infants die shortly after birth.

From 5% to 10% of patients with the malformation have less severe associated cardiac anomalies such as right aortic arch (7%), ostium secundum atrial septal defects, or patent ductus arteriosus.\textsuperscript{54,56,57,71}

The rarity of IAA with APW is such that among 472 neonatal patients with IAA reported in a Congenital Heart Surgeon’s Society study, 20 (4%) had IAA with APW\textsuperscript{53} (Fig. 44-2).

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

In infants with isolated APW, symptoms and signs of heart failure usually develop early in life, and their presentation is similar to that of infants with a large VSD. These infants are generally small, underdeveloped, and tachypneic, and they tend to have repeated respiratory infections.\textsuperscript{73}

On examination, the left precordium is prominent because of marked cardiomegaly. The second heart sound at the base is usually accentuated. The murmur is usually only systolic and of variable intensity.\textsuperscript{D2,M5,N1} In about 15% of patients, it is continuous because the APW is smaller and pulmonary hypertension less than usual.\textsuperscript{M5,N1} When the left-to-right shunt through the defect is large, there are peripheral signs of rapid aortic runoff (e.g., jerky or collapsing peripheral pulses), but these signs are not evident when heart failure is marked or pulmonary vascular resistance is severely elevated.

Chest radiograph and electrocardiogram (ECG) findings are similar to those of infants and young children with VSD or large patent ductus arteriosus, giving evidence of left and right ventricular enlargement and large pulmonary blood flow.\textsuperscript{B4} Left atrial enlargement (a result of large pulmonary blood flow) is usually prominent.

Differential diagnoses before special study include large patent ductus arteriosus (see Chapter 37), truncus arteriosus (see Chapter 43), and, in patients beyond the infant age group, VSD with aortic regurgitation (see Section II of Chapter 35) and ruptured sinus of Valsalva aneurysm (see Chapter 36).

Since the early 1990s, diagnosis has relied exclusively on two-dimensional (2D) echocardiography.\textsuperscript{M1,P1,S1,T4} Nevertheless, other imaging techniques are useful. Garver and colleagues correlated echocardiography, angiography, and magnetic resonance imaging (MRI) to achieve accurate diagnosis in APW.\textsuperscript{G1} Prior to the advent of 2D echocardiography,
cardiac catheterization and cineangiography were used to provide the definitive diagnosis and identify associated cardiac anomalies. Cardiac catheterization shows blood oxygen saturation in the pulmonary artery is elevated over that in the right ventricle and right atrium in most cases. Occasionally, oxygen saturation in the right ventricle is increased over that in the right atrium, which may suggest VSD or truncus arteriosus until cineangiography shows this to be from pulmonary valve regurgitation associated with APW. Ascending aortic angiography shows rapid filling of the pulmonary trunk through the APW, as well as separate aortic and pulmonary valves. Because location of the APW varies and coronary arteries may arise from the pulmonary trunk, visualization of all anomalies must be accurate.

**NATURAL HISTORY**

APW is a rare malformation, occurring in about 0.2% of cases of congenital heart disease. There is no known tendency for APWs to close spontaneously. The natural history of infants with large APWs is at least as unfavorable as that of infants with persistently large VSD (see Natural History in Section I of Chapter 35). In the absence of surgical correction, mortality in the first year of life has been estimated at 40%. In fact, patients with large APWs are rarely seen in childhood or adult life, and those who survive beyond early life have important pulmonary vascular disease. This natural history is, therefore, similar to that of surgically untreated older patients with large VSD.

**TECHNIQUE OF OPERATION**

Because APW often coexists with other important cardiac anomalies, the basic technique of repair must be modified and adapted to the individual situation. However, every effort should be made to accomplish a one-stage repair. A special combination is APW and anomalous origin of the right pulmonary artery from the ascending aorta, in which the APW may be left open anatomically but functionally closed by connecting it to the orifice of the right pulmonary artery by one of several techniques.

The discussion that follows pertains specifically to isolated APWs. Cardiac catheterization and cineangiography were used to provide the definitive diagnosis and identify associated cardiac anomalies. Cardiac catheterization shows blood oxygen saturation in the pulmonary artery is elevated over that in the right ventricle and right atrium in most cases. Occasionally, oxygen saturation in the right ventricle is increased over that in the right atrium, which may suggest VSD or truncus arteriosus until cineangiography shows this to be from pulmonary valve regurgitation associated with APW. Ascending aortic angiography shows rapid filling of the pulmonary trunk through the APW, as well as separate aortic and pulmonary valves. Because location of the APW varies and coronary arteries may arise from the pulmonary trunk, visualization of all anomalies must be accurate.

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Chapter 44 Aortopulmonary Window

![Figure 44-3](image)

**Figure 44-3** Repair of type I aortopulmonary window (APW). **A,** Operation is performed on cardiopulmonary bypass with aorta occluded. APW is exposed through a transverse aortotomy. It is located just above sinotubular junction. Origin of left coronary artery is identified because it may have a close relationship with inferior margin of APW. **B,** APW is closed with a polyester, polytetrafluoroethylene, or pericardial patch to create a partition between aorta and pulmonary trunk. Left coronary artery is protected from inclusion in suture line.

cannulation site. Care is taken to identify and protect the right pulmonary artery during this dissection and while placing the aortic clamp. A single venous cannula may be used, or the cavae may be cannulated directly. The right atrium is opened and a pump-oxygenator sump sucker placed across the foramen ovale into the left atrium.

As soon as CPB has been initiated and core cooling begun, a side-biting clamp (e.g., small Cooley clamp) is placed across the window from the pulmonary trunk side to occlude the window; alternatively, separate tourniquets may be placed on left and right pulmonary arteries. The aortic occlusion clamp is positioned exactly at the place provided by the prior dissection. Cold cardioplegic solution is injected into the ascending aorta or retrogradely via the coronary sinus (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3).

Repair can be done through either the aorta or pulmonary trunk, and even the older technique of complete division has given good results. However, an initial approach through the aorta is generally recommended to facilitate clear identification of the aortic valve and right and left coronary orifices in relation to the defect. The aorta is opened transversely at the level of the APW (Fig. 44-3, **A**). Both coronary arteries must be identified. If one is anomalously positioned in the pulmonary trunk, the patch for closure of the window must be positioned so that both coronary ostia are on the aortic side of the patch. Small or moderate-sized APWs may be closed by direct suture, using one or two rows of continuous 4-0 polypropylene sutures. A large window is closed with a polyester, polytetrafluoroethylene (PTFE), or pericardial patch sewn into place with continuous 4-0 or 5-0 polypropylene sutures (Fig. 44-3, **B**). The aortotomy incision is then closed with one row of continuous polypropylene sutures. The remainder of the operation, including the de-airing procedure, is carried out as usual (see “De-airing the Heart” in Section III of Chapter 2).
PART VII  Congenital Heart Disease

This technique allows visualization of the left coronary ostium and orifice of the right pulmonary artery and provides a secure partitioning of the ascending aorta from the pulmonary trunk. Unless there is aneurysmal thinning around the window, this technique seems useful.

A modification of this technique is required when the right coronary artery arises from the pulmonary trunk just to the left of the anterior wall of the APW. Then the anterior incision into the window curves to the left into the pulmonary trunk to create a flap of anterior pulmonary trunk wall. The flap should be large enough to cover the entire window. It is sewn into position over the window with a continuous stitch passing through the aortic wall, the patch, and the pulmonary trunk wall. This technique allows visualization of the left coronary ostium and orifice of the right pulmonary artery and provides a secure partitioning of the ascending aorta from the pulmonary trunk. Unless there is aneurysmal thinning around the window, this technique seems useful.

Alternatively, a vertical incision may be made in the anterior wall of the APW itself, more or less transecting its anterior half. After carefully identifying orifices of the right pulmonary artery and left coronary artery, the patch for closure is sutured to the posterior, superior, and inferior walls of the window. The incision into the window is then closed by incorporating the front edge of the patch, with each stitch passing through the aortic wall, the patch, and the pulmonary trunk wall. This technique allows visualization of the left coronary ostium and orifice of the right pulmonary artery and provides a secure partitioning of the ascending aorta from the pulmonary trunk. Unless there is aneurysmal thinning around the window, this technique seems useful.

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polypropylene stitch. Repair is completed by closing the defect in the pulmonary trunk with a pericardial patch. Rarely, the right coronary artery arises from the anterior aspect of the pulmonary trunk at some distance from the APW. In that situation, the right coronary artery can be taken as a button from the pulmonary trunk, mobilized, and reimplanted into the aorta at a site distinct from the APW, which is closed with a separate patch. Similar methods (flap reconstruction or reimplantation) can be used to repair APW with an anomalous origin of the left coronary artery from the posterior wall of the pulmonary trunk.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care is as usual (see Chapter 5). The hemodynamic state is generally excellent because the left ventricle is large, no ventriculotomy has been made, and duration of myocardial ischemia is less than 1 hour. When repair has been performed in a neonate or infant, care appropriate to this age group is used (see Section IV, Chapter 5).

RESULTS

Early (Hospital) Death

Hospital mortality is low after repair of APW unless unusual circumstances are present; no deaths occurred among 18 patients undergoing primary repair at UAB and the University of California at San Francisco (Table 44-1), and one death occurred among 11 infants reported by Tiraboschi and colleagues. Even with coexisting major anomalies or low birth weight, risk of total repair may also be low.

Time-Related Survival

Time-related survival is excellent when the operation is performed in infancy. McElhinney and colleagues followed patients for up to 25 years after operation. Eighteen patients with Richardson type I or II were operated on at age 6 months or less. Eleven were categorized as complex because of operability described for patients with VSD are applicable to those with large APWs (see Indications for Operation in Section I of Chapter 35).

<table>
<thead>
<tr>
<th>Age (Months)</th>
<th>UAB* n</th>
<th>UCSF* n</th>
<th>Hospital Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3</td>
<td>2</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>3–6</td>
<td>6</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>6–12</td>
<td>12</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>12–24</td>
<td>24</td>
<td>1</td>
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</tr>
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<td>48</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>8</td>
<td>0</td>
</tr>
</tbody>
</table>

*1967 to July 1, 1983.

Key: CL, 70% confidence limits; UCSF, University of California at San Francisco.

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### Definition

Anomalous origin of a pulmonary artery from the ascending aorta is a condition in which the right pulmonary artery (RPA) or rarely, the left pulmonary artery (LPA), arises from the ascending aorta in the presence of separate aortic and pulmonary valves and without interposition of ductal tissue. This condition is sometimes referred to as hemitrunicus. Hemitrunicus is also used to describe a subset of truncus arteriosus (see Chapter 43). Rarely, both right and left pulmonary arteries arise from the ascending aorta in the presence of two separate semilunar valves.

Origins of one or both pulmonary arteries from the transverse aortic arch via a ductus arteriosus or collateral arteries and from the descending thoracic aorta via collateral arteries are not discussed; these conditions are most commonly part of tetralogy of Fallot, but they can occur in the presence of other intracardiac defects or even with normal intracardiac morphology (see Chapter 38). When both the RPA and LPA or only one pulmonary artery arise from the ascending aorta with a common semilunar valve, the condition is a subset of truncus arteriosus (see Chapter 43).

### Historical Note

The first description of this entity was by Frantzel, who in 1868 reported the case of a 25-year-old woman dying in heart failure, with the RPA arising from the ascending aorta and an aortopulmonary window. In 1914, Doering reported aortic origin of the RPA in an infant dying at age 8 months whose only associated anomaly was a patent ductus arteriosus. Bopp, in 1949, gave a detailed report of this condition; since then, and with development of cardiac catheterization and angiography, other cases have been reported.

In 1957, Caro and colleagues corrected the malformation by disconnecting the RPA from the ascending aorta and connecting it with an interposition graft to the pulmonary trunk. The patient, a 23-year-old man, died a short time after operation. The first successful repair, which was in a 12-month-old infant, was reported in 1961 by Armer and colleagues. They interposed a graft between the pulmonary trunk and distal end of the divided RPA and closed a coexisting patent ductus arteriosus. In 1967, Kirkpatrick and colleagues reported the first successful cases of retroaortic direct anastomosis of the divided RPA to the pulmonary trunk. The first report of successful surgical treatment of aortic origin of the LPA, in a 6-week-old infant, was by Herbert and colleagues in 1973.

### Morphogenesis and Morphology

#### Morphogenesis

Anomalous origin of the RPA from the ascending aorta is related to development of the aortopulmonary septum by fusion of the right and left conotruncal ridges. As such, this defect has developmental morphogenesis similar to aortopulmonary window (see Chapter 44). Severe unequal partitioning of the aortopulmonary trunk by conotruncal ridges results in more dorsal development of the aorta. In this situation, the right sixth aortic arch originates solely from the ascending aorta and is not related to the pulmonary trunk. The result of severe conotruncal ridge malalignment is anomalous origin of the RPA from the ascending aorta, which has been classified by Richardson and colleagues as aortopulmonary septal defect type III.

#### Morphology

**Anomalous Origin of Right Pulmonary Artery**

The RPA usually arises from the right or posterior aspect of the ascending aorta (Fig. 45-1) in this condition, but occasionally it arises from the leftward posterior aspect. Its origin is usually within 1 to 3 cm of the aortic valve. Uncommonly, it arises from the distal portion of the ascending aorta just proximal to the origin of the brachiocephalic
When the RPA arises anomalously from the ascending aorta and no other anomalies are present, pulmonary vascular beds of the two lungs may be similar despite differences in origin of the pulmonary arteries. Occasionally, pulmonary and tricuspid valves are dilated as a result of right heart failure, and the tricuspid leaflets may be thickened and edges rolled. Origin of the RPA from the ascending aorta is an isolated lesion in about 20% of cases. In the remainder, the most common coexisting lesion is patent ducus arteriosus, present in about 50% of cases.

Other less common associations are with tetralogy of Fallot, ventricular septal defect, aortopulmonary window, coarctation of the aorta, interrupted aortic arch, and atrial septal defect. Severe contralateral (left) pulmonary vein stenosis may coexist. The vein stenoses are typically tubular, with dilatation of the left pulmonary veins proximal to the stenoses. Also, Sievers and colleagues report coexisting subtotal obstruction of the left pulmonary vein orifices by a membrane that was excised at operation.

**Anomalous Origin of Left Pulmonary Artery**

Origin of the LPA from the ascending aorta is rare. It occurs as an isolated lesion in about 40% of cases, usually coexisting with right aortic arch. In contrast to origin of the RPA from the ascending aorta, the most common associated anomaly is tetralogy of Fallot. Then, the aortic arch may be left sided. Tetralogy of Fallot with absent pulmonary valve syndrome is also observed (Fig. 45-2).

**Anomalous Origin of Both Pulmonary Arteries**

Origin of both RPA and LPA from the ascending aorta has been reported in one patient who had no other cardiac anomaly. The origin was by way of a short single trunk coming off the posterior aspect of the ascending aorta, with the pulmonary trunk arising normally from the right ventricle and connected only to a patent ductus arteriosus. Repair was attempted unsuccessfully at age 11 days.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

When the condition is isolated except for a patent ductus arteriosus, the patient characteristically presents early in infancy with respiratory distress and heart failure. Frequently the infant is acutely ill. There may be cyanosis from (1) venous admixture in the lungs or (2) reversed shunting through a patent ductus arteriosus or a patent foramen ovale resulting from right heart failure.

There are no typical auscultatory findings, and murmurs may or may not be present. When present, the murmur is usually systolic and heard along the left sternal border. Rarely, it may be continuous as a result of kinking or stenosis of the artery. The peripheral pulses are jerky or bounding because of rapid runoff from the aorta into the lung and consequent left-to-right shunting. Electrocardiographic findings are not diagnostic and usually indicate biventricular and right atrial enlargement. Cardiomegaly is usually severe on the chest radiograph, with the heart assuming a globular shape. Pulmonary plethora is usually of similar degree bilaterally.

When tetralogy of Fallot is present with severe pulmonary stenosis, clinical features are dominated by the tetralogy. The condition may be suspected, however, because the lung supplied by the anomalously arising artery is usually plethoric, whereas the other lung is oligemic. Since the early 1990s, correct diagnosis and assessment have been adequately made with two-dimensional echocardiography alone, making cardiac catheterization unnecessary.

![Figure 45-1](image1.png) Origin of right pulmonary artery (RPA) from ascending aorta, also referred to as aortopulmonary septal defect type III (see Chapter 44). RPA takes its origin from right lateral aspect of ascending aorta. There is a large blood flow shunt from aorta to RPA.

![Figure 45-2](image2.png) Heart specimen from 1-month-old infant viewed from in front. The left pulmonary artery arises from ascending aorta and crosses in front of the dilated right pulmonary artery that arises normally from the pulmonary trunk. This infant had tetralogy of Fallot with absent pulmonary valve. Key: Ao, Aorta; LAA, left atrial appendage; LPA, left pulmonary artery; LV, left ventricle; RAA, right atrial appendage; RPA, right pulmonary artery; RV, right ventricle; Tr, trachea. (From Calder and colleagues.)
lethal condition. About 70% of surgically untreated patients are dead by age 6 months and 80% by age 1 year (Fig. 45-6). Intractable heart failure is the usual mode of death.

Pulmonary hypertension in the anomalous pulmonary artery is uniformly present, and commonly it is also present in the normally connected pulmonary artery. This finding is supported by Pool and colleagues’ observation that provide additional information. Pressure in the pulmonary artery arising from the aorta is systemic in almost all cases, because ostial stenosis is rare. As already noted, pressure in the pulmonary artery that arises normally is usually also elevated to systemic or suprasystemic levels. Accurate measurement of pulmonary and systemic blood flows is difficult in this situation but not critical, because the infants usually present with clear clinical evidence of increased pulmonary blood flow. Pulmonary vascular resistance in the normally connected lung can be calculated and is a useful guide to operability—and an essential guide in older patients.

Cineangiography is diagnostic, and a right ventriculogram or pulmonary angiogram opacifies only the normally connected pulmonary arteries. Antegrade or retrograde aortography shows the pulmonary artery that arises from the ascending aorta (Fig. 45-4). Cineangiography is also used to define other cardiac anomalies that may be present.

In neonates and infants in whom catheterization is not critical, computed tomography angiography can confirm morphologic details suspected by echocardiography (Fig. 45-5).

**NATURAL HISTORY**

Anomalous origin of a branch pulmonary artery from the ascending aorta is rare, reportedly accounting for 0.12% of all congenital heart defects. Nearly all cases involve the RPA. As of 2004, 136 cases of RPA from the aorta had been reported, and from 2004 to 2010, at least 35 additional cases appeared in the literature. In 2003, Prifti and colleagues reviewed the reported experience with LPA from the aorta and found 77 cases; however, many of these appear to have had LPA origins from the descending thoracic aorta or from a ductus, with a high association with tetralogy of Fallot, and thus likely represent a different lesion. It is a lethal condition. About 70% of surgically untreated patients are dead by age 6 months and 80% by age 1 year (Fig. 45-6). Intractable heart failure is the usual mode of death.

Pulmonary hypertension in the anomalous pulmonary artery is uniformly present, and commonly it is also present in the normally connected pulmonary artery. This finding is supported by Pool and colleagues’ observation that
pulmonary hypertension develops in 19% of infants born with unilateral absence of a pulmonary artery and no associated malformations, and that ligation of one pulmonary artery within 24 hours of birth in five calves resulted in severe pulmonary hypertension in the opposite lung within 2 months. Surprisingly, Keane and colleagues report no important obstructive vascular changes in either lung in most patients dying in the first 6 months of life. This does not mean that pulmonary hypertension was not present, just that pathologic changes were not evident.

Among older patients, pathologic evidence of hypertensive pulmonary vascular disease is usually present, often to a similar extent in the two lungs, sometimes greater in the right and sometimes greater in the left. It is likely that the natural history of isolated origin of the LPA from the ascending aorta is similar, but too few patients have been observed to establish this.

**TECHNIQUE OF OPERATION**

Preparations for operation, median sternotomy, and cardiopulmonary bypass (CPB) are those normally used (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2), as are the techniques for myocardial management (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion,” and “When Needed] Warm Cardioplegic Induction” in Chapter 3). The technique is described for anomalously arising RPA; it is similar when the LPA is affected.

Once the pericardium has been opened, the anomalously originating RPA is visualized coming from either the posterior or right lateral aspect of the ascending aorta (Fig. 45-7, A). It passes into the right hemithorax behind the superior vena cava. The aorta is completely dissected from the pulmonary trunk, and the ductus arteriosus is dissected out at this point.

The purse-string sutures and preparation for CPB are made as usual, except that care is taken to place the aortic cannula far enough downstream so that the aorta may be occluded distal to the aortic origin of the RPA (see Fig. 45-7, A). A single venous cannula is placed into the right atrium. CPB is established as usual, and as soon as it has begun, a temporary arterial clamp is placed across the RPA.

The ligamentum arteriosum or ductus arteriosus is ligated and specifically divided. Division allows improved mobility of the pulmonary trunk so that the connection to the RPA can be performed with minimal tension. A vent catheter is placed in the left atrium through a purse-string in the right upper pulmonary vein. After the aorta is occluded well distal to the RPA, cold cardioplegia is administered. The clamp is removed from the RPA, which is then thoroughly mobilized beneath the superior vena cava out to the lobar branches.

The pulmonary artery is then disconnected from the ascending aorta (see Fig. 45-7, A). The defect left in the ascending aorta is closed by a pericardial patch or other patch material (Fig. 45-7, B). In some cases, it may be possible to close the aorta transversely by direct suture. The aorta is rotated anteriorly and leftward. The right side of the pulmonary trunk is pulled out from beneath the aorta (see Fig. 45-7, B), and a longitudinal incision is made in it. An anastomosis is made between the end of the well-mobilized RPA and the side of the pulmonary trunk (Fig. 45-7, C). A 7-0 polypropylene suture is used, sewing from within the vessels posteriorly and working external to the vessels anteriorly. The completed repair establishes continuity between the RPA and pulmonary trunk, eliminating the shunt (Fig. 45-7, inset).

An alternative technique that achieves greater length on the RPA was described by van Son and Hanley (Fig. 45-8, A). After the aorta is occluded, it is incised transversely at the level of RPA origin. The aortic incision is continued posteriorly, leaving a generous cuff of posterior wall around the origin of the RPA. Position of the left coronary artery is noted and its ostium protected from injury. An incision is made in the right lateral wall of the pulmonary trunk so as to create an anteriorly based flap (Fig. 45-8, B). An anastomosis of the RPA to the pulmonary trunk is created with the two flaps forming the proximal segment of the RPA (Fig. 45-8, C). The ascending aorta is reconstructed by end-to-end anastomosis (Fig. 45-8, D).
Figure 45-7 Repair of anomalous origin of right pulmonary artery (RPA) from ascending aorta. A, Aorta is occluded near origin of brachiocephalic artery above anomalous origin of RPA. This requires cannulating the distal ascending aorta or aortic arch. RPA is removed from aorta (dashed line). B, Opening in ascending aorta is repaired by prosthetic patch. Right lateral aspect of pulmonary trunk is mobilized and delivered to the right. An opening is made into the pulmonary trunk. C, An end-to-end anastomosis of RPA to pulmonary trunk is constructed using continuous stitches of 6-0 or 7-0 polypropylene or polydioxanone suture. Inset, Repair restores normal continuity of pulmonary arteries and eliminates shunting from aorta to RPA.
Chapter 45  Origin of the Right or Left Pulmonary Artery from the Ascending Aorta

RESULTS

When origin of the RPA or LPA from the ascending aorta is an isolated condition (apart from patent ductus arteriosus), operation can be a low-risk procedure even in critically ill small infants (Table 45-1). This has been confirmed in other small individual institutional experiences, each ranging from 1 to 16 cases, with little or no early mortality.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Management usually given to infants after intracardiac surgery is used (see Chapter 5). Pulmonary hypertensive crises can be expected early postoperatively, and the infant is treated accordingly (see “Pulmonary Hypertensive Crises” under Pulmonary Subsystem in Chapter 5).

**Figure 45-8**  Repair of anomalous origin of right pulmonary artery (RPA) from aorta using autogenous flaps of aorta and pulmonary trunk.  

A, Ductus arteriosus is doubly ligated and divided. Aorta is transected at level of anomalous origin of RPA. Posteriorly, as indicated by dotted line, the transection incision separates at midpoint of aorta to encompass origin of RPA, thereby creating a flap of aorta attached to the RPA. Two parallel incisions (dashed lines) are made on the pulmonary trunk at proposed site of anastomosis of RPA. Incisions are joined posteriorly (dotted line) to create an anteriorly based flap on the pulmonary trunk.  

B, Aortic and pulmonary artery flaps are shown. Sufficient length is created to allow tension-free anastomosis of RPA to pulmonary trunk.  

C, Tissue flaps are anastomosed with continuous stitches of 6-0 polyglyconate suture, creating a proximal extension from pulmonary trunk to RPA.  

D, Aorta is reanastomosed in end-to-end fashion anterior to RPA to complete the repair.
tetralogy of Fallot with absence of the pulmonary valve or pulmonary vein stenosis, risk of death increases. Survivors of repair in infancy, with or without patent ductus arteriosus, have generally done well and have normal pulmonary artery pressure late postoperatively and presumably a normal life expectancy.\textsuperscript{6,8,11,23} Stenosis can occur at the anastomotic site of the RPA.\textsuperscript{7,14} It can be effectively treated by surgical revision or catheter angioplasty.\textsuperscript{2,12,21} Ascending aortic stenosis has been reported at the site of pulmonary artery removal.\textsuperscript{2,12,21} Ventilation and perfusion are usually normal in both lungs late postoperatively.\textsuperscript{21}

At least an intermediate-term good result can be obtained in some older patients. Juca and colleagues reported a satisfactory decrease in RPA and LPA pressure in a patient who was 20 years old at operation.\textsuperscript{11,12} Long and colleagues reported normalization of pulmonary vascular resistance in both lungs in a patient repaired at age 23 years with stenosis of the anomalous pulmonary artery but severe LPA hypertension due to a ductus arteriosus.\textsuperscript{11}

**INDICATIONS FOR OPERATION**

Diagnosis of origin of RPA or LPA from ascending aorta in infancy is an indication for urgent operation. This is true regardless of pulmonary vascular resistance in the two lungs, because these changes are usually reversible, at least in infants operated on before age 6 to 12 months. In rare cases of presentation beyond infancy, excessive elevation of pulmonary vascular resistance in the normally connected lung is a contraindication to operation.\textsuperscript{72} However, experience is insufficient to state the exact level of pulmonary vascular resistance in the normally connected lung that makes patients inoperable.

If the resistance is normal in the normally connected lung, repair is indicated. The anomalously connected lung will never have infinite resistance, so connecting it to the pulmonary circuit will always lower pulmonary vascular resistance. The difficulty lies in assessing resistance in the anomalously connected lung prior to repair. Pressure and flow to the normally connected lung can be easily measured at catheterization, and thus resistance in that lung can be calculated. Pressure, but not flow, to the anomalously connected lung can be easily measured, thus resistance cannot be calculated. A nuclear medicine lung perfusion scan can be used to estimate the flow ratio to each lung, and when this is combined with other pressure and flow data from catheterization, resistance can be calculated independently in each lung, helping to determine operability.

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INTRODUCTION

Congenital anomalies of the coronary arteries represent a varied group of lesions. Taken together, they are relatively common, seen in 1% to 5% of the population, depending on the method of detection. Many lesions are incidental findings with little or no consequences, but approximately 20% have the potential to cause coronary ischemia and its sequelae.

Box 46-1 presents a useful classification of all congenital coronary artery lesions. Some of these—an anomalous or eccentric location of a coronary artery ostium, multiple ostia, and duplication of coronary arteries—have no physiologic importance but may be important if other cardiac procedures are required. Others lesions such as myocardial bridging, ectasia or aneurysm, and small fistulas may or may not have to be surgically repaired, depending on whether or not they have physiologic consequences.

The most important lesions include large coronary arteriovenous fistula, anomalous connection of a coronary artery to the pulmonary trunk, and anomalous connection of a coronary artery to the wrong aortic sinus. All require surgical correction, or occasionally other intervention. This chapter focuses on these three lesions. A discussion of the more minor and incidental lesions outlined in Box 46-1 can be found in the review by Kayalar and colleagues.65

Box 46-1  Classification of Coronary Artery Anomalies

<table>
<thead>
<tr>
<th>Anomalies of Origin and Course</th>
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</thead>
<tbody>
<tr>
<td>I. Anomalous location of coronary ostium:</td>
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<tr>
<td>a. High ostium</td>
</tr>
<tr>
<td>b. Commisural ostium</td>
</tr>
<tr>
<td>II. Anomalous origin of coronary artery from opposite sinus with one of four courses:</td>
</tr>
<tr>
<td>a. Interarterial</td>
</tr>
<tr>
<td>b. Transseptal</td>
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<tr>
<td>c. Retroaortic</td>
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<tr>
<td>d. Prepulmonic</td>
</tr>
<tr>
<td>III. Anomalous origin of coronary artery from pulmonary trunk:</td>
</tr>
<tr>
<td>a. Type 1: Left coronary artery</td>
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<tr>
<td>b. Type 2: Right coronary artery</td>
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<tr>
<td>c. Type 3: Circumflex coronary artery</td>
</tr>
<tr>
<td>d. Type 4: Left and right coronary arteries</td>
</tr>
<tr>
<td>IV. Single coronary artery</td>
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<tr>
<td>V. Multiple ostia</td>
</tr>
<tr>
<td>VI. Anomalous origin of coronary artery from noncoronary sinus</td>
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<tr>
<td>VII. Duplication of coronary arteries</td>
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<table>
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<tr>
<th>Anomalies of Intrinsic Coronary Arterial Anatomy</th>
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<tbody>
<tr>
<td>I. Congenital ostial stenoses</td>
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<td>II. Coronary artery ectasia or aneurysm</td>
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<td>III. Myocardial bridging</td>
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<tr>
<th>Anomalies of Termination</th>
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<tbody>
<tr>
<td>I. Congenital coronary artery fistula</td>
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<tr>
<td>II. Extracardiac termination</td>
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</table>

Modified from Kayalar and colleagues.65

Section I  Coronary Arteriovenous Fistula

DEFINITION

A congenital coronary arteriovenous (AV) fistula is a direct communication between a coronary artery and the lumen of any one of the four cardiac chambers, the coronary sinus or its tributary veins, or the superior vena cava, pulmonary artery, or pulmonary veins close to the heart. Fistulous coronary connections that occur in congenital pulmonary and aortic atresia (see “Right Ventricular Coronary Artery Fistulae” under Morphology in Chapter 40 and “Other Associated Cardiac Anomalies” under Morphology in Chapter 49) are excluded from this chapter.

HISTORICAL NOTE

A congenital coronary AV fistula was first described by Krause in 1865.61 The first report in the English literature was that of Trevor in 1912, who described autopsy findings in a case with a fistula from the right coronary artery into the right ventricle. The patient died from associated endocarditis.73 Autopsy reports from Blakeway89 and from Halpert32 followed. The first report of surgical correction was in 1947 by Biorck and Crafoord,87 who discovered a fistulous connection to the pulmonary trunk at thoracotomy in a patient presumed to have a patent ductus arteriosus. It was closed with sutures. Probably the first reported case of a fistula that was correctly diagnosed preoperatively was that of Fell and colleagues in 1958,82 and the first report of repair using cardiopulmonary bypass (CPB) was that of Swan and colleagues in 1959.61,63 Currarino and colleagues described the use of angiography in diagnosis in 1959.515

MORPHOLOGY

Coronary Artery Site

The right coronary artery or its branches are the site of the fistula in 50% to 55% of cases.12,112 The left coronary artery is involved in about 35%, and both coronary arteries in 5%.82 The fistulous artery is almost invariably part of a normally distributed coronary artery with a normal branching pattern. The fistula occurs either in the main vessel that continues beyond the fistula (a side-to-side pattern) or at the termination of the main vessel itself, or at a branch (an end artery).55 Rarely, the involved artery is anomalous.11 The coronary artery proximal to the fistula is always dilated and elongated and may be serpiginous, and the degree of these changes is roughly proportional to the size of shunt through the fistula. Usually, dilatation is uniform throughout, but it may become aneurysmal anywhere along its course. Rarely, a giant aneurysm occurs involving the whole artery. This is particularly prone to occur in fistulae from the right coronary artery entering either the posterior wall of the left ventricle11,10,03 or right ventricle17 (Fig. 46-1). Although such aneurysms enlarge progressively,11,18 rupture is rare. Should the artery continue beyond the fistula, it reduces abruptly to a diameter smaller than expected. It is probable that in such cases a
coronary steal phenomenon occurs. There is no convincing evidence that these “feeding arteries” are unusually susceptible to developing arteriosclerosis.

Site of Fistulous Connection

Fistulous connections between the coronary artery and heart may enter any of the four cardiac chambers, the coronary sinus or its tributary veins, or the great arteries or veins adjacent to the heart (pulmonary trunk, proximal pulmonary veins or proximal superior vena cava, or left superior vena cava). There are, however, certain predilections. More than 90% of fistulae open into right heart chambers or their connecting vessels. True AV fistulae to the veins themselves (coronary sinus or its major branches or venae cavae) are uncommon. Thus, about 40% connect to the right ventricle, 25% to right atrium, 15% to 20% to pulmonary artery, 7% to coronary sinus, and only 1% to superior vena cava.

Fistulae entering the right side of the circulation cause rapid systolic and diastolic runoff from the aorta and a left-to-right shunt. The Qp/Qs is seldom larger than 1.8 and is often less, and arterial pulse pressure is seldom greatly widened. About 8% of fistulae drain into left heart chambers or their tributaries, usually the left atrium, less often the left ventricle (about 3%), and rarely the proximal pulmonary veins. Left heart fistulae are not, of course, AV fistulae but arterioarterial (arteriocameral, arteriosystemic) and therefore do not produce a left-to-right shunt. There may be important runoff from the aorta during both systole and diastole when fistulae enter the left atrium, or only during diastole when they enter the left ventricle, because fistulae usually close off during systole, and because there is no pressure gradient. Volume overload on the left ventricle is therefore similar to that produced by aortic regurgitation.

Information on sites of fistulous connections comes in large part from numerous collective reviews of this subject, and most patients were surgically treated.

The right atrium and right ventricle are the most frequent sites of connection for cases requiring surgery. In angiographic series, the most frequent site of connection of small coronary fistulae not requiring surgical therapy was the pulmonary trunk. Fistulae (localized and diffuse) to the left heart are more common in coronary angiographic series than in surgical series.

Size and Multiplicity of Fistulae

In surgically treated cases, the fistulous opening, when single, is seldom larger than 2 to 5 mm (Fig. 46-2) and usually has fibrous margins, although uncommonly it may itself be aneurysmal as in the first reported case. Occasionally there may be several openings or a localized angiomatous network of vessels. Among the 58 patients reported from the Texas Heart Institute, multiple fistulae were identified in 16% and an angiomatous lesion in 10%; the fistula was aneurysmal in 19%. In a number of instances (no doubt many times the number reported in surgical series), the fistula is small and is recognized only because of high-quality cineangiography. As in other sites, most fistulae to the left ventricle are single. In a small group of patients, however, there is a diffuse sponge-work of tiny connections from a number of, if not most, branches of the left coronary and sometimes also the right coronary artery (Fig. 46-3). These presumably represent persistence of embryonic trabecular spaces.

Cardiac Chambers

The chamber or vessel into which the fistula connects is variably affected. When the right atrium receives the fistula, it tends to become considerably dilated, whereas the right ventricle and pulmonary trunk show less change (apart from that to be expected from an increase in pulmonary blood flow) until heart failure occurs and they participate in cardiomegaly. Similarly, the left ventricle tends to remain normal in size despite a fistulous connection to it, probably because runoff occurring only in diastole is seldom large and seldom comparable with that occurring in severe aortic regurgitation. Left ventricular hypertrophy may be present. Rarely the left atrium becomes aneurysmally dilated.

The coronary sinus may also become aneurysmal and may rupture; this is the only reported site of preoperative rupture in this condition. It is possible that runoff through the coronary sinus is limited by the coronary sinus ostium. Arterialization of the coronary sinus occurs, and possibly in relation to this, there is an unusually high prevalence of heart failure in such patients.

Infective Endocarditis

The fistula is the site of endocarditis in about 5% of cases and is attributed to turbulence.

Associated Lesions

Most coronary AV fistulae occur as isolated lesions, but there may be coincidental congenital or acquired lesions of almost any type. In the series reported by Urrutia-S and colleagues, 21 of 58 patients had associated lesions such as atrial septal defect, ventricular septal defect, and acquired valve or coronary disease.
Figure 46-2  Cineangiogram frames in right anterior oblique projection in two patients with coronary arteriovenous fistulae from main right coronary artery (RCA) to right ventricle (RV).  

A, Dilated RCA runs in its usual position in atrioventricular groove, and beyond fistula (arrow) it continues around acute margin to divide into posterior descending and inferior left ventricular (posterolateral segment) branches (not seen).  

B, RCA is again shown to be normally positioned and very dilated and tortuous. Fistula (arrow) arises from posterior descending branch about halfway along posterior interventricular groove and lies therefore at termination of this vessel.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Age at Presentation
Most patients present late in life, occasionally in childhood, rarely in infancy.

Symptoms
Most patients considered for operation are asymptomatic and present either because of a continuous murmur or mild cardiomegaly and plethora on chest radiograph. Some 80% of patients under age 20 years are asymptomatic, whereas only 40% of those older are without symptoms. Patients with small fistulae are being detected because of coronary angiography for other conditions. They are typically asymptomatic and presumably will continue to be so.

The most common symptoms are effort dyspnea and fatigue from the left-to-right shunt. Angina is uncommon (about 7%) and myocardial infarction rare (about 3%). It is postulated that these ischemic symptoms are due to coronary artery steal.

Heart failure occurs in 12% to 15% of patients presenting for operation but is much more common in older patients, as is angina. Thus, in the review by Libethson and colleagues, only 6% of patients under 20 years of age had heart failure, but 39% of those 20 years or older did. Heart failure can occur in infants with large shunts and in the occasional child with a large right coronary–left ventricular fistula comparable with an aortico–left ventricular tunnel. The likelihood of older patients having heart failure is not directly related to shunt size; rather, it is presumably related to a long-standing modest left-to-right shunt, as in the case of atrial septal defect. Heart failure is more common in patients with fistulous connection to the coronary sinus (50% vs. 14% in the overall group as reported by Ogden and Stansel). It may also be more common with onset of atrial fibrillation, which occurs more often when the connection is to the right atrium.

When infective endocarditis occurs, presentation may be with chills and fever.

Diagnosis
Diagnosis is often strongly suspected from physical signs, but it may be difficult to distinguish coronary AV fistula from other lesions with rapid aortic runoff and continuous murmurs such as patent ductus arteriosus, ventricular septal defect with aortic regurgitation, ruptured sinus of Valsalva aneurysm, and in infancy, aortico–left ventricular tunnel. In coronary AV fistula, there is usually a continuous murmur that is maximal to the right of the sternum when the fistula enters the right atrium, and usually at the lower left sternal edge when it enters the right ventricle or left ventricle. However, when the pulmonary trunk is involved, the murmur is situated as in a patent ductus arteriosus. When the fistula enters the left ventricle, the murmur is usually only diastolic.

A systolic thrill is occasionally palpable when the fistula lies anteriorly (entry into right atrium or right ventricle). When the shunt and aortic diastolic runoff are large, pulse pressure...
is wide and the pulse jerky.Rarely, infants with a connection to the left ventricle may present with full-blown signs of severe aortic regurgitation.

The electrocardiogram (ECG) is entirely normal in about half of surgical patients and shows evidence of right or left ventricular overload in the remainder. The chest radiograph may also be normal or may show mild cardiomegaly and plethora. Cardiomegaly is more marked when heart failure appears. There may be evidence of right or left atrial enlargement, and occasionally the dilated and tortuous or aneurysmal coronary artery or fistulous site may distort the cardiac silhouette. This is most obvious when a giant aneurysm of the right coronary artery drains to the left ventricle, although this is rare.

Two-dimensional (2D) echocardiography can detect importantly enlarged coronary arteries and may also confirm specific chamber enlargement. Thus, diagnosis of a coronary AV fistula can be made by 2D and Doppler echocardiography if the fistula is large enough (Fig. 46-4). Echocardiography, however, is not definitive.

Cardiac catheterization, aortography, and selective coronary angiography have long been the gold standard for definitive diagnosis and planning of either surgical repair or coil occlusion by interventional catheterization (Figs. 46-5 and 46-6; also see Figs. 46-2 and 46-3). Left-to-right shunts are calculated, and right heart pressures are measured.

Computed tomography angiography (CTA) can accurately define the morphology of the fistula in both adults and young children, in cases that will not require hemodynamic measurements to make management decisions, it may be the diagnostic procedure of choice.

NATURAL HISTORY

The natural history of coronary AV fistula is not known precisely, but its general outlines are clear. The fistula, if not present at birth, develops early in life. Likely, small fistulae remain small, and moderate fistulae slowly increase in size, although there may be little change over 10 to 15 years. Onset of dyspnea, heart failure, and angina can occur in young patients with large fistulae. However, because the shunt is usually only moderate, symptoms often do not appear until later in life consequent to long-standing moderate left ventricular volume overload. Daniel and colleagues found from a review of the literature that if heart failure did not occur early in infancy, it would be virtually unknown until age 20. The maximum prevalence of heart failure occurs in the fifth and sixth decades.
The other event that may precipitate symptoms and cause premature death is infective endocarditis, which occurs in about 5% of patients and may develop at any age.\textsuperscript{19,25,52} Aneurysm formation develops with increasing frequency over time, occurring in 9% of children and 14% to 29% of adults.\textsuperscript{52,54} Spontaneous rupture is rare,\textsuperscript{11} even though the feeding coronary artery or the fistula itself may become aneurysmal, and as with other aneurysms, there is progressive dilatation of the sac.\textsuperscript{1,10} Rupture has not been reported in children.\textsuperscript{52} Libethson and colleagues found that among 173 reported patients with mean age 24 years, fistula-related death occurred in 6%: 1% in those presenting younger than age 20, and 14% in those presenting later (mean age 45 years).\textsuperscript{19} Spontaneous closure of a fistula has been recorded\textsuperscript{25,31,52,59} but is rare.

**Figure 46-4** Two-dimensional echocardiogram and color-flow Doppler interrogation of coronary artery fistula. A, Right coronary artery (RCA) to right ventricular (RV) fistula is demonstrated. Note increased diameter of coronary artery. B, Color-flow Doppler signal showing turbulence at fistulous site entering right ventricle. Key: Ao, Aorta; CF, coronary fistula.

**Figure 46-5** Cineangiograms in two patients with small fistulae to pulmonary trunk. A, Right anterior oblique projection. Fistula (arrowhead) is supplied by small branches from second diagonal and proximal left anterior descending coronary arteries (LAD). Pulmonary trunk (PT) opacifies faintly during part of each cardiac cycle. Operation is not indicated. B, Left anterior oblique projection. Fistula (arrow) is supplied by two branches from proximal LAD (origin of superior one is overlapped by shadow of cardiac catheter). PT opacified faintly. This lesion was closed at time of atrial septal defect repair. Key: Ao, Aorta; Cx, circumflex artery.

**TECHNIQUE OF OPERATION**

Approach in all patients is through a median sternotomy, with preparation made for use of CPB (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). After opening the pericardium, site of the fistula and location, size, and pathology of the coronary artery leading to it are noted. CPB is indicated:

1. When the artery is dilated and tortuous, to prevent catastrophic hemorrhage during closure of the fistula
2. When the fistula is relatively inaccessible, such as when it is in the left atrioventricular groove or distribution of the circumflex or distal right coronary artery
3. When the fistula is in the course of the coronary artery rather than at its termination, so that the fistula itself can be closed without ligation of the coronary artery
4. When an aneurysm requires excision
Precise location of the coronary AV fistula is determined and marked with a stitch before establishing CPB, because this is difficult to do later. After establishing CPB, the aorta is clamped. While the fistula is digitally closed, cold cardioplegic solution is administered. When the chamber into which the fistula opens is an atrium or the pulmonary trunk, the chamber is opened and the fistula closed from within with over-and-over sutures supplemented with a pledgeted mattress suture.

Cold cardioplegic solution can be infused both to identify the entry point of the fistula in the opened chamber and to test security of closure. When the fistula enters a ventricle or when the coronary artery is large and continues beyond the fistula, the coronary artery itself is opened and the fistula closed with a running suture, followed by closure of the arteriotomy with 6-0 or 7-0 polypropylene sutures. Use of a running mattress suture beneath the artery through the fistulous site is not recommended because this may lead to fistula recurrence.

Alternatively, if the fistula enters the right ventricle, right atrium, or pulmonary trunk, once CPB is established, the pulmonary trunk or right atrium, as appropriate, is opened without clamping the aorta. A pressurized blood stream emitted from the fistula makes its identification easy. This technique is especially helpful if the fistula enters the trabeculations of the right atrium or right ventricle. Closure from within the chamber is performed, and elimination of the blood stream confirms efficacy of closure.

When a large aneurysm is present (see Fig. 46-1), it should be excised. If the aneurysm is localized over the fistula site, excision entails trimming away the edges of the dilated vessel and resutting its walls to create an artery of near-normal size. This is possible because the posterior wall invariably consists of strong tissue. This is necessary only when the artery continues beyond the site of the fistula. When it is an end artery, the aneurysm is completely excised and the vessel remnants oversewn. When the aneurysm involves most of the feeding coronary artery (see Fig. 46-1), there is usually no option but to unroof it completely and close the coronary artery proximal and distal to the sac, the latter closure including the fistula site. In such circumstances, it is always appropriate to consider use of coronary artery bypass grafting (CABG) using either a saphenous vein or internal thoracic artery to the vessel beyond the fistula, but this may not be possible when the coronary artery is too small.

After completing the repair, if a left-sided chamber has been opened, it is aspirated for air. The remainder of the operation is completed as usual (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). Fistulous connection may be safely closed without CPB when it represents the termination of a major coronary artery branch into an easily accessible site and indicators for CPB are absent. In such instances, a suture ligature is placed around the “feeding” coronary artery very close to the fistulous connection. The fistula is then temporarily completely closed (verified by complete ablation of the thrill), and the ECG is monitored for several minutes. If there are no ECG changes, the ligature is tied down and another suture ligature placed for additional security. When the fistula is less clearly localized and consists of multiple vessels, secure closure requires a running suture that encompasses all involved vessels and the underlying wall.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Patients are managed as described in Chapter 5.

**RESULTS**

**Survival**

**Early (Hospital) Death**

Hospital mortality for repair of coronary AV fistula in the absence of giant aneurysm formation approaches zero. A literature review by Liberthson and colleagues indicates a mortality of 4% (CL 2.5%-6.2%) in 173 patients. Giant aneurysms almost always involve the right coronary artery, necessitating complete aneurysm excision and usually regrafting of the remaining right coronary system; risk of ischemia and arrhythmia increases in this situation. Of 10 reported patients with right coronary artery–left ventricular fistula, 3 (30%; CL 14%-51%) died postoperatively. Operative complications are rare. Myocardial ischemia, either temporary or with infarction, has been reported in 5% of cases, and fistula recurrence in 4%. With use of the techniques described here, these complications have become uncommon.

**Time-Related Outcomes**

Late results of repair are excellent. Edis and colleagues report that essentially all patients in whom the fistula was eradicated remain in New York Heart Association (NYHA) class I. Lowe and colleagues found no late deaths and no recurrent fistulas among 22 survivors of repair, with a mean follow-up of 10 years. Although involvment of the greatly dilated leading artery can occur when repair is performed in early life, this is not the case in adults.
INDICATIONS FOR OPERATION

Some believe that prognosis of a surgically untreated coronary AV fistula is excellent, and operation is indicated only if symptoms are present. However, in view of the probability that at least some of these fistulae will increase in size and therefore eventually produce symptoms and heart failure, the tendency for development of infective endocarditis, the low probability of spontaneous closure, and the safety and efficacy of operation, it is recommended that diagnosis of a coronary AV fistula is an indication for operation unless the shunt is small ($Q_p/Q_s < 1.3$).

SPECIAL SITUATIONS AND CONTROVERSIES

Use of various interventional catheter-delivered occluding devices and coils has been reported to treat coronary AV fistulae successfully. These techniques are increasingly being considered the therapy of choice for appropriately selected patients. In a nationwide survey conducted between 1996 and 2003, 85% of treated patients were managed surgically and 15% with interventional techniques.

Section II  Anomalous Connection of Left Coronary Artery to Pulmonary Trunk

DEFINITION

In anomalous connection of left coronary artery to pulmonary trunk, the whole of the left main coronary artery or only the left anterior descending or circumflex branch connects anomalously to the proximal pulmonary trunk or very rarely to the proximal right pulmonary artery. Branching pattern of the anomalously connecting left coronary artery remains normal. The right coronary artery arises normally from the aorta and has a normal branching pattern. Collaterals from the right coronary artery feed the left coronary artery, in which flow is reversed, so that the left coronary artery drains into the pulmonary artery. Very rarely, both coronary arteries connect to the pulmonary artery by a single trunk.

HISTORICAL NOTE

In 1886, Brooks in Dublin described, apparently for the first time, anomalous connection of a coronary artery to the pulmonary trunk, and in 1908, Abbott described anomalous connection of left coronary artery to pulmonary trunk. Bland, White, and Garland in 1933 described the clinical syndrome associated with the anomaly, based on their experience with a 3-month-old infant who died from it. The pathophysiology, as suggested by Brooks in his original paper, is impoverished left ventricular myocardial blood flow—despite good collaterals between right and left coronary arteries—because of retrograde flow from left coronary artery to pulmonary trunk. Edwards supported this hypothesis, as did Case and colleagues in 1958. The latter also reported the postmortem observation that radiopaque dye injected into the ascending aorta passed out through the normal right coronary artery and, by collaterals, filled the left coronary artery in retrograde fashion.

Sabiston and colleagues verified retrograde flow at the first successful operation for the anomaly in 1959 by measuring a striking increase in left coronary artery pressure when its anomalous connection to the pulmonary trunk was occluded. Actual demonstration of left-to-right shunt into the pulmonary trunk was by Augustsson and colleagues in 1962 and by Rudolph and colleagues in 1963.

Earliest surgical attempts to ameliorate the condition were indirect. The first attempt was apparently by W.J. Potts, who created an aortopulmonary (AP) fistula to increase saturation in the pulmonary trunk (personal communication, 1955). Kittle and colleagues banded the pulmonary artery, and Paul and Robbins used pericardial poudrage. These procedures are obsolete.

Successful ligation of the anomalous left coronary artery connection by Sabiston and colleagues in 1959 was followed by a similar report from Rowe and Young in 1960. As early as 1953, Mustard reported attempts to anastomose the turned-down left common carotid artery to the anomalous left coronary artery that he detached from the pulmonary trunk together with a button of pulmonary trunk wall. Apley and colleagues attempted a similar procedure using the subclavian artery in 1957. Meyer and colleagues first used this latter procedure successfully to create a two-artery coronary system in 1968, and others including Pinsky and colleagues reported such a repair.

In 1966, Cooley and colleagues reported use of coronary artery bypass vein grafting from the aorta to the left main or proximal left anterior descending artery, after closing the left coronary ostium from within the pulmonary trunk. The next procedure to evolve was translocation of the anomalous coronary artery from pulmonary trunk to ascending aorta. Such a procedure was performed unsuccessfully in 1972 using hypothermic circulatory arrest. This was first performed successfully for the rare condition of anomalous connection of the right coronary artery to pulmonary trunk (where the artery lies anteriorly and is more readily translocated) by Tingelstad and colleagues in 1971, and for the left coronary artery by Neches and colleagues in 1974. The latter also described successful interposition of a free left subclavian artery segment between the left coronary artery and the back of the ascending aorta.

In 1979, use of a tunnel within the pulmonary trunk to connect the ostium of the anomalous coronary artery to the aorta via an AP window was introduced. It was created either of pericardium, as described by Hamilton and colleagues, or of pulmonary artery wall, as described by Takeuchi and colleagues. Arciniegas and colleagues modified this concept by placing a free subclavian artery graft inside the pulmonary trunk. Reconstructive techniques have been devised to permit implanting coronary arteries that are remote from the aorta. Use of temporary ventricular assistance in infants has been an important adjunct to postoperative management. The aneurysmal left ventricular wall was excised unsuccessfully in 1960. This procedure, combined with ligation of the left coronary artery, was subsequently performed successfully by Turina and colleagues in 1973 and Fleming and colleagues in 1975.
MORPHOGENESIS AND MORPHOLOGY

Morphogenesis

Embryologic information indicates that the proximal coronary arteries grow from the peritruncal area into the aorta, with formation (normally) of single orifices for both left and right coronary arteries. Therefore, the phrase “the anomalous artery arises from” is inappropriate. For that reason, the former term, anomalous origin, has been abandoned in this text for anomalous connection.

Morphology

The anomalous left main coronary artery connects most often to the sinus of Valsalva immediately above the left or posterior cusp of the pulmonary trunk and rarely from that above the right cusp. The left main coronary artery is of variable length, but usually divides into anterior descending and circumflex branches within 5 or 6 mm of its origin. Collateral communications between right and left coronary arteries are always present, but vary in extent and are grossly visible in only a few cases, mainly in adults. Uncommonly, only the circumflex branch connects anomalously to the pulmonary trunk, and rarely only the anterior descending branch.

Very rarely, the left main coronary artery or only the circumflex artery connects to the right pulmonary artery near its origin rather than to the pulmonary trunk. Even more rarely, both the left and right coronary arteries connect to the pulmonary trunk (see “Total Anomalous Connection of Coronary Arteries to Pulmonary Trunk” under Special Situations and Controversies later in this section).

The left ventricle is always hypertrophied and usually greatly dilated, with dilatation often involving primarily the left ventricular apex. Diffuse left ventricular fibrosis is virtually always present, and patients dying in infancy usually have evidence of recent and old anterolateral myocardial infarction. Fibrosis is most marked in the subendocardial layer. Focal calcification may be present in fibrotic areas. Secondary subendocardial fibroelastosis of variable degree is usually present. However, a considerable amount of left ventricular dysfunction, in infants at least, must be ischemic in origin, in view of the dramatic improvement in left ventricular function that can result from an operation that creates a two-artery coronary system. Improvement in left ventricular function in a patient with coronary artery disease is difficult to distinguish from that of myocardial ischemia.

The chronic ischemia accompanying this lesion results in devitalization (or adaptive response) of the myocardium at a cellular and biochemical level. The devitalized myocardium has been termed hibernating myocardium (see “Myocardial Cell Stun ning” under Damage from Global Myocardial Ischemia in Chapter 3). The devitalized muscle slowly recovers over the time described once adequate blood flow and oxygen delivery are established.

Several pathologic features may result in mitral valve regurgitation. There may be extensive fibrosis and sometimes calcification in the papillary muscles, leading to papillary muscle dysfunction. Endocardial fibroelastosis may involve the mitral apparatus, with fusion and shortening of chordae tendineae. Also, papillary muscles may be abnormally positioned, which may lead to mitral regurgitation. Extensive left ventricular fibrosis can produce left ventricular and mitral anular dilatation and mitral regurgitation. Reversible left ventricular ischemia must, to some degree, contribute to the mitral valve regurgitation in infants, because in many cases regurgitation has been observed to decrease to an important extent after surgical treatment and creation of a two-artery coronary system.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Infant Presentation

Symptoms may be recognized within a week or so of birth. When there are no other anomalies, these are seldom severe enough to warrant referral before age 2 months. Presumably, high postnatal pulmonary artery pressure limits runoff into the pulmonary trunk, so there is less coronary steal, and myocardial dysfunction is gradual in onset rather than sudden. Circumural pallor and blueness are often present. The cardiac symptom is poor feeding. The baby takes the first 2 to 3 ounces well but then stops; there is breathlessness and sweating, and the baby may draw up the knees, arch the back, and uncommonly, cry or scream. The presumed cause is angina. As a result of the feeding problem, weight gain is poor. Few infants with these symptoms improve spontaneously. Usually by age 2 to 3 months, there is overt heart failure with persistent tachypnea and tachycardia. The infant by then is seriously ill and occasionally moribund.

Clinical signs are difficult to distinguish from those of cardiomyopathy or endocardial fibroelastosis. There may be a nonspecific systolic murmur at the base, or a more definite apical pansystolic murmur caused by mitral regurgitation and an apical gallop rhythm. A continuous murmur is not audible in infants. A precordial lift is common in association with marked and frequently gross cardiomegaly. Hepatomegaly also is present, and rales are heard throughout the lungs. The ECG is frequently helpful in diagnosis, because it usually shows anterolateral infarction with Q waves and ST-segment elevation in lateral chest leads and evidence of left ventricular hypertrophy. However, left ventricular hypertrophy alone may be reflected in the ECG. Myocardial enzymes may be elevated. In addition to cardiomegaly, interstitial pulmonary edema is evident on the chest radiograph.

Echocardiography shows a dilated, poorly contracting left ventricle (with ejection fraction typically <20%) and reveals the functional status and morphology of the mitral valve. In infants otherwise thought to have dilated cardiomyopathy, 2D and pulsed Doppler echocardiography may detect an abnormally large right coronary artery and anomalous connection of the left coronary artery to the pulmonary trunk, with retrograde flow in it (Fig. 46-7). This technique can also be used to identify an anomalously connecting right coronary artery.

Although definitive diagnosis is often made by echocardiography, current practice requires cardiac catheterization and cineangiography. An aortogram demonstrates the single right coronary artery arising from the aorta, and retrograde filling of the left coronary artery that produces a varying degree of opacification of the pulmonary trunk (Fig. 46-8). A left ventriculogram can be used to assess left ventricular function and degree of mitral regurgitation. It may also demonstrate coronary anatomy, making an aortogram unnecessary. Left ventricular end-dia stolic pressure is always elevated but may be lower than anticipated from viewing the typically very poor ejection fraction on echocardiography. Right heart
catheterization may show an increase in blood oxygen content at pulmonary artery level.

**Adult Presentation**

Collateral circulation from the right coronary artery is apparently adequate to prevent massive infarction, because few patients presenting later in life report a history of hospitalization in infancy, although there may have been feeding difficulties. When severe symptoms do not occur in infancy, presentation is often delayed to beyond age 20 years. Some adults remain asymptomatic or complain only of fatigue, dyspnea, or palpitations. About half have effort angina. There usually is a nonspecific systolic murmur, sometimes an apical pansystolic murmur from mitral regurgitation, and occasionally a continuous murmur over the upper left sternal edge due to retrograde flow from the coronary artery into the pulmonary trunk. Occasionally, mitral regurgitation dominates the clinical picture, producing heart failure. In an earlier era, some of these patients were operated on for mitral regurgitation or died without diagnosis of anomalous connection of left coronary artery to pulmonary trunk having been made.

The resting ECG is virtually always abnormal, with ST-T segment changes or evidence of old anterolateral infarction. Exercise ECG usually shows an abnormal ischemic response, and stress thallium myocardial imaging is usually abnormal. The chest radiograph may be normal or may show cardiac enlargement. Cineangiography shows more prominent collaterals from the right coronary artery in adults than in infants and usually a near-normal left ventricular ejection fraction, but with anterolateral hypokinesia. Mitral regurgitation occasionally is severe.

Individuals with anomalous left anterior descending or anomalous circumflex coronary artery typically present in adulthood rather than infancy. In the rare case that all coronary arteries arise from the pulmonary artery, death early in life is almost a certainty.

**NATURAL HISTORY**

Anomalous connection of the left coronary artery to the pulmonary trunk is rare, occurring in 0.26% of patients with congenital heart disease undergoing cardiac catheterization. About 65% of infants born with it die during the first year from intractable left ventricular failure (Fig. 46-9). However, they uncommonly do so in the first 2 months. Explanation for this symptom-free interval is not entirely clear, because extensive left ventricular scarring, particularly of the subendocardium, and evidence of old and recent infarction are usually present by then. It likely results, however, from a combination of initially elevated pulmonary...
Figure 46-8  Biplane cineangiographic frames in 3-month-old infant with anomalous connection of left coronary artery to pulmonary trunk.  
A-B, In right anterior oblique projection.  
C-D, In left anterior oblique projection. In A and C, right coronary artery (RCA) fills directly from aorta, and prominent conal branch collaterals are visible. In B and D, there is delayed retrograde filling of left anterior descending (double arrowheads) and circumflex arteries (single arrow). Whiff of contrast can be seen in the pulmonary trunk (x) in D.

Figure 46-9  Freehand depiction of survival without surgical treatment of patients with anomalous connection of left coronary artery to pulmonary trunk. (Figure is based primarily on collective review of 140 cases by Wesselhoeft and colleagues.)*

artery pressure, which limits the runoff, and gradual accumulation of myocyte dysfunction and loss.

If death does not occur during the first year, the hazard lessens considerably and the chronic phase of natural history is reached. Survival to this stage may be related to presence of rich interarterial collaterals, possibly associated with a slightly restrictive opening between left coronary artery and pulmonary trunk. Supporting this is the continuous murmur heard in about 5% of patients. Many such patients are in good health, and a few have normal ECGs.* Survival beyond the first year may also be related to marked right coronary dominance, with this vessel supplying not only the diaphragmatic portion of the left ventricle but also much of the septum and lateral wall.* Patients with this arrangement may occasionally only have papillary muscle ischemia and fibrosis, and mitral regurgitation may dominate the clinical picture.

Most patients who survive infancy continue to be at risk of death from chronic heart failure secondary to ischemic left ventricular cardiomyopathy. Those who survive until the
fourth decade are at less risk of death from heart failure (see Fig. 46-9), and those few patients who live to the fifth and sixth decades occasionally die suddenly, as do older patients with long-standing ischemic heart disease (see “Death” under Natural History in Chapter 7). In adult patients, myocardial ischemia and fibrosis are prominent, and occasionally, extensive myocardial calcification develops. However, left ventricular ejection fraction is only moderately depressed or normal in most of these patients.\(^{510}\)

**TECHNIQUE OF OPERATION**

**Constructing a Two-Artery Coronary System**

Optimally, operation is undertaken with the idea of constructing a two-artery coronary system in all patients. Translocation of the anomalous coronary artery into the aortic root appears to be the most direct and therefore advisable procedure, but it is not always possible. Smith and colleagues found the distance between the midpoint of the empty left aortic sinus and posterior aspect of the anomalously connected coronary artery to vary between 2 and 18 mm.\(^{312}\) The longer of these distances probably precludes direct implantation and makes the tunnel (Takeuchi) repair necessary.\(^{51}\)

Other methods of creating a two-artery coronary system may be less desirable. In critically ill infants, a case may still be made for use of simple ligation of the anomalously connected coronary artery, especially if used as a temporary maneuver to resuscitate a patient presenting in cardiac arrest. However, this seems less desirable in an era when mechanical assist devices are available even for the smallest infants. In seriously ill infants, ventricular fibrillation is likely to develop before the heart can be cannulated and CPB commenced. Therefore, vigilance is required to maintain an optimal hemodynamic state during preparations for operation and cannula for CPB.

Operation is best done with CPB at 18°C to 28°C (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2), although left coronary artery translocation has recently been reported using normothermic CPB and a continuously beating heart.\(^{54}\) After sternotomy, the pericardium is opened without touching the heart, because even the slightest trauma can induce ventricular fibrillation. Preferably, arterial cannulation of both the aorta and pulmonary trunk is used with a bifurcated system to maximize myocardial perfusion once CPB is started. Single venous cannulation is used. Immediately before commencing CPB, tourniquets are placed around the left and right pulmonary arteries. The tourniquets are tightened as CPB is initiated to prevent perfusion steal into the pulmonary bed from the pulmonary trunk arterial cannula. A left-sided vent is placed through a purse-string in the right upper pulmonary vein.

Myocardial protection during aortic clamping is particularly important for two reasons: the existing compromised state of the myocardium, and the potential for inadequate delivery of cardioplegic solution to the left ventricle. Preferably, cardioplegic solution is delivered simultaneously into the aortic root and pulmonary trunk using a bifurcated cardioplegia delivery system to maximize protection of the left ventricle.

Alternatively, some surgeons use only one arterial cannula (in the aorta) and deliver cardioplegia only into the aortic root. It is critically important to occlude the branch pulmonary arteries at the initiation of CPB and through cardioplegia delivery using this technique.

After completing cardioplegia, the pulmonary trunk cannula and branch pulmonary artery tourniquets are removed. A transverse incision is made in the pulmonary trunk just downstream to the commissure of the pulmonary valve. When the opening of the anomalously connecting left coronary artery is posterior or right-sided, the coronary artery translocation technique is used. When the opening is on the left-sided aspect of the pulmonary trunk, the tunnel operation\(^{71}\) should be considered.

**Tunnel Operation (Takeuchi Repair)**

Taking care to avoid injury to the aortic valve, a button of aortic wall about 5 to 6 mm in diameter is excised at a point at which the left wall of the aorta is in contact with the right side of the pulmonary trunk (Fig. 46-10, A). Directly opposite this, a button is excised from the right wall of the pulmonary trunk (Fig. 46-10, B [also see A]). These openings are sewn together with continuous 7-0 polypropylene to create an aortopulmonary window.

Using a flap of anterior pulmonary trunk wall hinged on the right, the anterior wall of the tunnel is created, completing the tunnel conveying blood from the aortopulmonary window across the back of the pulmonary trunk to the anomalously connecting left coronary artery (Fig. 46-10, C [also see B]). The large defect in the anterior wall of the pulmonary trunk is reconstructed with a patch of pericardium, pulmonary artery allograft, or polytetrafluoroethylene (PTFE) (Fig. 46-10, D). Occasionally, this operation narrows the immediately supravalvar portion of the pulmonary trunk sufficiently to require a transanular patch.

The remainder of the operation is completed in the usual fashion (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). Weaning the patient from CPB may require patience, intravenous nitroglycerin, and monitoring left and right atrial pressures.

**Left Coronary Artery Translocation**

When the left coronary artery connects to the posterior or right-sided aspect of the pulmonary trunk (Fig. 46-11, A), the transverse pulmonary trunk incision is continued until the trunk is transected (Fig. 46-11, B).\(^{64,118,52,51}\) The incision is arranged so that a sizable button of pulmonary artery wall around the coronary ostium is excised (see Fig. 46-11, B). The left coronary artery is carefully mobilized for a short distance. An opening is made in the adjacent left posterolateral portion of the aorta (Fig. 46-11, C). The button around the coronary ostium is anastomosed to the aorta with 7-0 monofilament absorbable sutures, the pulmonary trunk is reconstructed by end-to-end anastomosis, and the coronary artery explant site is patched (see Fig. 46-11, C).

**Subclavian–Left Coronary Artery Anastomosis**

This procedure may be indicated when the anomalous coronary ostium within the pulmonary trunk is remote from adjacent aorta, making direct coronary translocation impossible and Takeuchi repair difficult. Initial CPB management uses a single aortic cannula, with attention to myocardial perfusion similar to that already described, but because the aortic root is not opened or manipulated, aortic clamping and cardioplegia are not necessary.
Figure 46-10  Tunnel operation (Takeuchi repair).  

A, After instituting cardiopulmonary bypass using techniques to maximize myocardial preservation, the initially small transverse pulmonary arteriotomy, made to confirm the unfavorable position of the anomalous coronary ostium for direct translocation, is extended to develop an anterior pulmonary arterial wall flap. It is based on the right lateral aspect of the pulmonary trunk. Dotted lines indicate (1) positions of buttons on adjacent aortic and pulmonary arterial wall that are to be removed, and (2) extent of incisions used for anterior pulmonary arterial flap.  

B, Anterior pulmonary arterial wall flap has been fully developed, and aortopulmonary window anastomosis is created using a running 7-0 monofilament absorbable suture. During creation of the aortopulmonary window, care should be taken to avoid direct injury or distortion of the semilunar valve cusps and commissures.  

C, Aortopulmonary window suture line has been completed, and the anterior pulmonary arterial wall flap has been used to create the tunnel connecting aortopulmonary window and remote ostium of anomalous coronary artery. This anastomosis is also performed with a running 7-0 monofilament absorbable suture. Great care should be taken as the suture line approaches the ostium of the coronary artery to avoid distorting the proximal coronary artery.  

D, Remaining defect in the anterior wall of the pulmonary trunk is now reconstructed with an appropriately shaped patch of either glutaraldehyde-treated autologous pericardium, pulmonary artery allograft arterial wall tissue, or polytetrafluoroethylene. A running monofilament nonabsorbable suture is used. Size of patch should be generous to avoid supravalvar pulmonary stenosis.
The left subclavian artery is dissected as far distally as possible and then ligated and divided at this level (Fig. 46-12). It is important that adequate length of left subclavian artery is achieved; otherwise, kinking at the subclavian origin is possible following anastomosis. The connection of the coronary artery to the pulmonary trunk is identified and the coronary mobilized on a generous button of pulmonary sinus tissue. The coronary artery is mobilized appropriately to allow the anastomosis to be performed without tension or kinking. The preferred method of anastomosis is end-to-end connection of subclavian artery to coronary button using a running 7-0 monofilament absorbable suture.

After completing the anastomosis and establishing flow through the reconstructed area, the proximal aspect of the subclavian artery should be examined carefully to ensure that no tension or kinking is present. The coronary explantation site on the pulmonary trunk can be closed primarily or, if preferred, with a small patch of autologous pericardium, pulmonary artery allograft, or PTFE, using a running monofilament nonabsorbable suture. Alternatively, the left coronary
The coronary artery is mobilized over an appropriate length so that there is no tension as the artery is brought over to the aortotomy site. A running 7-0 monofilament absorbable suture is used to create the coronary to aortic anastomosis. Also shown is the pulmonary trunk end-to-end reconstruction and reconstruction of the coronary explantation site using a patch of glutaraldehyde-treated autologous pericardium, pulmonary artery allograft, or polytetrafluoroethylene.

The patient’s anatomy may not permit this operation to be performed without excessive tension or kinking of the subclavian artery, so the surgeon must always have an alternative procedure in mind.

Other Techniques for Assisting Translocation
A number of techniques have been described to increase the likelihood of translocation of the anomalous coronary into the aorta for coronary arteries remote from the aorta. The coronary artery can be extended by autologous flaps of aorta and pulmonary artery, or it can be excised with a button of pulmonary artery, mobilized to reach the aorta, and anastomosed within the aortic lumen, a technique attributed to Yacoub. One such technique is shown in Fig. 46-13.

Coronary Artery Bypass Grafting
Techniques for CABG are the same as those used for internal thoracic artery grafting in the surgical treatment of arteriosclerotic coronary artery disease (see under Indications for Operation later in this section; see also Technique of Operation in Chapter 7). Even in small patients, the left internal thoracic artery can be used.

Ligation of Left Coronary Artery
This procedure may be carried out in the simplest manner through a limited left anterolateral fourth interspace incision. The pericardium is opened in front of the phrenic nerve after mobilizing the thymus from its upper part. A ligature is tied around the tip of the left atrial appendage to retract it superiorly. The anomalous connection of the left coronary artery is immediately obvious, and is rapidly dissected and ligated close to the pulmonary trunk wall with a single transfixing suture or metal clip. Venous collaterals around the artery may require cautery control. The pericardium is loosely closed and chest closed with or without drainage. The entire procedure can be completed within 30 to 45 minutes.

In the current era, this procedure may be applicable as an interim measure to stabilize critically ill patients before more formal revascularization. CPB may be used, especially if the anomalous coronary artery connects to the pulmonary trunk posteriorly. Using a single venous cannula, perfusion at 37°C, and no aortic clamping, the pulmonary trunk is opened transversely and the origin of the left coronary artery oversewn with a few simple sutures reinforced with a pledgeted mattress suture. CPB time is approximately 15 minutes.

SPECIAL FEATURES OF POSTOPERATIVE CARE
Care of patients undergoing repair of anomalous connection of left coronary artery to pulmonary trunk is the same as that for other patients undergoing cardiac surgery (see Chapter 5). A left atrial pressure monitoring catheter should be used. In critically ill small infants, low cardiac output can be anticipated during the first few postoperative days, and appropriate measures applied (see “Cardiovascular Subsystem” in Section I of Chapter 5). These measures may include use of temporary left ventricular assistance (see “Temporary Ventricular Assistance” in Section I of Chapter 5).
RESULTS

Survival

Early (Hospital) Death

Early mortality reported for heterogeneous groups of patients is almost valueless because of the powerful effect of risk factors in this setting, the small number of patients in all reported series, and the effect of “patients too sick for operation” on mortality after surgery. These factors also make difficult an appropriate comparison of outcomes after various surgical procedures. There is a suggestion, supported by physiologic arguments, that outcome following simple ligation is not as good as with more formal revascularization (Tables 46-1 and 46-2). Mortality in various subsets from series reported from 1975 to 1980 ranged from 0% to 75%. Certain trends have emerged over time. Series reported since 1995 emphasize operations that result in a two-artery coronary system and also document excellent survival (mortality 0% to 14%). Improved postoperative support, including use of temporary ventricular assistance, may play an important role.

Time-Related Outcomes

Few appropriate studies of long-term survival have been conducted. In one study, no late deaths were recorded in 21 patients with a mean follow-up of 6.5 years (range 2 months to 18 years) and a total of 145 patient-years of follow-up. Similar midterm results have been reported by others, supporting the position that most patients survive long term after any of the described procedures.

Modes of Death

Most hospital deaths result from acute cardiac failure.

Incremental Risk Factors for Premature Death

No formal analysis provides information regarding incremental risk factors for premature death. Presumably, there is an early, rapidly declining hazard phase for death; a low constant phase of hazard follows, conditioned by status of the left ventricular myocardium.

Preoperative status of the left ventricle is also the important risk factor for death during or early after repair, with depressed shortening fraction identified in one analysis of 39 patients. This status determines functional state of the patient, which is also a powerful risk factor for death.

Important risk factors are also a risk factor for death early (and perhaps late) after repair, but this is correlated with status of the left ventricle. As with older studies (see Fig. 46-9), more recent reports seem to indicate that deaths are more frequent among infants.

Functional Status

Functional status is generally good late postoperatively. Of 21 patients assessed by Cochrane and colleagues, 18 were in NYHA class I and 3 in class II at midterm follow-up. Size of the left ventricle (including cardiothoracic ratio) is nearly always markedly reduced by operation, and signs of myocardial ischemia are reduced. Late postoperative functional status in patients operated on in infancy or in adult life appears to depend primarily on status of the left ventricle before operation, just as it does in arteriosclerotic ischemic heart disease (see “Left Ventricular Function” under Results in Chapter 7). Clearly, however, these patients are not normal. In 11 late survivors, myocardial flow reserve was reduced, and exercise tolerance was lower than normal.

Left Ventricular Function

Left ventricular function does not change immediately after operation, but it improves strikingly after several months in most surviving patients, as evidenced by reduction in cardiothoracic ratio (Fig. 46-14) and left ventricular end-diastolic and end-systolic volumes, return of left ventricular shape to normal in both diastole and systole, and increase in left
Figure 46-13  Technique for extending coronary artery. A, Pulmonary trunk is transected above level of pulmonary valve. A sleeve of pulmonary artery posterior wall is excised along with left coronary orifice. Inset, Partially excised pulmonary arterial wall in continuity with origin of left coronary artery (LCA). B, Upper and lower edges of this pulmonary flap are sewn together with a 7-0 or 6-0 monofilament suture in order to form a tube-shaped autologous graft 3 to 4 mm in internal diameter in continuity with origin of left coronary. C, Graft is sutured end to side into left posterior wall of ascending aorta with a 6-0 monofilament suture. Defect in pulmonary trunk is repaired with a fresh autologous pericardial patch. Key: RCA, right coronary artery. (From Wu and colleagues.)

Table 46-1  Age and Hospital Mortality after Operation for Anomalous Connection of Left Coronary Artery to Pulmonary Trunk

<table>
<thead>
<tr>
<th>Age ≤ Months</th>
<th>&lt;</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0-85</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>7</td>
<td>2</td>
<td>29</td>
<td>10-55</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0-38</td>
</tr>
<tr>
<td>12</td>
<td>24</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0-32</td>
</tr>
<tr>
<td>24</td>
<td></td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0-61</td>
</tr>
<tr>
<td>TOTAL</td>
<td>19</td>
<td>2</td>
<td>11</td>
<td></td>
<td>4-23</td>
</tr>
</tbody>
</table>

Table 46-2  Procedure and Early and Late Mortality after Correction of Anomalous Connection of Left Coronary Artery to Pulmonary Trunk

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Early Mortality</th>
<th>Late Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No.</td>
</tr>
<tr>
<td>Ligation</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Ostial closure</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Takeuchi</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Ligation/CABG</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td>24</td>
<td>4</td>
</tr>
</tbody>
</table>

Data from Arciniegas and colleagues.67
Key: CL, 70% confidence limits.

Data from Bunton and colleagues.21
*Lost to follow-up evaluation.
Key: CABG, Coronary artery bypass grafting (saphenous vein); CL, 70% confidence limits.
ventricular ejection fraction and left ventricular shortening during systole.\textsuperscript{50,57,68,88,89,10,11,10,12,10,58} (Fig. 46-15). These findings indicate that in many patients, severe left ventricular dysfunction present preoperatively is due to reversible devitalization of the myocardium, or myocardial hibernation, as opposed to myocardial stunning (see “Myocardial Cell Stunning” under Damage from Global Myocardial Ischemia in Chapter 3).

**Mitral Regurgitation**

Mitral regurgitation frequently exists at presentation in patients with anomalous connection of left coronary artery to pulmonary trunk. It is argued by some that the basis for the regurgitation is ischemic and is reversible, and therefore the mitral valve should not be addressed routinely at initial operation for the anomalous coronary artery.\textsuperscript{1,12} Others routinely perform mitral anuloplasty when regurgitation is severe.\textsuperscript{12} When operation is performed in infancy, even important mitral regurgitation can regress postoperatively, no doubt related to improved left ventricular function.\textsuperscript{B21,C12,S8} However, when mitral regurgitation is severe, it may not regress, and reoperation is required for regurgitation a few months to a few years later.\textsuperscript{B14,B21,C12,S15} In one study that carefully tracked mitral valve function following surgery, regurgitation did not improve in 38% of cases but remained severe.\textsuperscript{65}

**Effect of One-Artery Coronary System**

Whether a two-artery coronary system after repair confers a better outcome than a one-artery system remains arguable. Speculatively, a two-artery system would seem to be advantageous, and results of exercise testing in a small number of patients support this view.\textsuperscript{142} Evidently, coronary blood flow is increased either by simple ligation of the anomalous left coronary artery or by creating an aortic origin of left coronary flow. However, coronary perfusion pressure in much of the left ventricle must be greater after the second type of repair, because it is not dependent on collateral flow. As a result,

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**Figure 46-14** Change in cardiothoracic ratio after surgery for anomalous connection of left coronary artery to pulmonary trunk. Along horizontal axis is age in years at time of observation. “1 ACS” (left graph) indicates patients with one-artery coronary system postoperatively; “2 ACS” (right graph) indicates patients with two-artery coronary system postoperatively. Key: ACS, Artery coronary system; C.T., cardiothoracic; SCA, subclavian to coronary artery; SVG, saphenous vein graft. (From Arciniegas and colleagues.\textsuperscript{87})

**Figure 46-15** Change in left ventricular shortening fraction after surgery for anomalous connection of left coronary artery to pulmonary trunk. Depiction as in Fig. 46-14. Key: ACS, Artery coronary system; SCA, subclavian to coronary artery; SVG, saphenous vein graft. (From Arciniegas and colleagues.\textsuperscript{87})
early and long-term results should be better, although magnitude of the difference when all other risk factors are similar remains to be determined.

Conduit Patency after Two-Artery Repair

Conduit patency cannot be assumed because the patient is asymptomatic, as is obvious from the fact that many patients are asymptomatic after a one-artery coronary system repair. The Takeuchi tunnel conduit was found to be obstructed in one of three patients studied late postoperatively by Bunton and colleagues, while four PTFE tubes used in a similar fashion were all patent. Two of five young patients undergoing left subclavian–left coronary artery anastomosis were found to have occluded conduits 3 to 5 years postoperatively.

When saphenous vein bypass grafts are used in adults, graft patency may be higher than in arteriosclerotic coronary artery disease. Donaldson and colleagues reported four of five grafts were patent 14 years postoperatively. When the reports of Moodie and colleagues and Chiariello and colleagues are combined, 11 of 15 grafts were patent. However, concern remains about the potentially lethal effect of vein graft closure, particularly in view of demonstrated regression of right coronary artery collaterals following successful revascularization. Anthony and colleagues reported sudden death in a 9-year-old girl 5 months after saphenous vein bypass grafting; at autopsy the graft was occluded and had extensive intimal fibrous hyperplasia. Similar vein graft obliterative changes were observed by el-Said and colleagues.

Right Ventricular Outflow Obstruction after Tunnel Repair

Right ventricular outflow obstruction is a risk following Takeuchi tunnel repair, but use of a generous anterior pulmonary trunk patch apparently reduces risk of serious obstruction.

INDICATIONS FOR OPERATION

Diagnosis of anomalous connection of left coronary artery to pulmonary trunk in an infant, regardless of clinical status, is an indication for urgent operation. The recommendation that operation be delayed until an older age is no longer tenable. Diagnosis is an indication for operation in older patients. Creating a two-artery coronary system may be considered to be indicated in all situations, including critically ill infants, especially if the option of using left ventricular assistance is available. Proper myocardial management (as described under Technique of Operation in this section) is mandatory.

Translocation of the left coronary artery into the aorta is the optimal operation when anatomy is favorable, with the Takeuchi procedure as the second option in infants. In older patients, internal thoracic artery grafting is a reasonable second alternative when size of the graft permits (see “Internal Thoracic Artery” under Technique of Operation in Chapter 7). Some recommend leaving the mitral valve alone when operation is performed in young patients, even when it is severely regurgitant, because this usually regresses if operation is successful; however, others routinely perform mitral anuloplasty as part of the initial operation. In older patients, mitral repair or replacement may be required (see Technique of Operation in Section I of Chapter 11).

SPECIAL SITUATIONS AND CONTROVERSIES

Anomalous Connection of Right Coronary Artery, Circumflex Coronary Artery, or Left Anterior Descending Coronary Artery to Pulmonary Trunk

An anomaly rarer than anomalous connection of left coronary artery to pulmonary trunk is anomalous connection of right coronary artery to pulmonary trunk. As of 2006, 77 cases had been reported. Undoubtedly, this lesion occurs more frequently and is underdiagnosed because of the relatively benign nature of the lesion compared with anomalous connection of the left coronary artery to pulmonary trunk (Table 46-3). Diagnosis is usually made at autopsy or incidentally in asymptomatic adults. Occasionally the anomaly is associated with symptoms in an older child or adult or with sudden death. Surgical correction consists of excising the anomalous connection of the right coronary artery to the anterior aspect of the pulmonary trunk, along with a button of pulmonary arterial wall, and translocating it into the anterior aspect of the ascending aorta.

Anomalous connection of circumflex or left anterior descending coronary artery to pulmonary trunk is also less lethal than anomalous connection of left coronary artery to pulmonary trunk. Both are also rarer than right coronary anomalous connection. Indications for surgery and technique of operation are similar to those for anomalous connection of the right coronary artery. Operation is indicated at the time of diagnosis for all these variations.

Total Anomalous Connection of Coronary Arteries to Pulmonary Trunk

Rarely, all coronary blood flow originates from the pulmonary trunk, either with a single ostium and trunk from which all branches emerge or from two ostia close together, giving rise to left and right coronary systems. In less than half the cases reported, this has been an isolated anomaly. In such cases, mitral anuloplasty or replacement may be required. Operation is indicated at the time of diagnosis for all these variations.

Table 46-3  Comparison of Anomalous Right versus Left Coronary Artery Connection to Pulmonary Trunk

<table>
<thead>
<tr>
<th></th>
<th>Right Coronary Artery</th>
<th>Left Coronary Artery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>0.002%</td>
<td>0.008%</td>
</tr>
<tr>
<td>Age at presentation</td>
<td>&gt;2 years</td>
<td>&lt;1 year</td>
</tr>
<tr>
<td>Heart failure</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Ischemia</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Sudden death</td>
<td>Rare</td>
<td>Yes</td>
</tr>
<tr>
<td>Physical exam</td>
<td>Murmur</td>
<td>Heart failure, ±systolic murmur</td>
</tr>
<tr>
<td>ECG findings</td>
<td>Nonspecific</td>
<td>Ischemia, Q waves in I and aVL &gt;80%</td>
</tr>
<tr>
<td>Reimplantation</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Modified from Williams and colleagues. Key: ECG, Electrocardiogram.
Anomalous Connection of a Main Coronary Artery to Aorta

DEFINITION
This section focuses on a condition in which (1) either the left main coronary artery connects to the aorta in a site other than the left coronary sinus or sinutubular junction (identified by the ridge between the sinus and ascending aorta), or (2) the right coronary artery connects to a site other than the right coronary sinus or sinutubular junction. The anomalously connected artery frequently passes between the aorta and pulmonary trunk (interarterial course) before normally distributing to the myocardium, commonly has a proximal course running within the aortic wall (intramural course), and occasionally has an ostial stenosis.

All these morphologic variations have been associated with ischemia and clinical events. Whether the course between the great arteries plays a pathophysiologic role in all clinical events remains controversial. The anomalously connected artery does not always pass between the aorta and pulmonary trunk but may pass in a retroaortic, pre pulmonary, or transseptal course. Rarely the anomalous artery does not arise from the opposite coronary sinus, but rather from the posterior (“noncoronary” sinus). These variations are of concern only when there is ostial stenosis or an intramural course.

HISTORICAL NOTE
Chetlin and colleagues in 1974 described death from anomalous connection of left main coronary artery to right sinus of Valsalva, with the artery then passing posteriorly between aorta and pulmonary trunk and then behind the trunk before branching into left anterior descending and circumflex arteries. In 1984, Roberts and colleagues described anomalous connection of right coronary artery to left sinus of Valsalva, with the right coronary artery passing anteriorly between the aorta and pulmonary trunk before passing across the outflow portion of the right ventricle.

MORPHOLOGY
The morphology of anomalous connection of a main coronary artery to aorta is abnormal in a number of ways beyond connection to the wrong sinus. These abnormalities have important implications with respect to both the likelihood of ischemia-related clinical events and specific surgical management.

Anomalous Connection of Left Main Coronary Artery
Most commonly, two coronary ostia are close together side by side in more or less the center of the right sinus of Valsalva. The ostium of the anomalous left main coronary may be eccentrically placed, however, often high in the right sinus and close to the right-left commissure. Less commonly, there is a single enlarged ostium in the right sinus, giving rise to both the normal right coronary and the anomalous left main coronary arteries. The ostium may have other abnormal characteristics. It may be angulated as it arises from the aorta, its opening may be slitlike, or it may travel in an intramural course, running within the wall of the aorta for up to several centimeters.

The left main coronary artery almost always passes posteriorly in an interarterial course between the aorta and pulmonary trunk, and then behind the pulmonary trunk to branch at the usual site. Much more rarely, the anomalously connecting left main coronary artery passes forward and across the floor of the right ventricle (ventricular septum) to emerge and pass near to its usual point. Also rarely, it may also pass retroaortically, or anteriorly across the right ventricular free wall. Circulation may be left or right dominant. Finally, anomalous connection of left main coronary artery to non-facing aortic sinus occurs rarely and may be associated with abnormal angulation and slitlike orifice as well.

Anomalous Connection of Right Coronary Artery
Anomalous connection of right coronary artery to aorta appears to be considerably more common than anomalous aortic origin of left main coronary artery. It may connect to a separate ostium within the left sinus, to a separate ostium just above the commissure between left and right sinuses, or to one just above the sinutubular ridge over the left sinus. Less commonly, the right coronary artery may connect to a single ostium that also gives origin to the left main coronary artery, and this ostium may lie within the left sinus or over the commissure between left and right sinuses. The anomalously connecting right coronary artery may have all the other ostial abnormalities described for the anomalously connected left main coronary artery, and always passes forward in an interarterial course between the great arteries. Rarely, one or both coronary ostia may arise from the posterior (the normal noncoronary) sinus.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA
Anomalous connection of a coronary artery to the aorta results in no characteristic clinical or ECG features. A meta-analysis using a number of reasonable assumptions suggests that more than 99% are asymptomatic and will remain so (see Natural History). The true prevalence of this defect is unknown. The most accurate estimate probably comes from a prospective search for the defect in more than 2000 children with normal hearts, in which a prevalence of 0.17% was found, or in other words, about 1 to 2 per 1000 children. Studies based on cardiac catheterization typically show similar to higher prevalence, probably because of selection bias.
Patients who are symptomatic typically present in the second or third decade of life and may complain of angina or syncope, or they may present with sudden death. Rarely, patients present with symptoms as neonates, infants, or in the first decade of life. The anomalous connection is most commonly diagnosed by echocardiography. The ECG may be indicated for other reasons in asymptomatic patients, and the anomalous vessel is identified incidentally. In symptomatic patients, an ECG is typically the initial imaging study.

The purpose of imaging the vessel is to define several clinically relevant morphologic characteristics:

1. Presence of a single ostium or separate ostia
2. Exact position of the ostium within or near the sinus
3. Presence of an intramural course
4. Identification of a slitlike or angulated ostium
5. Identification of an interarterial course, and determination of whether the caliber of the artery is narrowed in this area

Echocardiography can accurately define the ostial position and interarterial course of the vessel. It can also sometimes reveal whether there are one or two ostia and whether there is an intramural course\(^6\) (Fig. 46-16). However, this modality may have difficulty demonstrating whether there are one or two ostia when these are closely spaced, and whether there is an intramural course when that course is a short segment. Because of these limitations, further imaging is indicated.

Magnetic resonance angiography, CT, and angio- 
graphy at cardiac catheterization all have been used to further characterize the morphology, but available data are insufficient to assess whether these imaging modalities are superior to echocardiography, particularly with respect to defining an intramural course (Fig. 46-17). One study compared the accuracy of catheter-based angiography and CTA in helping determine the origin and proximal course of the anomalous artery. CT was found to be more accurate in revealing the proximal course. Accurate CT images require gating, so this modality may be of less use in smaller patients because of their faster heart rates. A search is also made for objective evidence of reversible ischemia. Documentation of compression of the right coronary artery coursing between aorta and pulmonary artery, with the right coronary artery arising from the left main coronary artery, has been demonstrated angiographically in a patient with exertional angina.\(^1\)

**NATURAL HISTORY**

The natural history is controversial. A number of cases have been reported in which serious sequelae, including sudden death, have been ascribed to anomalous connection of coronary artery to left sinus of Valsalva (summarized by Berdoff and colleagues\(^6\) and Mustafa and colleagues\(^3\)). The relationship between sequelae and anomaly is not conclusive. Asymptomatic patients with the condition were observed by Berdoff and colleagues, with a mean age of 40 to 69 years and with normal segmental wall motion and a left ventricular ejection fraction of 60% to 80%\(^6\); no unfavorable events were experienced in a follow-up of 8 to 69 months. Sudden death in neonates may occur in the presence of this defect in rare cases, but causality is difficult to prove.

There are only rare cases of clinical events in individuals once out of the neonatal period, until the second decade is reached. The combined U.S. and Italian registries of sudden deaths in competitive athletes revealed 27 individuals dying with anomalous coronary arteries; all but one death occurred between ages 10 and 32 years. The other individual was 9 years old. In two thirds of the deaths, there were no previous events and no symptoms. The prevalence of sudden death in competitive athletes is about 1 : 100,000. About 20% of these are due to coronary anomalies; thus, the prevalence of sudden death due to a coronary anomaly is about 2 : 1,000,000 in competitive athletes.

Most clinical events, including sudden death, occur in the second and third decades of life, and more commonly in males. Events are likely to occur during or just after exertion. Sudden death may be the initial event. If an individual lives into the third decade, new onset clinical events are extremely rare.

**TECHNIQUE OF OPERATION**

Several operations have been developed to relieve ischemia or potential ischemia. The choice of operation depends on the specific morphologic details, emphasizing the importance of accurate preoperative imaging (Fig. 46-18). Translocation of the anomalously connected artery to the correct sinus is indicated in several circumstances. This operation can usually be accomplished and will be effective when there are two reasonably widely spaced ostia, and when there is not an intramural course or angulated or slitlike ostium. The operation effectively removes the vessel from its vulnerable interarterial position. The technique of operation requires standard CPB and cardioplegic arrest. The coronary artery is dissected, mobilized, and translocated using the exact principles outlined for coronary translocation in the arterial switch operation for transposition (see Chapter 52).

Unroofing the proximal coronary artery is indicated when an intramural course is present (Fig. 46-19). This maneuver may be all that is necessary if the unroofing moves the effective ostium into the appropriate sinus. This
accomplishes two things: It relieves any stenosis in the intramural segment, and it moves the coronary lumen away from the interarterial position. Unroofing can be accomplished whether or not there is a single coronary ostium or separate ostia. Modified unroofing can be performed in some cases to avoid disturbing the commissure of the aortic valve. In this case, as in the arterial switch operation, care must be taken to excise the ostium with a button of sinus tissue that fully encompasses the intramural component. Also, in certain cases with an angulated or slitlike ostium but no true intramural element, ostial patching should be performed along with translocation.

When the morphology is that of a single coronary ostium without an intramural element, neither translocation nor
unroofing is possible. The goal of surgery is to eliminate the risk of the interarterial component of the vessel. CABG using the internal thoracic artery or a saphenous vein graft to the anomalously connected artery has been described. This option, however, is not recommended for several reasons. First, the long-term efficacy of the graft is uncertain in young patients. Second, the graft will be in competition with essentially normal antegrade flow through the anomalously connected artery, raising concern about graft thrombosis or, at the very least, adequacy of the graft when it may be acutely needed during transient compression of the anomalously connected artery. Instead of bypass grafting in this situation, moving the pulmonary trunk away from the aortic root so that the interarterial component of the anomalously connected artery is no longer at risk of compression should be considered. This can be accomplished in two ways, either translocating the distal pulmonary trunk leftward into the left pulmonary artery (Fig. 46-21), or translocating the right
pulmonary artery branch anterior to the aorta (Fig. 46-22), similar to the Lecompte maneuver in the arterial switch operation for transposition (see Chapter 52).

RESULTS

Early and midterm outcomes are generally excellent regardless of the specific operation, with mortality approaching zero and relief of symptoms in patients who are symptomatic preoperatively. Romp and colleagues report no mortality and relief of symptoms in nine previously symptomatic patients, all of whom underwent unroofing of an intramural artery. Of concern, however, despite lack of postoperative symptoms in 24 repaired patients, Brothers and colleagues were able to demonstrate signs of ischemia in almost 40% of patients evaluated with stress echocardiography, exercise stress testing, and stress myocardial perfusion scanning at a mean follow-up of 15 months after surgery. This same group of investigators also report that exercise capacity and quality of life were normal following surgical repair.

Indications for operation remain arguable. Ischemia, whether reversible or not, in the distribution of the anomalously connecting coronary artery is an indication for operation. A syncopal event, angina, or an episode of sudden death with resuscitation is an indication for operation, even if ischemia cannot be demonstrated at evaluation. In fact, ischemia typically is not elicited with stress testing.

Concerning morphology, such as intramural course, slit-like ostium, or narrowed caliber of the interarterial course, is probably an indication for operation, even in the absence of demonstrable ischemia. Existence of the anomalous connection with an interarterial course, but without symptoms and without other concerning morphologic characteristics, may be an indication for operation in individuals diagnosed in the second and third decades of life but probably not in those diagnosed later. Presence of the anomalous connection without ischemia, symptoms, or concerning morphologic characteristics is probably not an indication for operation in the first decade of life. Effectiveness of operation can be proved by absence postoperatively of any evidence of reversible ischemia.

SPECIAL SITUATIONS AND CONTROVERSIES

Presence of an anomalously connected vessel without other concerning morphologic characteristics in an asymptomatic child under age 10 years is probably not an indication for operation, but it is unclear whether such a patient should undergo operation once the second decade is reached if no clinical events have occurred. A survey of the Congenital Heart Surgeons Society regarding management practices underscores the marked heterogeneity of opinion regarding management of anomalous coronary arteries. There was strong but not unanimous agreement that evidence of ischemia warranted surgery. Less than 80% recommend referral for surgery with symptoms but no objective evidence of ischemia.

There is no consensus regarding the pathophysiologic importance of the interarterial course, especially when no narrowing of the vessel can be demonstrated in this area during imaging. The concern is that this region of the vessel
is at risk of transient narrowing or stretching during the dynamic conditions of exercise, when the wall tension of both the aorta and pulmonary trunk may increase from pressure and diameter changes. Although not recommended in young patients, use of interventional catheter-based techniques, including coronary artery stenting, has been anecdotally described for various coronary artery anomalies. These procedures are typically performed in previously undiagnosed adults who present with evolving acute myocardial events at the time of diagnostic, and potentially therapeutic, cardiac catheterization. CABG is also not recommended in young patients; however, it becomes a more attractive surgical option in older patients, particularly those presenting with symptoms or with associated arteriosclerotic disease. Excellent outcomes can be achieved. Brothers and colleagues have shown that familial screening in patients with anomalous coronaries yielded positive findings not attributable to chance alone, suggesting a genetic component for this disease.

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Congenital aortic stenosis is a cardiac anomaly in which narrowing at valvar, subvalvar, supravalvar, or combined (multiple) levels results in a systolic pressure gradient between the inflow portion of the left ventricle (LV) and the aorta beyond the obstruction. A spectrum of defects involves the aortic root, with some overlap of abnormalities. Congenital aortic stenosis in neonates and infants may be part of the constellation of hypoplastic left heart physiology (see “Coarctation as Part of Hypoplastic Left Heart Physiology” under Morphology in Section I of Chapter 48). This association is highly relevant to therapy.

Section I  Congenital Valvar Aortic Stenosis

DEFINITION

Congenital valvar aortic stenosis includes defects in which the major malformation involves the aortic valve cusps. An obstruction at valve level is caused by imperfect cusp development with cusp thickening and fusion. Cusp abnormalities can be severe in early life; when they are not, important obstruction may not develop until later in life when calcification occurs. This chapter discusses congenital valvar aortic stenosis only in the age range from birth to young adult life.

HISTORICAL NOTE

Congenital valvar aortic stenosis has been long recognized by morphologists. Initial efforts to find a surgical solution were made by Carrel and Jeger, who independently attempted experimentally to place conduits between left ventricular apex and aorta. In 1955, Marquis and Logan reported surgical treatment using dilators introduced through the LV apex, as did Downing in 1956. Also in 1956, valvotomy was performed by an open technique during inflow stasis with moderate hypothermia induced by surface cooling. The first report of its treatment by accurate valvotomy during cardiopulmonary bypass (CPB) was by Spencer and colleagues in 1958, although this had been performed at the Mayo Clinic in 1956 and was reported by Ellis and Kirklin in 1962.

MORPHOLOGY

Aortic Valve

The prevalences and precise nature of the various types of morphology of severely stenotic aortic valves and coexisting anomalies are incompletely understood for several reasons. First, it is difficult to obtain enough cases to constitute a reasonable sample of the spectrum of severe congenital valvar stenosis in neonates, infants, and children. Second, sources of data range from autopsy studies and surgical studies to echocardiographic and cineangiographic imaging in patients undergoing balloon valvotomy. Third, differing terminology contributes to incompleteness of morphologic data; ideally, not only should the morphologic nature of the cusps be defined, but also that of the sinuses of Valsalva, commissures (upper points of attachment of cusps to the aortic wall), and interleaflet triangles (fibrous or muscular tissue interposed between the sinuses in the subcusp LV outflow tract), as described by Angelini and colleagues for bicuspid valves.

In patients with stenosis severe enough to require operation in infancy or childhood, the valve is bicuspid in about 65% (Table 47-1). The valve usually consists of thickened...
stenosis can occur without fusion, resulting only from thickened cusps and a bicuspid configuration. If free edges of both thickened cusps are taut, they are then equal in length to the diameter of the aortic root and cannot open (Fig. 47-1, B). Most bicuspid valves will show three intercusp triangles on their ventricular side, indicating that three cusps were present in the developing valve. A bicuspid valve with only two definitive cusps is uncommon and usually is not stenotic early in life, rather presenting later in life with obstruction or regurgitation. A full discussion of the genetics, morphology, natural history, and therapeutic options for adult patients with a congenitally bicuspid aortic valve is found in Chapter 12.

In about 30% of patients the valve is tricuspid, with three thickened cusps of approximately equal size and three recognizable commissures that are fused peripherally to varying degrees, creating a dome with a central stenotic orifice. This type of valve is more favorable for valvotomy because all three commissures can usually be opened.

Less often (5%) the valve may have a unicuspid configuration with only one commissure (Fig. 47-2). This variety is more common in infants presenting with severe stenosis. Occasionally, however, the stenosis is not severe, and signs and symptoms develop in later life as the valve thickens and calcifies. A thickened unicuspid valve is inherently stenotic, whether the commissure is fused or not, unless the cusp is particularly redundant.

The cusps are approximately equal in size in only a small percentage of congenitally bicuspid or stenotic tricuspid valves. Likewise, the raphae are variable in thickness and length. Number of sinuses may not be the same number of cusps; most congenitally bicuspid and unicuspid (unicommissural) valves have three sinuses and three intercusp triangles.

Diffuse cusp thickening, most marked at the free cusp edges, contributes importantly to valvar stenosis. Thickening is more extreme in symptomatic neonates and infants, and cusps may be irregular and myxomatous or dysplastic in

<table>
<thead>
<tr>
<th>Valve</th>
<th>No.</th>
<th>% of 290</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicuspid</td>
<td>186</td>
<td>64</td>
</tr>
<tr>
<td>Tricuspid</td>
<td>89</td>
<td>31</td>
</tr>
<tr>
<td>Unicuspida</td>
<td>15</td>
<td>5</td>
</tr>
<tr>
<td>TOTAL</td>
<td>290</td>
<td>100</td>
</tr>
</tbody>
</table>

Data from Elkins and colleagues, 1960-1996.

Frequency may be underestimated because “bicuspid” valve with rudimentary commissures might better be termed unicuspid.

Table 47-1  Morphology of Congenital Valvar Aortic Stenosis in Surgical Patients Aged 1 Day to 26 Years
Shortness of breath and cyanosis may be present. In children and young adults, even important stenosis may be without symptoms. However, effort dyspnea, effort angina, or effort syncope, singly or in combination, usually indicates a severe lesion.

Dyspnea may be present with moderate stenosis.

**Signs**

In neonates and infants with severe valvar aortic stenosis, the most striking feature is small pulse volume with pallor, dyspnea, and at times cyanosis. Both the murmur and gradient across the valve may be unimpressive because of a low cardiac output. There also may be a hyperactive right ventricular impulse.
Clinical signs in children and young adults include an ejection systolic murmur (and thrill) at the base radiating to the carotid vessels, accompanied by a systolic ejection click. An aortic diastolic murmur is uncommon, particularly when compared with patients with discrete subvalvar stenosis. A severe lesion is characterized by palpable pulse of low volume and slow upstroke, single or reversed splitting of second heart sound, and sometimes third heart sound, and thrusting LV impulse.

Many investigators have concluded that physical signs are unreliable in assessing severity of valvar stenosis in children. However, physical signs can be used to differentiate among mild, moderate, and severe lesions in most patients, and severe lesions can always be distinguished from mild ones.

Electrocardiography

The electrocardiogram (ECG) usually shows severe LV hypertrophy but can be near normal. Right ventricular hypertrophy on the ECG may be associated with a left-to-right shunt at atrial level through a stretched patent foramen ovale and rarely a reversed shunt at ductus level.

Chest Radiography

The ascending aorta frequently is prominent in older children but is small in neonates and infants. Increased heart size is seldom seen except in neonates and infants in heart failure, in whom it may be marked. Radiologically demonstrable valvar calcification is rare in patients younger than age 25.

Noninvasive Studies

Two-dimensional echocardiography has become particularly important as a diagnostic tool. In neonates and infants, morphology and severity of narrowing of the valve and size, wall thickness, and contractility of the LV can be assessed. The congenitally stenotic aortic valve can be continuously reevaluated by Doppler ultrasound measurement of flow velocity across stenotic valves, which can be used to quantify transvalvar pressure gradient. Echocardiographic markers are useful for managing fetuses with important aortic stenosis. Serial measurements of fetal cardiac size and function may predict postnatal outcome.

Estimation of subendocardial oxygen requirements may be helpful in assessing severity of stenosis.

Cardiac Catheterization and Angiography

A systolic gradient across the aortic valve can be demonstrated at cardiac catheterization, usually through a retrograde aortic approach if possible or otherwise a transseptal approach. Cardiac output can also be measured so that valve area can be calculated. Systolic gradient greater than 75 mmHg or valve area less than 0.5 cm$^2$ is indicative of severe stenosis (see “Summary” in text that follows). Measuring gradient and valve area at cardiac catheterization has become less important as echocardiographic measurements have become more accurate. A raised LV end-diastolic pressure indicates LV failure or a fibrotic and noncompliant ventricle.

Angiography demonstrates thickened leaflets that form a dome in systole, with a localized jet of contrast entering the aorta (Fig. 47-6). Although this type of study is not reliable in assessing severity of stenosis, it can assess size of the aortic “anulus” and LV. An aortic root injection allows quantification of aortic regurgitation if present.

Summary

By a combination of clinical and hemodynamic assessments (echocardiography, cardiac catheterization), patients with congenital valvar aortic stenosis can be categorized as having mild, moderate, or severe obstruction. Mild implies that pulse volume and contour are normal, as is the second heart sound. Patients with these findings have an LV-aortic systolic pressure difference less than 40 mmHg at rest, with a mean of 20 mmHg. Patients with moderate stenosis have an

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**Table 47-2 Coexisting Cardiac Anomalies (Previously or Concurrently Repaired or Left Unrepaired) in Surgical Patients with Congenital Aortic Stenosis**

<table>
<thead>
<tr>
<th>Type of Stenosis</th>
<th>Associated Anomaly</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valvar ($n = 78$)</td>
<td>Isolated PDA</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>PDA + ASD</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>PDA + coarctation</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Isolated coarctation</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Isolated VSD</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>PDA + coarctation + VSD</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Left SVC</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>20 (26%)</td>
</tr>
<tr>
<td>Subvalvar ($n = 41$)</td>
<td>Isolated PDA</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>PDA + coarctation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Coarctation + congenital mitral stenosis</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>VSD + important PS</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Unroofed coronary sinus syndrome</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Left SVC + single coronary orifice</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>AR (3 mild, 2 important)</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>VSD</td>
<td>4</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>18 (44%)</td>
</tr>
<tr>
<td>Supravalvar ($n = 10$)</td>
<td>Pulmonary artery stenosis</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Left SVC</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Combined ($n = 7$)</td>
<td>PDA + coarctation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Congenital mitral stenosis</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>VSD</td>
<td>1</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>3 (43%)</td>
</tr>
</tbody>
</table>

*Data from 142 patients, UAB experience 1967-1982. Categories are mutually exclusive. Numbers in parentheses are percentages of the n of the type. Key: AR, Aortic regurgitation; ASD, atrial septal defect; PDA, patent ductus arteriosus; PS, pulmonary stenosis; SVC, superior vena cava; VSD, ventricular septal defect.*
abnormally small pulse volume on palpation and abnormal contour, and narrow inspiratory splitting of the second heart sound may be present. Such patients generally have systolic gradients less than 75 mmHg, with a mean of 20 to 50 mmHg. Patients with severe stenosis have a systolic gradient in excess of 75 mmHg and an abnormal pulse volume and contour, as well as a single second heart sound or reverse splitting. These patients have a mean calculated aortic valve area index of less than 0.5 cm² · m⁻².¹¹³

NATURAL HISTORY

Congenital valvar aortic stenosis is three to four times more common in males than in females and occurs in about 5% of Caucasians with congenital heart disease.

<table>
<thead>
<tr>
<th>Age at Operation</th>
<th>NYHA Functional Class (mean ± SD)²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Valvar (n = 78)</td>
</tr>
<tr>
<td>Weeks</td>
<td></td>
</tr>
<tr>
<td>≤ 1</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4.8 ± 0.45</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Months</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.0 ± 1.26</td>
</tr>
<tr>
<td>3</td>
<td>2.2 ± 0.98</td>
</tr>
<tr>
<td>Years</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1.7 ± 0.73</td>
</tr>
<tr>
<td>12</td>
<td>1.9 ± 0.74</td>
</tr>
</tbody>
</table>

¹Data from 142 patients, UAB experience 1967-1982.
²Patients were categorized into NYHA classes I to V, with class V indicating those undergoing emergency operation because of shock or metabolic acidosis. In the current era, isolated valvar aortic stenosis in newborns and infants is generally treated by percutaneous balloon valvotomy.

Presentation in Infancy

When neonates and infants present with valvar stenosis, the lesion is typically severe, with rapidly progressive heart failure and death within a few days to a few weeks of birth. Thus, most neonates and young infants come to intervention (currently with percutaneous balloon valvotomy) critically ill and in New York Heart Association (NYHA) class IV or V (Table 47-3). Many have other anomalies associated with the spectrum of the hypoplastic left heart physiology. Ten Harkel and colleagues noted a 5-year survival rate of 73% among patients presenting in infancy.⁷²

Presentation in Childhood

When symptoms are delayed beyond age 1 year, heart failure is rare, and survival without treatment generally is prolonged. Also, associated anomalies are less common. The Second Natural History Study of Congenital Heart Defects includes data on many patients treated for valvar aortic stenosis and followed for 25 years. Patients were 2 years or older at entry into the study, and 40% managed medically subsequently required surgical management. For patients presenting with LV-aortic pressure gradient greater than 50 mm Hg, 70% required surgical intervention. Almost 40% of patients required a second operation.

Survival is related to (1) sudden death in untreated children and (2) rate of progression of stenosis.

Sudden Death

Occurrence of sudden death varies between 1% and 19% of patients. Of 58 patients younger than 35 years old who died suddenly and were found to have congenital heart disease, three (5%) had aortic valve stenosis. Analysis of the literature and of a series of 218 patients with congenital valvar stenosis indicates that sudden death directly attributable to aortic stenosis is virtually confined to patients with a severe lesion. Sudden death in patients with no symptoms and normal physical findings except for the murmur of aortic stenosis has not been documented. Sudden death may occur...
in patients with a normal ECG, but this finding is not incompatible with severe stenosis. Thus, the true prevalence of sudden death in children and adolescents in whom surgery is deferred until the lesion is considered severe on clinical grounds is probably about 1%.

**Progression of Stenosis**

When congenital aortic valvar deformities are nonobstructive in infancy and childhood, less than 10% progress to mild obstruction within about 10 years. Leech, Mills, and colleagues obtained information on 26 patients aged 1 week to 29 years when first seen, and in whom diagnosis of nonobstructive aortic valve deformity was made based on an isolated aortic ejection sound. During a 5- to 16-year follow-up, two patients (7%; CI 2%-16%) developed signs of mild stenosis after 7 and 15 years. As more years pass, an undetermined time-related proportion of patients with deformed (usually congenitally bicuspid) aortic valves develop progressive thickening and calcification and ultimately important stenosis. Vollebergh and Becker suggest that minor inequality of size of tricuspid valves present from birth may lead to formation of senile or degenerative type of aortic valve stenosis presenting in the seventh or eighth decade of life.

When *mild* stenosis is present at first evaluation in childhood, progression is more rapid. Moderate or severe stenosis develops in about 20% of patients within 10 years and in 45% within about 20 years (Fig. 47-7). Even after this long interval, therefore, 55% of the mild lesions remain mild.

When *moderate* stenosis is present initially, the lesion becomes severe within 10 years in about 60% of patients (Fig. 47-8).

**Infective Endocarditis**

Spontaneously occurring infective endocarditis appears in less than 1% of patients. The reported incidence is 1.8 to 2.7 episodes per 1000 patient-years. Infective endocarditis may produce aortic regurgitation and may be a cause of death.

---

**Figure 47-7** Cumulative incidence curves (multiple decrement; see “Competing Risks” in Section IV of Chapter 6) for 153 patients presenting with originally mild congenital valvar aortic stenosis. Vertical bars represent 70% confidence limits. Mean age at presentation was 6.5 years (1 to 25 years) and mean follow-up 8.8 years (1 to 26 years). The one death was caused by infective endocarditis. Patients underwent operation when stenosis was considered severe. Percentages refer to distances between curves. Key: AS, Aortic stenosis. (From Hossack and colleagues.)

**Figure 47-8** Cumulative incidence curves for 54 patients presenting with originally moderate congenital valvar aortic stenosis (AS). Vertical bars represent 70% confidence limits. Mean age at presentation was 12 years (1–25 years) and mean follow-up 8.5 years (1–24 years). The two deaths were both sudden, in 4 and 9 years after presentation, in association with progression to severe stenosis. Percentages refer to distances between curves. (From Hossack and colleagues.)

**TECHNIQUE OF OPERATION**

**Percutaneous Balloon Valvotomy**

Percutaneous balloon valvotomy is often used for treating congenital valvar aortic stenosis, but a description of this technique is beyond the scope of this text. Its place in treating neonates is discussed under Special Situations and Controversies later in this section.

**Valvotomy in Neonates and Critically Ill Infants**

Closed techniques and surface cooling for hypothermic circulatory arrest have largely been replaced by aortic valvotomy on CPB using cold cardioplegic myocardial management.

Anesthetic and supportive management must be precise (see Section II of Chapter 4). Drifting downward of body temperature to 32°C to 34°C is probably advantageous. Preparation and median sternotomy are described under “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2. As the pericardium is being opened, care is taken to touch the heart as seldom as possible because ventricular fibrillation is easily provoked. The purse-string suture is placed for the aortic cannula, the patient heparinized, and the cannula inserted and connected to the arterial tubing. Only then is a purse-string suture placed around the right atrial appendage; if the heart fibrillates, CPB can be established in less than a minute. A single venous cannula is inserted, and CPB is begun with the perfusate at 34°C; the ductus arteriosus is ligated, perfusate taken to 20°C to 28°C, aorta clamped, cold cardioplegia administered, and the perfusate temperature is then taken to 34°C to 36°C. In the presence of aortic regurgitation to a degree that interferes with cardioplegia delivery, cardioplegia can be delivered via small olive tip catheters directly into the coronary ostia, or coronary sinus cardioplegia can be used.
A transverse aortotomy is made (Fig 47-9, A). Two stay sutures are placed on the upstream side of the aortotomy for exposure. The aortic valve is inspected to determine which of the commissures to incise. Only partially formed commissures should be incised; commissurotomy should not be performed where there is only a rudimentary raphe (Fig. 47-9, B).

Valvotomy is performed by dividing fused commissures with a knife to within 1 mm of the aortic wall; in neonates the cusps are often gelatinous, but every effort should be made to identify these commissures. It is important that even tension be placed on the two adjoining cusps so that incision is precise (Fig. 47-9, C). Only commissures with adequate cusp/commissural attachment to the aortic wall are opened, because division of rudimentary commissures produces regurgitation. Incisions are deepened in stages, and cusps on each side are evaluated for competence and lack of prolapse before each further incision. If further incising of the commissure might cause cusp prolapse, the incision is carried no further. Occasionally, myxomatous nodules can be excised from the cusp’s free edge, or fibrous thickening can be shaved off the ventricular aspect of one or more cusps. The aortotomy is then closed with a continuous suture. If there is any degree of aortic regurgitation by saline filling of the aortic root, a 6-0 polypropylene suture (Frater stitch) can be placed through the midpoint of each cusp and brought out through the closed aortotomy. The suture is removed when LV contraction begins.

The remainder of the procedure is completed as usual (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). A left atrial catheter should be positioned before discontinuing CPB. If the neonate is of suitable size for placing a transesophageal echocardiography (TEE) probe, the repair is evaluated before and after discontinuing CPB. LV and aortic pressures are measured and recorded before closing the chest.

Valvotomy in Older Infants, Children, and Adults

Preparation for operation, the incision, and preparations for CPB are described under “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2. Using a single venous cannula or caval cannulation, CPB is established at 28°C. A left atrial or LV vent is used. External cardiac cooling may be applied. The aorta is clamped and cold cardioplegic solution infused. The transverse aortotomy is made, and stay sutures are applied to the edges of the incision for exposure. Commissurotomy is performed as described.

The aortotomy is closed by continuous stitches, and the rest of the operation is completed as usual (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).
Cusp Reconstruction

Pericardial cusp extension valvuloplasty procedures (as described by Duran) to compensate for deficiency of valvar tissue and increase the coaptation surface area have been applied primarily to regurgitant aortic valves (see Chapter 12). More recently, encouraging midterm results with these techniques applied to congenital aortic stenosis support their inclusion as surgical options. Aortic cusp extension valvuloplasty may be considered as an adjunctive procedure to primary open valvotomy or in reoperative situations with recurrent aortic stenosis or regurgitation following previous valvotomy. Before proceeding with valve reconstruction, pre-operative echocardiographic studies should ascertain the absence of LV subaortic obstruction.

Following a median sternotomy, autologous pericardium is harvested, thoroughly cleaned of all fatty tissue and adhesions, treated with 0.625% glutaraldehyde solution for 3 to 5 minutes, and kept moist with normal saline. CPB, LV venting, and myocardial management are performed as described under “Valvotomy in Older Infants, Children, and Adults.”

An oblique aortotomy is made, and the aortic valve is evaluated for presence of complete but fused commissures and a raphe in congenitally bicuspid aortic valves. Each cusp is examined for thickness and mobility, free-edge irregularities, and tissue deficiency.

The valve is prepared for cusp extension by first thinning the thickened cusp edges. Fused commissures are incised out to the aortic wall, and subcommissural fusion or scar tissue is released to maximize cusp mobility. Bicuspid valves with a rudimentary raphe are tricupidized by incising through the fused cusp at the raphe all the way to the aortic wall (Fig. 47-10). The pericardial patches are each cut to a length determined by the diameter of the aorta, supplemented with an additional 15% to 20% to account for later pericardial shrinkage. Height of each patch is chosen to extend the line of coaptation of the repaired cusps about 5 mm higher than the highest cusp and to bring the extended cusps into a coaptation point in the center of the valve orifice. The pericardial extensions are sutured to each cusp with continuous 5-0 polypropylene, beginning in the center of the cusp and working toward the commissures. The extensions are attached to the aortic wall, creating neo-commissures at the level of the sinutubular junction. Ilbawi and colleagues recommend leaving a little excess pericardial patch at the commissural level, secured with a pledgeted mattress suture through the aortic wall. With all the patch extensions in place, the newly constructed extensions are trimmed to provide a uniform cusp height and symmetric coaptation surface (see Fig. 47-10).

Adequacy of the valve opening is examined, and initial valve competence is assessed by filling the aortic root with saline. Aortotomy closure and discontinuation of CPB are conducted as usual. Evaluation of valve function by TEE is performed before and following discontinuation of CPB. If aortic regurgitation is more than mild or if peak transvalvar gradient by TEE exceeds 30 mm Hg, consideration should be given to reestablishing CPB and revising the valve repair or, if improvement is not feasible, proceeding with valve replacement.

Aortic Valve Replacement in Children

When viewed at operation, the congenitally stenotic aortic valve may be too extensively deformed to be opened and remain reasonably competent. However, this situation is rare in primary operations in patients younger than age 10 and uncommon in those younger than 20. It is more common when multiple prior balloon valvotomies have been performed, and particularly when progressive or recurrent stenosis is accompanied by moderate or worse aortic regurgitation.

Aortic valve replacement in older children may be done in a standard fashion using a mechanical prosthesis (see “Isolated Aortic Valve Replacement” under Technique of Operation in Chapter 12). It may also be performed in the standard freehand manner using an aortic valve allograft (see “Allograft Aortic Valve” under Technique of Operation in Chapter 12) or a pulmonary valve autograft (see “Autograft Pulmonary Valve” under Technique of Operation in Chapter 12). Because the aortic root and LV-aortic junction may be quite small in young children who require aortic valve replacement, aortic root enlargement (see “Root-Enlarging Technique” under Technique of Operation in Chapter 12) or replacement (see “Replacement of Aortic Valve and Ascending Aorta, En Bloc” under Technique of Operation in Chapter 12) may be advantageous. An aortic allograft can be used as the replacement device, or a pulmonary autograft may be preferred. The autograft has the advantage of remaining unchanged and uncompromised by host reaction, and it also may grow.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Postoperative care after aortic valvotomy or other procedures discussed in this section are conducted in the manner generally used after intracardiac operations (see Chapter 5).

Whenever valvotomy is performed for congenital valvar aortic stenosis, long-term follow-up is indicated because of possible recurrence of stenosis requiring reoperation.

RESULTS

Early (Hospital) Death

Hospital mortality for surgical treatment of congenital valvar aortic stenosis in heterogeneous groups of patients younger than 20 to 25 years of age is largely an unhelpful value because of the important role of incremental risk factors for death and the selection processes by which treatments (or no treatments) are chosen.
Mortality varies widely among patient subsets, with few or no deaths after valvotomy in children and young adults.\(^5,17,79\) Mortality is higher in neonates, but the potential safety of an open approach in neonates with severe congenital aortic stenosis has been demonstrated.\(^7,19\) Still, the current preference in most centers is initial percutaneous balloon valvotomy. Multiple centers have achieved hospital mortalities of 15% or less in neonates.\(^51,28,15,20,3,78\) Again, however, mortality figures in heterogeneous groups of patients, even if all are neonates, are difficult to interpret, as demonstrated by Gaynor and colleagues\(^15\) and a Congenital Heart Surgeons’ Society (CHSS) analysis.\(^14\) In contrast to many situations in cardiac surgery, nearly all deaths after operation for congenital valvar aortic stenosis occur early postoperatively, most within 48 hours.

Success in salvaging such patients with emergency temporary extracorporeal membrane oxygenator (ECMO) or left ventricular assist device (LVAD) support has not been fully evaluated, but such support is advisable in the face of progressive circulatory failure (see “Treatment of Low Cardiac Output” in Chapter 5).

Hospital mortality after operations for congenital valvar aortic stenosis in patients older than age 1 year approaches zero.

**Time-Related Survival**

Overall survival up to 40 years is good after the primary operation for congenital valvar aortic stenosis in older infants and children.\(^38,79\) In very ill neonates and young infants, however, survival is compromised, primarily by high early risks.\(^7\)

A CHSS study of 320 neonates with critical aortic stenosis noted 1- and 5-year survival of 72% and 70%, respectively, among those receiving an initial procedure aimed at biventricular repair (Fig. 47-11).

**Modes of Death**

Almost all early deaths are in acute cardiac failure,\(^15\) and theoretically most should be preventable by (1) stabilization of critically ill neonates and others (with ECMO or LVAD support if needed) so that operation is not performed in NYHA class V patients as it was in the past,\(^12\) and (2) proper myocardial management. In neonates and young infants, however, many deaths result from (1) failure to appreciate the importance of coexisting components of the spectrum of the hypoplastic left heart physiology (see “Coarctation as Part of Hypoplastic Left Heart Physiology” under Morphology in Section I of Chapter 48), and (2) nonoptimal selection, in particular of a biventricular pathway rather than a single-ventricle pathway, at least in the present state of knowledge (see Indications for Operation later in this section).\(^14\)

Deaths occurring late after operation are in various modes, and inferences are made with difficulty. Thus “sudden death” has been reported as the mode of death in 12% of patients included in one long-term follow-up study, but the majority had severe residual or recurrent stenosis or severe aortic regurgitation.\(^1,14\) Among neonates for whom staging of repair is necessary for a univentricular pathway, few late deaths now occur between the cavopulmonary shunt stage and completed Fontan.\(^14\)

**Incremental Risk Factors for Premature Death**

**Coexisting Severe Left-Sided Cardiac Anomalies**

Left-sided cardiac defects (components of the spectrum of the hypoplastic left heart physiology, such as small aortic valve diameter, aortic hypoplasia, severe endocardial fibroelastosis, LV hypoplasia, extreme LV hypertrophy with small cavity size, and congenital mitral valve disease\(^22\)) are associated with high mortality after operation.\(^3,7,14\) (Table 47-4). These coexisting major cardiac anomalies, poor preoperative functional class, and young age at admission tend to occur together, and all are risk factors.

The important study by Karl and colleagues from Melbourne, Australia, emphasized the major role of these coexisting important cardiac anomalies in the early postsurgical mortality in neonates.\(^23\) No deaths (0%; CL 0%-19%) occurred after open valvotomy in neonates with no coexisting anomaly or only a patent duc tus, whereas early mortality was 47% (CL 39%-62%) among those with important coexisting cardiac anomalies.
Table 47-4  Incremental Risk Factors for Time-Related Death in Neonates with Critical Aortic Stenosis for Intended Biventricular Repair and for Initial Norwood Procedure

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Coefficient ± SE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Intended Biventricular Repair</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Higher Grade of endocardial fibroelastosis&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.53 ± 0.23</td>
<td>.02</td>
</tr>
<tr>
<td>Lower Aortic valve diameter z score at level of sinuses of Valsalva</td>
<td>0.36 ± 0.109</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Younger Age at entry&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.49 ± 0.53</td>
<td>.005</td>
</tr>
<tr>
<td><strong>Initial Norwood Procedure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smaller Diameter of ascending aorta&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.95 ± 0.40</td>
<td>.02</td>
</tr>
<tr>
<td>Presence of moderate or severe tricuspid regurgitation</td>
<td>0.86 ± 0.43</td>
<td>.05</td>
</tr>
</tbody>
</table>

Data from Lofland and colleagues.<sup>114</sup>
<sup>a</sup>Single early hazard phase (see Fig. 47-11, 8).
<sup>b</sup>Graded subjectively by echocardiographic appearance of left ventricular endocardial brightness and thickness: 0, None; 1, involvement of papillary muscles only; 2, papillary muscle with some endocardial surface involvement; 3, extensive endocardial surface involvement.
<sup>c</sup>Inverse transformation.
<sup>d</sup>Logarithmic transformation.

Poor Preoperative Functional Class

Advanced symptoms, or NYHA class IV and particularly class V, are associated with a considerably increased risk of death early after operation. Thus, for patients preoperatively in NYHA class I or II (most older infants and children), 15-year survival (all deaths, including those in hospital) after the primary valve operation is about 90%.<sup>44,87</sup> In preoperatively very ill neonates and young infants, 10-year survival is about 30%.<sup>83</sup> However, the risk of death in the constant hazard phase (after about 5 years postoperatively) is no greater in this group than in older patients.

These ideas came from an era when critically ill neonates and young infants were not resuscitated preoperatively by the infusion of prostaglandin E<sub>1</sub> (PGE<sub>1</sub>). This risk factor can be neutralized at a cost of only about 5% mortality among neonates by management that includes stabilization on PGE<sub>1</sub> and usually low-dose inotropic support.<sup>82</sup>

Type of Congenital Valvar Aortic Stenosis

In a few patients, a truly unicuspid or severely dysplastic bicuspid valve may be essentially uncorrectable.<sup>57</sup> In a few patients, the very small aortic anulus may prevent a satisfactory outcome. Again, these situations usually are found in very sick neonates and young infants. Currently such patients typically are managed by a staged protocol leading to a univentricular repair.<sup>134</sup>

Young Age

Very young age at operation is associated with a high risk of early death postoperatively.<sup>17,14,87</sup> However, in the past, most patients coming to operation as neonates have been in NYHA functional class IV or V. It is important to recall, however, that with contemporary medical management, survival after operation is possible in critically ill neonates and young infants.<sup>81,87,62,23,23,13,14,76,76</sup>

Table 47-5  Preoperative Functional Class and Functional Class When Last Traced Postoperatively in Patients Undergoing Primary Operation for Congenital Valvar Aortic Stenosis<sup>47</sup>

<table>
<thead>
<tr>
<th>Follow-up NYHA Class</th>
<th>Preoperative NYHA Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>I</td>
<td>22</td>
</tr>
<tr>
<td>II</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
</tr>
<tr>
<td>Dead</td>
<td>0</td>
</tr>
<tr>
<td>Uncertain</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>22</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data from 78 patients, UAB experience 1967-1982. Key: NYHA, New York Heart Association.

Functional Status

Most surviving patients, including those who have had reoperations, are in NYHA class I or II (Table 47-5). Objective evidence of improvement in functional capacity is provided by Whitmer and colleagues, who demonstrated marked regression of exercise-induced ST depression 1 year after operation, as well as an increase in mean total work and peak exercise systolic blood pressure.<sup>57</sup>

Electrocardiographic Changes

ECG evidence of LV hypertrophy may persist after valvotomy or valve replacement either because of residual stenosis or regurgitation or a progressive secondary cardiomyopathy. Intraoperative damage to the LV or preexisting ischemic myocardial fibrosis exacerbated by delaying operation can contribute to or cause this condition.<sup>57,225</sup> Usually, however, LV hypertrophy is reversible.

Left Ventricular Morphology and Function

Preoperative inordinate LV hypertrophy and wall thickness often found in children with congenital valvar aortic stenosis often regresses after successful valvotomy or valve replacement, which reduces LV afterload and increases systolic function.<sup>61</sup>

Residual or Recurrent Left Ventricular–Aortic Pressure Gradients

Pressure gradient usually is substantially reduced after valvotomy and persists for 5 to 10 years.<sup>31,35,318</sup> Thereafter, the gradient tends to rise steadily, occurring earlier and more frequently when valvotomy was necessary during the neonatal period or in infancy.<sup>57</sup> In patients with a good initial result, the later rise in gradient is mainly the result of progressive cusp immobility and calcification.<sup>81</sup> Recurrence and progression of LV-aortic pressure gradient is usually an indication for reintervention with either percutaneous balloon valvotomy or operation.

Following aortic cusp extension procedures with autologous pericardium, long-term durability of repair has been incompletely studied. Alsoufi and colleagues have...
emphasized the importance of satisfactory relief of aortic stenosis at the time of operation. Among 22 children who underwent this procedure, those with postoperative peak echocardiographic gradients of less than 30 mmHg had stabilization of their peak gradient over the next 2 to 3 years. However, progressive worsening of aortic stenosis was noted in those with early gradients exceeding 30 mmHg (moderate or greater aortic stenosis).

Aortic Regurgitation

Important aortic valve regurgitation is uncommon after valvotomy when the operation has been performed as described (see Technique of Operation earlier in this section). Moderate to severe regurgitation without residual stenosis is present at late follow-up in about 10% of patients, but some regurgitation is combined with moderate or severe residual or recurrent stenosis in an additional 15% to 20%. Postoperative regurgitation occurs more frequently when valvotomy is radical, and particularly when an attempt is made to convert a bicuspid into a tricuspid valve.

Infective Endocarditis

The incidence of endocarditis is not lessened by valvotomy and may even be somewhat higher than in the natural history.

Diastolic Heart Failure

Rarely, patients with severe valvar aortic stenosis who undergo surgical or balloon valvotomy as neonates or in infancy develop severe diastolic heart failure years later. Robinson and colleagues at Boston Children’s Hospital reported four such patients who presented 14 to 19 years after balloon valvotomy with heart failure and severe diastolic dysfunction. All had evidence of a confluent layer of LV subendocardial hyperenhancement demonstrated by gadolinium-enhanced magnetic resonance imaging that was documented by histopathology in two patients to be endocardial fibroelastosis (EFE). One patient experienced clinical improvement following aortic valve replacement and extensive EFE resection. Robinson and colleagues hypothesize that EFE may result from early (possibly in utero) and irreversible myocardial damage induced by subendocardial ischemia secondary to persistent pressure overload with decreased ventricular flow, which may gradually progress irrespective of relief of LV outflow obstruction.

Reintervention

As with time-related freedom from death, time-related depictions of freedom from reintervention and aortic valve replacement are of limited value when they are derived from a heterogeneous population.

In general, however, about 85% to 95% of children and young adults (excluding neonates and infants) are free of reintervention (usually valve replacement) for at least 10 years after the initial operation (Figs. 47-12 through 47-14). Then, although constant in the intermediate term, the hazard function (rate of reintervention) begins to rise. By 20 years after initial operation, only 60% of patients will be free of reintervention, and by 40 years only 10% will be free. The older the patient, the more likely it is that the reintervention will be valve replacement.

Reintervention appears to be required at a shorter interval and in greater prevalence when the initial intervention has been performed in neonatal life or infancy, and is more likely to consist of valvotomy than valve replacement. Greater frequency of reintervention may be related to generally higher residual gradients in these cases. Reintervention appears to be required more frequently when initial valvotomy has been performed by some method other than an open...
operation using CPB. Reintervention rate increases 15 years after operation from 0.73% per year to 2.3% per year ($P < 0.0001$).

Procedures done at reoperation are generally more varied than at initial operation (Table 47-6). A satisfactory repeat valvotomy is sometimes possible, especially when the initial operation has been done in infancy. At times, an overlooked second level of obstruction is found that requires treatment such as patch graft supravalvar enlargement, a Konno procedure (see Technique of Operation in Section II), or an aortic root replacement (see “Aortic Valve Replacement in Children” under Technique of Operation earlier in this section). These reoperations carry a low risk, but generally carry greater risk than primary operation (see Table 47-6).

Freedom from further reoperation following aortic valve cusp extension procedures has been variable, with freedom from subsequent aortic valve repair or replacement of 60% to 80% at 5 years and about 50% at 15 years. Durability of repair appears greater if a tricuspid valve can be created.

INDICATIONS FOR OPERATION

Initial Valvotomy

Neonates and Young Infants

In neonates and young infants with severe congenital valvar aortic stenosis, medical treatment is begun on an emergency basis. When the diagnosis is suspected before transport of a neonate to a cardiac surgical center in the first week or two of life, or as soon as such a patient, usually moribund or in metabolic acidosis, is admitted, prostaglandin $E_2$ is begun (see Indications for Operation in Chapter 49). This substance usually opens the ductus arteriosus, particularly if the neonate is just a few days old, improves systemic oxygenation, and relieves metabolic acidosis because the right ventricle can support both systemic and pulmonary circulations. The child’s condition should be stable and good before operation is begun.

Before intervention, care must be taken to distinguish the neonates or very young infants with isolated severe congenital valvar aortic stenosis from those whose anomaly is part of the spectrum of hypoplastic left heart physiology. When the anomaly is hypoplastic left heart physiology class III (see Table 48-1 in Chapter 48), the Norwood operation rather than aortic valvotomy is indicated; simple aortic valvotomy is futile. The criteria for using the more extensive operation are (1) mitral valve area less than 4.75 cm$^2$ · m$^2$; (2) LV inflow dimension less than 25 mm; (3) small LV, evidenced by a ratio between the apex-to-base dimension of the LV and that of the right ventricle of less than 0.8; or (4) transverse cavitary and aortic “anular” dimension of 6 mm or less.

In the Congenital Heart Surgeons multi-institutional study of decision making based on 362 neonates, greater intermediate-term survival was obtained by a strategy of an initial Norwood procedure vs. two-ventricle strategy if the arch was small, LV dysfunction was present, or LV outflow tract was small, particularly when less than 4 mm. Colan and colleagues have also developed and subsequently revalidated a scoring algorithm for decision making in neonates with aortic stenosis and a mitral valve $z$ value of greater than $-2$. In those patients in whom aortic valvotomy alone is indicated, the decision to use percutaneous balloon aortic valvotomy (see Special Situations and Controversies later in this section) or surgical valvotomy remains controversial. Surgical valvotomy may be accomplished by closed transventricular valvotomy, open surgical valvotomy with CPB, or using hypothermic or normothermic circulatory arrest. The preference is for surgical valvotomy using CPB, as well as more sophisticated methods of myocardial management than have been generally used. However, a large trial may be the only way to determine comparative outcomes in this complex setting.

Older Infants and Children

Severe congenital valvar aortic stenosis is an indication for operation in older infants and children. Symptoms of angina or syncope always indicate severe stenosis and thus are indications for operation. Conversely, severe stenosis requiring operation frequently occurs without symptoms, but in such circumstances there will usually be physical signs, particularly in the pulse and behavior of the second heart sound. Also, the ECG will usually show an LV hypertrophy pattern; an ECG that shows severe hypertrophy (important ST-T depression) is an indication for operation even if the gradient is less than 50 mmHg.

Mild congenital aortic stenosis is not an indication for operation. Because of the natural history, these patients require long-term periodic noninvasive reevaluation and invasive study and operation if indicated.

Older infants and children with moderate stenosis are a controversial group. Many recommend operation, and others recommend periodic reevaluation of LV-aortic gradient, subendocardial oxygen requirement, or valve area. Those against possibly premature operation argue that (1) sudden death is rare in children whose systolic gradient is 50 to 75 mmHg, (2) operation and probable valve replacement will still be necessary, and (3) valve replacement cannot be delayed by early operation. Therefore, operation usually is not recommended in this group, but is advised if stenosis becomes severe on repeated noninvasive follow-up.
Table 47-6  First Reoperation for Congenital Aortic Stenosis, According to Morphologic Category and Procedure at First Operation\textsuperscript{a}

<table>
<thead>
<tr>
<th>Category</th>
<th>Procedure</th>
<th>Prior Procedure</th>
<th>n</th>
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\textsuperscript{a}Data from 24 patients undergoing reoperation anywhere after initial operation at UAB, 1967-1982.

Key: AVR, Aortic valve replacement; LV-Ao, left ventricular to aortic.

Reoperation

When restenosis becomes severe or when symptoms develop with moderate restenosis, reoperation is indicated. Initially, dysplastic valve cusps should not be a contraindication to reoperation, because in a number of patients the cusps have been more normal in appearance at reoperation than in early life.\textsuperscript{22} Although repeat valvotomy or valve replacement is usually required, subvalvar stenosis may have also developed and must not be overlooked. Important subvalvar stenosis is often associated with a small “anulus,” as well as some supravalvar narrowing. In this case a Konno operation, aortic root replacement operation, or Ross-Konno operation may be advisable.

SPECIAL SITUATIONS AND CONTROVERSIES

Technique of Operation

Periodic enthusiasm for closed transventricular aortic valvotomy in critically ill neonates and young infants is motivated by high early mortality in this group.\textsuperscript{27} Closed transventricular dilations have been performed with Hegar dilators and balloon catheters designed for percutaneous use.\textsuperscript{25,27} Considering the early mortality, need for reintervention, and amount of valvar regurgitation produced, however, no convincing evidence indicates that this method is as good as or superior to the techniques described under Technique of Operation earlier in this section.\textsuperscript{23}

A few groups have preferred to perform valvotomy under inflow stasis at normothermia or mild hypothermia.\textsuperscript{23} Operation under these circumstances is a semiopen one, and forceful stretching or tearing of the valve may result if exposure is not ideal. In children, the method can be used safely, but 7 (26%; CL 17%-37%) of 27 patients followed up to 15 years by Stewart and colleagues had moderate or severe aortic valve regurgitation.\textsuperscript{28} Sink and colleagues reported two (25%; CL 9%-50%) hospital deaths among eight infants, six of whom were neonates.\textsuperscript{314}

Ilbawi and colleagues reported use of extended aortic valvuloplasty in which the commissurotomy incision is extended into the aortic wall around the cusp insertion, mobilizing the valve cusp attachment at the commissures and freeing the
aortic insertion of the rudimentary commissure. They showed reduced aortic valve gradients compared with standard aortic valvotomy at 1.7 years after operation. The method has possible merit, but has not had wide application. Kadri and colleagues, as well as Tolan and colleagues, have described similar operations in which the raphe or fused commissure of the larger cusp of a bicuspid aortic valve is incised, and a triangular piece of pericardium is folded and inserted between the free edges of the incised raphe. Auto- logical or bovine pericardium is attached to the free edges of the incised raphe and vertically to the aortic wall. This procedure produces a tricuspid valve and restores the deficient intercusp triangle, preventing cusp prolapse. Experience with this and other cusp reconstruction procedures (see “Cusp Reconstruction” under Technique of Operation earlier in this section) is limited, so caution should be used in applying these methods until more is known about their efficacy in palliating aortic valve stenosis.

### Percutaneous Balloon Aortic Valvotomy in Neonates, Infants, and Children

Percutaneous balloon aortic valvotomy for severe aortic stenosis in neonates was described by Ruppenthal and Neuhaus in 1985 and Lababidi and Weinhaus in 1986. A large experience with this technique has accumulated since then, well summarized in the neonatal group by Zeevi and colleagues from Boston Children’s Hospital. They found no difference when the results were compared with those of surgical valvotomy in a previous era. Similar results have been reported by others. New technology may improve results further.

In the Congenital Heart Surgeons multi-institutional study, 110 neonates for whom the strategy for management was biventricular repair were treated by either surgical ($n = 28$) or percutaneous balloon ($n = 82$) aortic valvotomy. Propensity score adjustment (see “Clinical Studies with Nonrandomly Assigned Treatment” in Section I of Chapter 6) was used to account for procedure selection bias and achieve comparability of patient characteristics. Time-related survival to age 5 years was similar after surgical and percutaneous balloon aortic valvotomy, as was risk of reintervention.

Moore and colleagues studied midterm results of balloon dilatation of congenital aortic stenosis performed at Boston Children’s Hospital in 148 children, all more than 1 month old. Mortality was 0.7% and was successful in 87% of patients, with average peak gradient reduction of 56±20%. At 8 years postoperatively, 95% were alive, but only 50% were free of another intervention (surgical or repeat balloon aortic valvotomy). Aortic valve regurgitation of grade 3 or higher occurred immediately after the procedure in 13% (CL 10%-16%) and was a major factor in determining another intervention.

Gatzoulis and colleagues compared results of balloon aortic valvotomy in 34 children (8 neonates) and surgical valvotomy in 17 children (7 neonates) treated between 1988 and 1993. Results were equivalent. Two deaths occurred in each group, attributable to small LVs. Peak gradient reduction was equivalent.

Shim and colleagues showed that repeat balloon aortic valvotomy is an effective palliative procedure for children with aortic valve stenosis. Repeat balloon aortic valvotomy provided immediate gradient reduction comparable with the results reported with initial balloon valvotomy, with no increased risk of developing aortic regurgitation.

Hawkins and colleagues followed 60 patients for 1 to 110 months after balloon aortic valvotomy. Operation was required in 23 patients (38%), and aortic valve operation was required in 5% to 7% of patients per year after balloon aortic valvotomy. Aortic valve regurgitation was the predominant indication. Aortic valve repair (valvotomy) was possible in 9 of 23 patients requiring operation after balloon aortic valvotomy. Aortic valve replacement was required in the remaining 14 patients.

Sandhu and colleagues showed that balloon aortic valvotomy can be effective in young adults with congenital aortic stenosis. Of 15 patients aged 16 to 24 years having balloon aortic valvotomy, three required aortic valve replacement for high residual gradient or severe aortic valve regurgitation. Immediate reduction of the pressure gradient by 55% persisted for an average of 1.5 years. Equivalent results were found in 70 children.

Beneficial results of balloon aortic valvotomy in adult patients, especially those with degenerative aortic stenosis, are not long lasting, and restenosis occurs in most patients within 6 months. Wang and colleagues reviewed results of balloon aortic valvotomy in adults, including results from two large registries. They concluded that long-term survival for adults after balloon aortic valvotomy is similar to the natural history of untreated severe aortic stenosis. Survival for patients having balloon valvotomy alone at 3 years was less than 25%, vs. almost 90% for those having balloon aortic valvotomy followed by aortic valve replacement. Balloon aortic valvotomy is reserved only for those patients who are not candidates for aortic valve replacement because of comorbidity illness or advanced age. Balloon aortic valvotomy has not been effective in reducing risk of noncardiac surgery or acting as a bridge to future aortic valve replacement (see Special Situations and Controversies in Chapter 12).

Even with these data, it remains difficult to evaluate balloon aortic valvotomy and determine its effectiveness compared with surgical valvotomy. Immediate, early, and probably midterm results appear to be equivalent to operation in the neonate and child and perhaps in the young adult with congenital aortic stenosis. Long-term results are not currently available. Balloon aortic valvotomy is not effective treatment for adult patients, especially when aortic stenosis is the degenerative type. Application of percutaneous balloon aortic valvotomy seems to be determined by local preference at present.

### Section II Congenital Discrete Subvalvar Aortic Stenosis

#### DEFINITION

Congenital discrete subvalvar aortic stenosis is an obstruction beneath the aortic valve caused by either a short, localized, fibrous or fibromuscular ridge or a longer diffuse fibrous tunnel. “Diffuse subvalvar aortic stenosis” is a phrase best not used to avoid confusion; it was originally used to
distinguish what is now termed *hypertrophic obstructive cardiomyopathy* (HOCM) from congenital aortic stenosis (see Chapter 19). K13 Subvalvar aortic stenosis may also be a part of other cardiac anomalies. In these situations, the obstruction may be fibromuscular and indistinguishable from the entity discussed here or may consist of a localized muscular bar or shelf (e.g., in coarctation or aortic arch interruption with VSD) or abnormalities of the mitral valve. In other words, subvalvar aortic stenosis, as well as valvar stenosis, may be part of the spectrum of hypoplastic left heart physiology.

**HISTORICAL NOTE**

The first description of discrete subvalvar stenosis is attributed to Chevers in 1842. C18 In 1956, Brock and Fleming from Guys Hospital in London published an early report of diagnosing the condition during life using transventricular puncture to measure LV pressure. B21 The catheter was then advanced across the aortic valve from below and the level of obstruction demonstrated. Brock reported results of transventricular dilatation in 1959. B23 Spencer and colleagues published the first substantial report of treatment using CPB in 1960. S18 The lesion was illustrated clearly in patients operated on at the Mayo Clinic between 1956 and 1960. S4, S5

The long fibrous tunnel form of the stenosis was described by Spencer and was later reemphasized by Reis and Morrow and colleagues. R7 Its effective treatment under difficult circumstances became possible with the introduction of aortoventriculoplasty by Rastan and Koncz, and independently by Konno and colleagues in 1975. K15, R2, R3 Complete relief of subvalvar stenosis without sacrifice of the aortic valve became possible with the introduction of the modified Konno operation in 1978 (see Technique of Operation later in this section). The aortoseptal approach was introduced by Vouhe and colleagues in 1984. V5 An alternative form of treatment, LV-aortic conduit, was developed about the same time. C21, N5

**MORPHOLOGY**

**Left Ventricular Outflow Tract**

**Localized Subvalvar Aortic Stenosis**

The localized form of discrete subvalvar aortic stenosis may be fibrous or fibromuscular. The fibrous form involves a spectrum of pathology varying from a discrete short fibrous ridge, a thicker but still discrete fibromuscular shelf, to a long fibrous tunnel. When a fibrous ridge is firmly adherent to the hypertrophied septum anteriorly and to the left, the condition is termed *discrete fibromuscular stenosis*. K12, N4

Whether isolated, localized, or only muscular, subvalvar stenosis occurring as an entity separate from HOCM is controversial.

An obstructing localized circumferential fibrous shelf or ridge may be situated at any level between the nadir of the aortic cusps and the free edge of the anterior mitral leaflet, as well as anywhere along the aortic-mitral anulus. An immediately subvalvar fibrous ridge may be adherent to the base of the aortic cusps (only the right or all three), but more often it is separated from the cusps by several millimeters. Such a high (distal) ridge tends to be narrow, and unless there is severe LV hypertrophy, the remainder of the outflow beneath it remains relatively normal. R12 A low (proximal) fibrous ridge may be attached almost at the hinge line of the anterior mitral leaflet, but most frequently it occupies an intermediate position well above this and several millimeters below the aortic valve (Fig. 47-15). Usually the ridge is 2 to 3 mm thick and is more prominent anteriorly and laterally than posteriorly on the aortic-mitral anulus. The ridge may be present as a complete fibrous diaphragm, however, and the stenotic orifice may be central and circular or eccentric and slitlike. The aortic-mitral anulus is longer than normal in hearts with discrete subvalvar aortic stenosis, and on average, the diameter of the aortic valve anulus is smaller than normal. R12 The muscular ventricular septum beneath the right aortic cusp shows a variable degree of hypertrophy and prominence, and in severe cases may contribute importantly to the stenosis.

**Tunnel Subvalvar Aortic Stenosis**

Much less common, tunnel stenosis presents as a circumferential irregular zone of fibrosis commencing at or close to the LV-aortic junction (“anulus”) and extending...
downward for 10 to 30 mm. Tunnel stenosis has varying degrees of severity, and its spectrum blends into localized subvalvar aortic stenosis. In its most severe form—the form that requires a special surgical procedure—the stenotic tunnel is long and the diameter of the aortic anulus small, even though aortic valve cusps are normally formed. In patients with less severe disease, the tunnel may be shorter and aortic anulus normal in size; morphology then resembles localized fibromuscular discrete subvalvar aortic stenosis. These gradations explain the differing prevalences in reported series. Fibrous stenosis is sufficiently long to justify the term tunnel in about one fifth of cases of congenital subvalvar aortic stenosis; the full-blown entity with anular hypoplasia is rare.

Aortic Valve
The aortic valve is usually tricuspid and either entirely normal or has some diffuse cusp thickening. Trivial or mild aortic regurgitation is present in about two thirds of patients. The aortic valve, however, may be bicuspid, and congenital commissural fusion may produce varying degrees of valvar stenosis. The valve may have been damaged by endocarditis, a complication of subvalvar stenosis, which can result in severe regurgitation. Rarely, the subaortic membrane may be infected. Bases of valve cusps are thick when a high-lying fibrous ridge is continuous with them. Infrequently, supravalvar as well as valvar stenosis coexists with the subvalvar narrowing. This combination is at the mild end of the spectrum of hypoplastic left heart physiology.

Left Ventricle
The LV is usually concentrically hypertrophied. Subendocardial ischemia, and probably fibrosis, occur in subvalvar aortic stenosis as well as in congenital valvar stenosis. Rarely, there may be excessive hypertrophy of the septum (vs. thickening of the posterior LV wall) and muscle fiber disorientation histologically. This histology complicates the distinction in a few patients between discrete subvalvar aortic stenosis and HOCM.

Roberts and his group have noted coronary artery luminal narrowing due to structural wall changes of intramural coronary arteries in both humans and dogs with fibrous subvalvar aortic stenosis. These changes have not been observed in valvar aortic stenosis.

Coexisting Cardiac Anomalies
Discrete subvalvar aortic stenosis occurs as an isolated anomaly in only about half to two thirds of patients coming to operation. Coexisting anomalies include a VSD that is frequently large, and the fibromuscular obstruction is then often located immediately below (upstream to) the VSD. When there is aortic arch interruption and patent ductus arteriosus or occasionally coarctation, localized muscular subvalvar stenosis may be associated with a subpulmonary VSD and occasionally tetralogy of Fallot, atrial septal defect, aortopulmonary window, sinus of Valsalva aneurysm, and aneurysm of the membranous ventricular septum may also coexist, occurring more frequently in pediatric surgical patients.

The complex relationship between VSD and discrete subvalvar aortic stenosis is further evidenced by stenosis developing after spontaneous closure or narrowing of the VSD. Typical discrete subvalvar aortic stenosis may also develop both before and after repair of a complete atrioventricular (AV) septal defect, repair of coarctation, LV-to-aorta internal rerouting in double outlet right ventricle or transposition with VSD, and other forms of congenital cardiac anomalies.

Other Types of Discrete Subvalvar Aortic Stenosis
Localized subvalvar aortic stenosis may be caused by morphomechanism other than those just described. In an autopsy series that included complex congenital heart disease, Freedom and colleagues found the typical fibrous or fibromuscular variety to be the least common in infancy. Mitral valve anomalies involving accessory tissue or leaflet malposition (including that found in AV septal defects) may be a cause of obstruction and may occur in the absence of functional abnormality of the mitral valve or other cardiac anomalies. Localized muscular obstructions related to abnormal infundibular development or malalignment are frequent and often associated with a VSD and aortic coarctation or interruption. A developmental complex described by Shone and associates consists of a parachute mitral valve and LV outflow tract obstruction that usually includes localized fibromuscular subaortic stenosis. Discrete muscular subvalvar aortic stenosis may develop after pulmonary trunk banding for VSD.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Symptoms
Symptoms of congenital subvalvar aortic stenosis are similar to those of the valvar variety. About 25% of patients requiring operation are asymptomatic despite presence of important obstruction.

Signs
A systolic ejection murmur is heard, but a click is rare. There is an unimpressive aortic diastolic murmur in 65% of patients. It is secondary either to (1) cusp thickening with or without adherence of the fibrous ridge to the cusps or (2) effects of eddy currents produced by the subvalvar stenosis upon aortic valve closure.

When severe stenosis is present, the pulse is slow rising, the second heart sound is single or paradoxically split, a third and occasionally fourth heart sound are audible, and a mid-diastolic murmur may be heard at the apex, usually in association with a fibrotic obstruction that limits anterior mitral leaflet movement. It is important to recognize, particularly in children, that one or more of these signs may be minimal or absent despite severe obstruction.

Occasionally, aortic regurgitation may be caused by severe congenital cusp deformities or infective endocarditis. When endocarditis occurs on the aortic valve, signs of regurgitation produced by cusp destruction may be less than expected because a tight fibrous stenosis beneath the valve may limit aortic runoff. Moreover, vegetations on the fibrous shelf itself may increase subaortic obstruction.
Two-dimensional echocardiogram in localized discrete subvalvar aortic stenosis. Fibromuscular ridge is observed narrowing left ventricular outflow tract below aortic valve.

**Figure 47-16**

Chest Radiography

The ascending aorta is not usually dilated in the chest radiograph, and valvar calcification is absent. The LV is usually enlarged.

Electrocardiography

The ECG usually shows severe LV hypertrophy.

Echocardiography

Two-dimensional echocardiography can be diagnostic, accurately demonstrating and outlining the obstructing shelf\(^{12,3,5}\) (Fig. 47-16). The technique is so sensitive that it can demonstrate a subvalvar discrete lesion before a gradient develops. Color flow Doppler imaging sufficiently defines the gradient across the obstruction to allow a definitive decision regarding operation. Siggrusson and colleagues suggested that the angle formed by the septum and aorta (aortoseptal angle) may have prognostic value in patients with discrete subaortic stenosis,\(^{12,3}\) because it is steeper in patients with subaortic stenosis than in normal persons. They suggested this anatomic feature may be causative in development of this condition. M-mode echocardiography is helpful in differentiating this lesion from HOCM.\(^{11,3}\)

Cardiac Catheterization and Cineangiography

Cardiac catheterization shows a systolic pressure gradient below the valve on withdrawal of the catheter across the LV outflow tract. When the fibrous ridge is immediately beneath the valve, the gradient may be apparent at valve level. Postectopic pressure pulse response is normal, and the aortic pulse contour does not show an accessory wave; these features distinguish the lesion from HOCM.

Angiography supports the definitive diagnosis.\(^{3,12,3,4}\) The tilted left anterior oblique (LAO) view provides good visualization of the fibrous ridge because it overcomes the foreshortening of the LV outflow tract region present in the conventional LAO projection (Figs. 47-17 through 47-19). Level and thickness of obstruction can be accurately defined in this manner, and additional valvar stenosis and regurgitation also can be evaluated.

Summary

In discrete subvalvar aortic stenosis, features characteristic of HOCM are usually absent. Rarely, however, particularly in severe forms of fibrous subvalvar aortic stenosis,\(^{11}\) including the tunnel variety,\(^{3}\) there may be abnormal systolic anterior motion (SAM) of the mitral leaflet and an abnormal posttropic response. These signs indicate either a particularly prominent anterior muscular shelf or, in patients who also show an abnormal septal to posterior wall thickness ratio on echocardiography (with disorientation of the muscular pattern of hypertrophy histologically), associated HOCM.

**NATURAL HISTORY**

Discrete subaortic stenosis is present in 8% to 30% of patients with congenital LV outflow tract obstruction.\(^{11,5,3,11,3,4}\) Rather, obstruction is often absent in early life and then becomes evident and progressively more severe in childhood or young adulthood.\(^{11,11,5,3,11,8}\)

The subvalvar gradient has first appeared several years after an early study in infancy before VSD and coarctation repair. Also, the lesion appears infrequently after age 30, suggesting that survival beyond this time is rare without surgery or that the lesion gradually takes on the appearance of HOCM.\(^{11}\)

Pyle and colleagues provided further support for these concepts in their study of fibrous subaortic stenosis in Newfoundland dogs.\(^{59}\) In these animals, subaortic stenosis was never present at birth but was important by 12 weeks of age. Evidence also shows that stenosis might be an inherited trait. A familial occurrence has been reported in humans.\(^{11,14,3}\)

Reports of serial cardiac catheterizations indicate that discrete subvalvar aortic stenosis progresses quite rapidly,\(^{10,4,1,5,3,4,24,4}\) probably more rapidly than valvar stenosis. Such features probably explain why, in published surgical series in which ages of patients are listed, the youngest patients operated on are age 3 to 6 years and surgery is uncommon beyond age 20.\(^{15,3,11,5,12,1,3,3,5,3,18}\)

Aortic regurgitation, often associated with discrete subvalvar aortic stenosis, is progressive and caused by cusp thickening from poststenotic turbulence.\(^{34}\) Cusp thickening most likely explains the frequency of endocarditis before and after surgical excision of the membrane.\(^{34,1,2,3,3,2,3,3,0}\)

**TECHNIQUE OF OPERATION**

Resection of Localized Subvalvar Aortic Stenosis

Preparation for operation for congenital subvalvar aortic stenosis in children is accomplished as described for valvotomy in Section I. Fig. 47-20 shows anatomic relationships of the subaortic fibromuscular ridge.

A transverse aortotomy is made (Fig. 47-21, A). The aortic cusps are retracted and the subvalvar fibrous ridge exposed. Beginning beneath the nadir of the right coronary cusp, a vertical incision is made through the ridge and into the underlying muscle, with depth of incision proportional to estimated septal thickness (Fig. 47-21, B). A second incision parallel to the first is made through the ridge below the commissure between right and left aortic valve cusps. Excision of the fibromuscular ridge begins by carrying a vertical incision circumferentially between the parallel incisions.
Figure 47-17  Left ventricular cineangiogram in crani-ally tilted left anterior oblique projection in patient with localized discrete fibrous subvalvar aortic stenosis, in diastole (A) and early systole (B). A thin ridge obstructing left ventricular outflow tract about 1 cm below aortic valve is well profiled and indicated by white arrows. In systole, aortic valve is domed (arrows), indicating a valvar abnormality in addition to subaortic ridge. Key: a, Ante-rior mitral leaflet; Ao, aorta; L, left; LV, left ventricle; N, noncoronary sinus; R, right coronary sinus.

Figure 47-18  Left ventricular cineangiogram in cranially tilted left anterior oblique projection in patient with fibromuscular subvalvar aortic stenosis. Cineangiogram frame in systole shows thick fibromuscular outflow obstruction commencing just beneath aortic valve. Aortic cusps fail to open completely but show no doming. Diverticulum just below obstructing shelf on septal aspect of outflow tract represents a surgically closed ventricular septal defect (arrow).

Figure 47-19  Left ventricular cineangiogram in lateral projection in patient with tunnel subvalvar aortic stenosis. Cineangiogram frame in late systole shows outflow tract narrowing 1 cm below aortic ring and extending down into base of left ventricle. Anterior mitral valve leaflet forms posterior margin of stenotic zone (arrows) and is prevented from moving back to its normal systolic position. Anterior (septal) margin of outflow tract shows irregular encroach-ment by obstructing fibromuscular tissue.
Chapter 47 Congenital Aortic Stenosis

(Fig. 47-21, C), removing fibrous tissue and myocardium deep into the ventricular septum until the mitral apparatus is encountered at the leftward extremity of the LV outflow tract. In this process, care is taken not to penetrate the ventricular septum and produce a VSD. As the dissection is carried down over the anterior mitral leaflet, only the fibrous ridge is removed, shaving it off the leaflet or mitral-aortic anulus with the knife or a Freer septum elevator (Fig. 47-21, D). Dissection is carried rightward as far as the mitral leaflet and mitral-aortic anulus extend.

Returning anteriorly, only the fibrous ridge is shaved off the muscular septum to the right of the nadir of the right coronary cusp using a knife or septum elevator (see Fig. 47-21, D). The ridge excision is carried rightward over the membranous septum. This technique preserves the integrity of the underlying bundle of His and cores out the entire subvalvar stenosis as a single mass. When the fibromuscular ridge is attached to the undersurface of the belly of one or more of the aortic cusps, it is carefully shaved away from the cusp tissue.

The procedure is not considered complete unless a generous amount of muscle has been removed leftward of the nadir of the right coronary cusp. If only the fibrous component has been enucleated, a deep trough of muscle is cut from the ventricular septum anteriorly. The trough is centered beneath the commissure between the right and left aortic valve cusps as in the operation for HOCM (see Technique of Operation in Chapter 19). This step is of value even when the fibrous ridge is immediately subvalvar, because the ventricular septum is always hypertrophied.

Yacoub and colleagues propose mobilization of the left and right fibrous trigones along with extensive resection of all components of the subvalvular fibrous ring. Their proposal is based on the concept that the aortic and mitral orifices interact, with the fibrous trigones acting as a hinge mechanism for movement of the subaortic curtain and anterior mitral leaflet during the cardiac cycle. The incision to resect the fibrous ring is extended laterally at the location of the left and right fibrous trigones to excise this fibrous tissue in continuity with the obstructing ring. Resection of the left fibrous trigone carries the risk of creating an opening to the outside of the heart or into the anterior mitral leaflet, and injury to the conduction system could occur during resection of the right fibrous trigone. The technique was used in 57 consecutive patients operated on over the course of 25 years without these complications occurring. Pressure gradient over the LV outflow tract after the repair ranged from 0 to 30 mmHg (mean 8 mmHg), and no change in gradient was observed on follow-up assessment.

After determining that the ventricular septum has not been perforated and aortic valve cusps have not been damaged, the aortotomy is closed and the remainder of the procedure accomplished as described under Technique of Operation in Section I for valvotomy.

Ross-Konno Procedure

Aortic valve replacement may be required in some older children or adults when important aortic valve regurgitation coexists with severe subaortic stenosis. Modification of the Ross and Konno procedures is used in these patients (Ross-Konno procedure). CPB is established using either two can- nulae for venous uptake (with venae cavae tourniquets) or a single two-stage cannula, with the atrial uptake placed deep in the atrium at the inferior vena cava (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Oxygenated blood is returned through a cannula in the ascending aorta. The aorta is occluded and cold cardioplegia adminis- tered through a cannula in the coronary sinus (see “Technique of Retrograde Infusion” in Chapter 3), directly into the coronary ostia, or both. The ascending aorta is divided and aortic valve excised. The coronary ostia are mobilized with a rim of sinus aorta, and the noncoronary sinus aorta is removed (see Chapter 12). The pulmonary trunk is removed from the right ventricular (RV) outflow tract in the usual manner for a Ross procedure (see “Autograft Pulmonary
Figure 47-21  Repair of discrete fibromuscular subvalvar aortic stenosis. A, Operation is performed on cardiopulmonary bypass with aorta occluded. Cold cardioplegic solution is infused to achieve total electromechanical arrest. A transverse aortotomy is made. B, Subaortic ridge is exposed by retracting right coronary cusp. Broken lines indicate proposed incision points. C, Scalpel is used to make two incisions through fibromuscular ridge, with one below the commissure between right and left aortic valve cusps and the other parallel to first incision and beneath the nadir of right coronary cusp. Septal myocardium is removed deeply between the two incisions. D, Fibrous ridge is dissected from the septum to the right and over anterior leaflet of mitral valve using a Freer septum elevator. Deep incision of ventricular septum carries hazard of heart block. Similarly, deep incision over anterior leaflet of mitral valve risks its perforation.

Valve” under Technique of Operation in Chapter 12). A slightly longer portion of the RV outflow tract below the pulmonary valve may be removed (Fig. 47-22, A). A short incision is made through the fibrous tissue of the aortic valve attachment at the nadir of the right coronary sinus into the ventricular septum, as in the Konno procedure (Fig. 47-22, B). This incision is not as deep into the septum as in the Konno procedure, however, and should not extend beyond the medial papillary muscle (Lancisi) of the tricuspid valve to avoid injury to the first septal branch of the left anterior descending coronary artery. The fibromuscular subaortic ridge is excised and septal myocardium shaved from the left side to reduce thickness of the hypertrophied ventricular septum in order to widen the LV outflow tract and completely relieve the obstruction (Fig. 47-22, C). The pulmonary autograft is then attached to the LV outflow tract (Fig. 47-22, D). The lengthened tongue of the attached RV outflow tract is inserted to the depth of the incision in the
Figure 47-22  Repair of complex subvalvar aortic stenosis requiring aortic valve replacement by pulmonary autograft (Ross-Konno procedure).  

A, Operation is performed on cardiopulmonary bypass with aorta occluded and cold cardioplegia infusion for myocardial management. Aorta is divided and aortic valve excised. Coronary arteries are mobilized with a button of sinus aorta. Rest of sinus aorta is removed. Pulmonary trunk is divided at its bifurcation and removed from right ventricular outflow tract. An extension of the anterior wall of right ventricular outflow tract may be included to fill defect in ventricular septum created by the Konno incision.  

B, An incision is made into ventricular septum (Konno) at the midpoint of right coronary sinus of Valsalva. This incision is not nearly as deep into ventricular septum as in the classic Konno operation, and ordinarily would not pass the depth of the medial papillary muscle (Lancisi) of the tricuspid valve to avoid injury to first septal branch of left anterior descending coronary artery.  

C, Subaortic obstructing ridge is cut away from ventricular septum on left side. Hypertrophied ventricular septum is shaved down on left side to achieve an unobstructed left ventricular outflow tract.  

D, Pulmonary autograft is attached to ventricular septum with interrupted polypropylene stitches. Anterior extension of right ventricular outflow tract may be beneficial when incision of ventricular septum is extensive and deep.
ventricular septum. If no extra length of RV outflow tract has been removed, the pulmonary autograft is simply inserted deep into the LV outflow tract. The operation is completed as described for the Ross procedure (see “Autograft Pulmonary Valve” under Technique of Operation in Chapter 12).

Repair of Tunnel Stenosis by Aortoventriculoplasty (Konno Operation)

When a tunnel type of subaortic stenosis coexists with hypoplasia and narrowing of the LV-aortic junction, aortoventriculoplasty is a reasonable procedure, using the modification described by Misbach and Ebert and colleagues and others. The preliminaries and preparations for CPB are identical to those described earlier for congenital valvar aortic stenosis (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). CPB is established using two caval cannulae and caval taping, because the RV will be opened. The aorta is occluded, cold cardioplegic solution is infused, and perfusate temperature is stabilized at 20°C to 25°C. Through a small oblique right atriotomy incision, the pump-oxygenator sump sucker is placed across a naturally occurring or surgically created foramen ovale.

Before establishing CPB, position of the right coronary artery must be accurately noted, and a marking stitch placed leftward from this to indicate the RV incision site. A vertical aortotomy is made beginning about 10 mm downstream to the level of the right coronary artery (Fig. 47-23, A). The incision is carried well to the left of the right coronary artery and onto the RV over the junction of the contiguous portions of right and left coronary cusps. The right ventriculotomy may be made first to visualize the pulmonary valve cusps, because these lie near the point of entry of the incision into the RV. After the RV is opened, the scissors are positioned with one blade in the LV through the aortotomy and one in the RV through the ventriculotomy; a scissors cut is made to the left side of the nadir of the right coronary cusp (see Fig. 47-23, A). This incision is carried far enough into the two ventricles to gain access below (or upstream to) the tunnel stenosis. The newly created and enlarged anulus is sized, and an appropriately sized mechanical valve prosthesis is chosen. A double-velour collagen or gel-coated polyester graft is fashioned to form an oval-shaped patch. Beginning at the inferior angle of the incision in the ventricular septum, this patch is sewn into place from the RV side out to beyond the aortic anulus and posteriorly through it. A triangular patch of polyester is attached to the primary aortic patch with the anteriorly placed valve stitches (Fig. 47-23, B). Horizontal mattress sutures in the anterior aspect of the prosthesis are passed through the patch. The remainder of the polyester patch is sutured into place to enlarge and close the aortotomy (Fig. 47-23, C).

The triangular polyester patch is used to close the RV opening (see Fig. 47-23, C). The patch must be wide enough to enlarge the RV outflow tract as compensation for projection of the enlarged LV outflow tract into the RV outflow tract. Particular care is taken to anchor the patch at the junction of RV and aorta so that hemostasis is secure in that area.

The left atrial suction device is removed from across the foramen ovale. The foramen is closed, then the right atrium. The remainder of the operation is carried out in the usual manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Aortoventriculoplasty by “Mini” Aortic Root Replacement

Enlarging the subvalvar and valvar area of the LV outflow tract can also be accomplished using biological material, either an ascending aorta valved allograft or a pulmonary artery valved autograft. The operation is begun in the same manner as the Konno operation, extending the incision into the ventricular septum as far toward the apex as required by the extent of subaortic stenosis; incision into the aorta is kept as short as possible. The aorta is then transected just downstream to the distal extent of the vertical incision, and the coronary ostia with generous buttons of surrounding sinus wall are removed from the aorta. The remnant of aortic root and valve cusps are then excised, leaving a fringe of aortic wall attached to the LV-aortic junction. The V-shaped defect in the ventricular septum is filled in with a polyester patch. This reconstructs and enlarges that portion of the LV outflow tract to which the aortic valved allograft (or pulmonary valved autograft) is attached proximally. The graft is sewn into place, and the coronary buttons are implanted. Finally, the opening in the anterior RV wall is closed with a patch, using a triangular piece of pericardium sutured into the incision and distally onto the anterior aspect of the graft.

The anterior mitral leaflet may be left in place on an aortic valved allograft and used to fill in the ventricular septum. However, this dictates the orientation of the valved cylinder, which may be disadvantageous because the curvature of the aorta is brought anteriorly and to the right. This problem can be overcome by using an aortic allograft with attached anterior mitral leaflet to widen the LV outflow tract posteriorly into the anterior leaflet of the mitral valve, as suggested by Milsom and Doty. This places the allograft in anatomic position for treating the complex but localized subvalvar aortic stenosis.

Modified Konno Operation

The modified Konno operation, originally described in the first edition of this book, is effective in patients with difficult and complex localized subaortic stenosis or tunnel stenosis when the aortic anulus and valve are normal. This procedure has also been found to be useful in other patients.

Preparations for operation and establishment of CPB are exactly as described for the Konno operation (see “Repair of Tunnel Stenosis by Aortoventriculoplasty [Konno Operation]” earlier in this section). The aorta is occluded, cold cardioplegic solution infused, and a suction device placed across the foramen ovale (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). Because the Konno operation usually would not be done with a normal-sized anulus and valve, a transverse aortotomy is made just as for the operation for aortic valvotomy (see Section I of this chapter) or resection of discrete subaortic stenosis as described earlier in this section (Fig. 47-24, A). When it has been determined that the usual procedures will not enlarge the LV outflow tract sufficiently, the RV is opened through a transverse incision about 2 cm inferior (upstream) to the level of the pulmonary valve cusps. A right-angled clamp is passed
Aortoventriculoplasty (Konno operation) and aortic valve replacement. **A**, Vertical aortotomy is directed slightly rightward of the commissure between left and right coronary cusps of aortic valve. As incision is being made, orifice of right coronary artery is visualized, and incision passes clearly leftward of this. Right ventricle (RV) is opened with a oblique incision, pulmonary valve is located, and the two incisions are joined. Before or after excising aortic valve, an incision is made into base of the right coronary cusp just to the left of its nadir. This incision is extended into ventricular septum and toward apex of left ventricle. It is leftward of conduction system. **B**, Patch of collagen-coated polyester is cut into a diamond shape and attached to ventricular septum. A second triangular-shaped patch is fashioned for closing RV outflow tract. This patch and a prosthetic valve are attached to the primary patch at the level of the aortic anulus. A single suture line will suffice for this portion of the reconstruction. Prosthetic valve is attached directly to aortic anulus.
from the aortotomy through the aortic valve and into the left side of the LV outflow tract and positioned 1 cm or so upstream to the valve. The tip of the clamp can be palpated through the ventricular septum, and at that point an incision is made in the septum from the RV side (Fig. 47-24, B). It is extended inferiorly for about 1 cm, parallel to the LV outflow tract and thus at an angle to the RV outflow tract. The incision through the ventricular septum is now extended superiorly with great care to keep it clearly upstream to the aortic valve (Fig. 47-24, C). Hypertrophied myocardium of the ventricular septyum is removed to thin it out and relieve obstruction. As described for the Konno operation, an oval patch is trimmed from a double-velour collagen-coated polyester graft. This is sewn into place so as to enlarge the LV outflow tract (Fig. 47-24, D). The right ventriculotomy and aortotomy are closed with continuous sutures (Fig. 47-24, E).

Valve-Preserving Technique for Enlarging Left Ventricular Outflow Tract and Mitral Anulus

Jonas and colleagues have described an operation for enlarging the LV outflow tract and mitral anulus in patients with tunnel subaortic stenosis, often as a component of Shone syndrome and therefore associated with mitral stenosis and hypoplasia of the mitral anulus. The aortic valve, if normal, is preserved. The operation consists of an incision from the aorta through the commissure between the left and noncoronary cusps of the aortic valve. The incision is extended into the roof of the left atrium and across the anulus of the mitral valve. The mitral valve is removed and replaced with a mechanical prosthesis. A triangular patch is used to enlarge the mitral anulus and close the left atrium. The aorta is reclosed, preserving the aortic valve. Some regurgitation of the aortic valve may occur, but this is not necessarily negative, because it serves to hasten growth of the aortic anulus.

RESULTS

Early (Hospital) Death

Hospital mortality for repair of localized subvalvar aortic stenosis is low but has not quite approached zero. In a combined series of 314 patients compiled from the literature, with operation performed primarily in an earlier era, mortality was 4.8% (CL 3.5%-6.4%).

Extensive operations, such as aortoventriculoplasty by the Konno or Rastan technique, have a higher mortality. In older children and young adults, aortoventriculoplasty has been performed with hospital mortalities of 5% to 15%.

Although experience is limited, results for the Ross-Konno procedure have been good. Reddy and colleagues, Daenen and colleagues, and Brown and colleagues all report mortalities under 10% for series of 11 to 14 patients. The operation can be successfully accomplished even in neonates.

Time-Related Survival

About 85% to 95% of heterogeneous groups of children and young adults coming to operation for discrete subvalvar aortic stenosis are alive 15 years later.

Incremental Risk Factors for Premature Death

Absence of formal multivariable analysis of a sizable and representative group of patients undergoing appropriate surgical treatment handicaps the effort to identify incremental risk factors in patients with subvalvar aortic stenosis.

However, the nature of the morphology is clearly the dominant risk factor. The tunnel form of subvalvar aortic stenosis
Figure 47-24  Modified Konno operation, used only for complex or recurrent discrete subaortic stenosis or tunnel stenosis with normal-sized aortic valve and anulus. 

A, Ascending aorta is opened through small transverse incision to inspect valve and guide incision into ventricular septum. Transverse incision is made in infundibulum of right ventricle. 

B, An incision is then made through ventricular septum parallel to direction of left ventricular outflow tract, keeping incision well anterior to the level of the muscle of Lancisi (i.e., well to the left) to avoid heart block or central right bundle branch block. Usually a finger or instrument is passed through aortic valve to protect it while making this incision. 

C, Fibromuscular components of subvalvar stenosis are excised as much as possible. Incision in septum is carried to within 1 to 2 mm of aortic valve anulus. 

D, Left ventricular outflow tract is widened by inserting a patch. 

E, Ventriculotomy and aortotomy are closed with continuous sutures.
and small aortic anulus increase the risk of premature death. Increased risk in the early hazard phase after operation is related to more extensive operations required for optimal therapy. Increase in the later hazard phase is related to the tendency of patients with these complex morphologies to have persistent stenosis or develop restenosis that requires complex reoperations.

Morphologic risk factors can be eliminated by using an appropriate but extensive surgical procedure as the initial operation and by making it safe and durable by optimal myocardial management and improved techniques.

Complications
Complications of the resection procedure are rare with current techniques, but include complete heart block, iatrogenic VSD, hemorrhage, and injury to the mitral valve. Reddy and colleagues reported that 1 of 11 patients (9%; CL 1.5%-28%) required a permanent pacemaker after aortoventriculoplasty.

Functional Status
Functional status of surviving patients is generally good. Of 38 surviving and traced patients in the UAB experience, 31 (82%; CL 73%-88%) were in NYHA functional class I and six (16%; CL 6%-24%) in NYHA class II. Whitmer and colleagues have shown objective evidence of improved exercise tolerance.

Hemodynamic Status
Most patients, including those with the less severe forms of tunnel stenosis, have an excellent hemodynamic result late (10 years) postoperatively. The operation usually results in a dramatic immediate gradient reduction, which is sustained or improved over the subsequent 10 years. In a few patients, gradient is mildly increased 5 to 10 years postoperatively compared with measurements in the operating room, but these data are difficult to interpret because of the variability of postrepair operating room measurements.

Sreeram and colleagues suggested that intraoperative echocardiography provides better morphologic information about obstructive lesions of the LV outflow tract and enables immediate assessment of the adequacy of operative repair. Kuralay and colleagues suggested that use of intraoperative transesophageal echocardiography in adult patients allows optimal resection of the obstruction and reduces complications such as complete heart block and VSD. Results from simple resection are less good in patients with severe tunnel stenosis. Wright and colleagues found that in six patients, mean LV-aortic gradient was reduced from 102 to 72 mmHg. This was a smaller reduction in gradient (30 ± 17 mmHg) than was achieved in patients with discrete subvalvar aortic stenosis (52 ± 40 mmHg) (P for difference < .05). The advantages of the Konno or modified Konno procedure in this setting are clear.

Recurrence and Reoperation
Stewart and colleagues found that about half of their patients having operations for localized and diffuse forms of subvalvar aortic stenosis required reoperation, some as long as 17 years after the initial procedure. The hazard function for reoperation increased at 5 years. Serraf and colleagues analyzed long-term results including risk factors for recurrence and reoperation in 160 patients followed for a median of 13.3 years. Freedom from reoperation at 15 years was 85%. Recurrence and reoperation were most influenced by coarctation of the aorta and immediate postoperative LV outflow tract gradient.

Brauner and colleagues followed 75 patients an average of 6.7 years after operation for subvalvar aortic stenosis. They found 18 recurrences in 15 patients (20%). The linearized hazard of recurrence and reoperation was 3.8% per patient-year. When patients had a preoperative LV outflow tract gradient greater than 40 mmHg, risk of reoperation was sevenfold higher, suggesting that early intervention or more extensive operation may prevent recurrence, reoperation, and secondary progressive aortic valve disease. In discussing these findings, Freedom conjectured that the problem of recurrence may be more complex and somehow related to abnormal cellular response in the LV outflow tract. Recalling earlier work of Ferrans and colleagues in which at least five cell layers are present in resected subvalvar fibrous rings, Freedom called for better understanding of the fundamental mechanisms of mechanical stress and genetic regulation of the endothelial surface of the LV outflow tract in subvalvar aortic stenosis.

Recent discrete subvalvar stenosis is usually indistinguishable morphologically from the primary disease, although its recurrent rather than persistent nature has been documented. This entity of recurrent discrete subvalvar stenosis is to be clearly distinguished from persistent subvalvar stenosis after an inadequate initial operation, although their effect and treatment are the same.

Aortic Regurgitation
Some investigators have suggested that aortic regurgitation may progress after a satisfactory operation. Typically, however, aortic regurgitation remains trivial or mild unless endocarditis occurs. Serraf and colleagues found that relief of subvalvar aortic stenosis improved the degree of aortic regurgitation in 86% of patients (CL 80%-91%) with preoperative aortic regurgitation.

INDICATIONS FOR OPERATION
Because obstruction from localized congenital subvalvar aortic stenosis tends to progress rather rapidly, and because the propensity for sudden death when it becomes severe is presumably the same as in severe congenital valvar aortic stenosis, operation is advisable whenever the stenosis is moderate (LV-aortic gradient > 50 mmHg) or severe. When the stenosis is severe (gradient > 100 mmHg), operation without delay is indicated. Resection of the subvalvar obstruction is usually the initial procedure of choice.

When the diagnosis has been made but obstruction is mild (LV-aortic gradient less than 50 mmHg), reevaluation with echocardiography is indicated every 6 months because rapid progression can occur. However, some evidence indicates that intervention at an earlier age and at a lower gradient (30 mmHg) may improve late results, depending on the extent of relief of obstruction at the initial operation.
When discrete subvalvar stenosis is long (tunnel stenosis), and perhaps particularly when it is recurrent, simple resection is usually not effective. In these circumstances, an initial modified Konno operation is indicated.

When there are multiple levels of LV outflow tract obstruction or major associated cardiac anomalies, the general indications previously described pertain, but each patient must be considered with respect to individual morphology and circumstances. The Ross-Konno aortoventriculoplasty is the most generally applicable procedure, because the autograft may grow, and if it does it is the preferred technique in young patients. Either the Konno procedure or the “mini” aortic root replacement may also be used.

SPECIAL SITUATIONS AND CONTROVERSIES

Type of Operation

Simple resection of a discrete subaortic membrane (or shelf) has been recommended by some as equivalent to membrane resection plus transaortic myectomy in terms of likelihood of restenosis. However, Lupinetti and colleagues and Barkhordarian and colleagues found that adding septal myectomy to resection of discrete subvalvar aortic stenosis reduced the frequency of reoperation.

Aortoseptal Approach for Tunnel Stenosis

The modified Konno procedure provides only a limited exposure of the subvalvar area. Vouhe and colleagues have used an “aortoseptal approach” similar to the Konno operation, but without the need to replace the aortic valve. A longitudinal incision in the aorta is carried obliquely down toward the top of the adjacent portions of right and left aortic cusps. A roughly transverse incision is made in the RV infundibulum, beginning at a point just over this. The aortic and RV incisions come together just over the top of the left anterior fibrous trigone. The aortic “anulus” is now divided through the trigone, going exactly between adjacent extremities of left and right cusps; this can be done without damaging the cusps. This incision is carried well into the ventricular septum, as in the Konno procedure, opening the LV outflow tract widely. After resecting obstructing tissue, the septal incision is closed, the left anterior fibrous trigone reconstructed, and the RV and aortic incisions closed. The authors also describe widening the LV outflow tract with a polyester patch in closing the septal incision, as in the modified Konno procedure. The aortic valve is replaced if it is part of the obstructing process or if it is regurgitant.

Left Ventricular–Aortic Conduit

The LV-aortic conduit (apicoaortic conduit) operation has enjoyed some popularity in the past. Norwood and colleagues reported a hospital mortality of 22% (CL 8%-45%) with use of this technique in infants. Complications both early and late postoperatively are common, and 4 (24%; CL 12%-39%) of 17 hospital survivors reported by Brown and colleagues required reoperation, as did 7 (78%; CL 55%–92%) of 9 hospital survivors reported by Di Donato and colleagues. Currently, few indications exist for the procedure in cases of congenital aortic stenosis. Cooley and colleagues revived interest in apicoaortic conduits with a report of its use in seven patients with complex LV outflow tract obstruction. They used a transthoracic approach to avoid redo sternotomy and compromise to coronary arteries, the conduction system, and other valves. Two patients died of respiratory insufficiency (29%; CL 10%-55%). The others survived and were improved by operation.

Section III Congenital Supravalvar Aortic Stenosis

DEFINITION

Congenital supravalvar aortic stenosis is an obstruction caused by localized or diffuse narrowing of the aortic lumen commencing immediately above the aortic valve.

HISTORICAL NOTE

The first description of supravalvar aortic stenosis is attributed to Mencarelli in 1930. It was seldom recognized, however, until Denie and Verheugt emphasized in 1958 that supravalvar stenosis could be differentiated from other varieties of aortic stenosis by retrograde arterial catheterization. In 1959, Morrow and colleagues pointed out the usefulness of angiography in diagnosis.

In 1961, Williams, Barratt-Boyce, and Lowe described the association of supravalvar aortic stenosis with unusual “elfin” facies and mental retardation, a syndrome that was soon confirmed by others. This constellation of signs and symptoms has since been referred to as Williams syndrome or elfin facies syndrome. In 1964, Beuren and colleagues reported 10 cases of this syndrome, all associated with multiple peripheral pulmonary artery stenoses. Watson and Bourassa and Campeau had also noted this association a year earlier. The similarity between the facies of patients with supravalvar aortic stenosis and severe infantile hypercalcemia was noted in 1963 by Hoofit and colleagues and Black and Bonham Carter. Garcia and colleagues reported the first patient with Williams syndrome and a documented history of infantile hypercalcemia. The occurrence of a familial form of supravalvar stenosis without elfin facies was reported by Sissman and colleagues in 1959. Nakinski and colleagues reported supravalvar aortic stenosis in monozygotic twins without phenotypic features of Williams syndrome.

Successful operation for supravalvar stenosis using patch graft enlargement of the noncoronary sinus of Valsalva was reported by McGoon and colleagues in 1961, the first patient being operated on in 1956. Before this publication, successful procedures using a similar technique had been performed.

In 1960, Hara and colleagues successfully performed an excision and end-to-end aortic anastomosis in a patient with supravalvar aortic stenosis, as did Chard and Cartmell. Hancock satisfactorily relieved the stenosis by excising the intimal ridge without patch enlargement. Neither of these procedures is currently recommended.

Most surgeons have placed the patch into the noncoronary sinus of Valsalva, but in Williams and colleagues’ original report, it was placed into the right sinus to relieve any narrowing between the right cusp and aortic wall. Doty
and colleagues recommended using a double-flanged patch that extends into both noncoronary and right sinuses, incising the stenosing ring at points 180 degrees apart. Resecting the remaining stenotic ring above the left coronary sinus may be performed to enhance the repair. Their report introduced the concept of more anatomic repair of the aortic root and led to a number of modifications of the classic operations for supravalvar aortic stenosis. Subsequent modification of their extended aortoplasty technique employed incision in the left coronary sinus and repositioning of the commissure between left and right coronary cusp of the aortic valve to achieve a more anatomic repair. Steinberg and colleagues proposed a modification of extended aortoplasty in which an additional separate incision is made across the sinotubular junction into the left coronary sinus of Valsalva to the right of the left coronary ostium. This incision is closed around an oval-shaped prosthetic patch, and the primary Y-shaped incision is closed with a pantaloon-shaped patch.

Brom introduced an even more symmetric aortoplasty, enlarging all three sinuses of Valsalva by a three-patch technique. The first patient was operated on using this method in 1978, but the technique was not published until 1988. The aorta is transected distal to the obstruction and incisions made into each of the three sinuses. Pericardial patches are inserted into each of the aortic sinuses to relieve the obstruction while retaining normal geometric relationships of the aortic root.

Myers and Waldhausen and colleagues described a technique of repair that is symmetric and obviates need for prosthetic patch material. The aorta is divided distal to the obstruction, and incisions are made into each aortic sinus. Distally, three incisions are made in the ascending aorta corresponding to the position of the commissures of the aortic valve. The aorta is mobilized sufficiently to advance the ascending aorta into the incisions in the aortic root.

**MORPHOGENESIS AND MORPHOLOGY**

**Supravalvar Stenosis**

*Morphogenesis*

The vascular pathology of supravalvar aortic stenosis and Williams syndrome results from mutations involving the elastin gene on chromosome 7q11.23. These mutations include intragenic deletions, translocations, and complete deletion of the elastin gene, suggesting that a quantitative reduction in elastin during vascular development is pathogenically important. Point mutations of the elastin gene (ELN) are especially important in supravalvar aortic stenosis. Stamm and colleagues found Williams syndrome in 61% of patients treated operatively for supravalvar aortic stenosis, and more recently the clinical diagnosis was supported by the chromosome 7q11.23 abnormality.

*Morphology*

Stenosis may be localized or diffuse. Most often the narrowing is localized to the supravalvar area of the aorta just above or at the most superior level of the attachments of the valve commissures. Narrowing of the aorta at this point is usually apparent externally; in association with some dilatation of the sinuses of Valsalva and absence of poststenotic dilatation, this produces an hourglass appearance. In addition, variable intimal thickening in the form of an internal shelf increases the stenosis and may obstruct or even close the ostium of the left main coronary artery (see “Coronary Arteries” later in this section).

Less often, the narrowing is diffuse, extending throughout the length of the ascending aorta and even beyond into the arch and into the origins of brachiocephalic arteries.

**Other Aortic Lesions**

Supravalvar aortic stenosis should be considered a complex anomaly of the aortic root. Too often the surgeon focuses attention on only the defect at the sinus rim; narrowing and thickening of the sinus rim are fundamental to the morphology, but this defect involves more anomalies. Thickening of the aortic media and intimal hyperplasia reduces aortic circumference at the sinus rim. The morphologic process may not be circumferential but may involve only the sinus rim over one or two sinuses. The sinuses of Valsalva beneath the thick and short sinus rim may be abnormal or hypoplastic. Ostia of the coronary arteries may be obstructed not only by the overhanging thick sinus rim, but also by an aortic cusp that becomes bound down or fused to the aorta at the sinus rim.

The aortic valve cusps are reported to be thickened in about 30% of patients with supravalvar aortic stenosis. True valvar stenosis resulting from leaflet fusion is rare. The aortic valves are actually involved in every case, because the relationships of the commissures are distorted as they are drawn close together by the shortened and thickened sinus rim. This distortion produces a characteristic buckling of the free edge of the aortic cusp. The free edge of the aortic cusp has normal length in most young patients. It buckles as it accommodates to the shortened space at the sinus rim. The buckled aortic cusps become part of the obstruction within a space too small to accommodate them properly. Thickening of the edges of the aortic cusps, however, is eventually produced by turbulent blood flow from stenosis at the sinus rim. The thickened valve cusps then become an even more important part of the stenosing process.

The aortic anulus may occasionally be hypoplastic. Subvalvar stenosis of the LV outflow tract may also be part of this total deformity of the aortic root. McElhinney and colleagues focused attention on the fact that supravalvar aortic stenosis involves not only the supravalvar aorta but the entire aortic root in the 36 patients who were operated on consecutively over 6 years. Procedures were required on the aortic valve in 39%, which agrees closely with the series reported by Delius and colleagues. In that series, resection of the subvalvar LV outflow tract was performed in 11 patients, and two patients underwent procedures on the coronary arteries. Four patients had aortic root deformity so severe that the entire root was replaced with a pulmonary autograft (Ross procedure). The authors compared their series to six others and found similar high frequency of associated pathology and LV outflow tract procedures.

Bicuspid aortic valve is common (6 of 15 patients, 40% in the series of Delius and colleagues).

**Coronary Arteries**

The aortic valve cusp free edges near the aortic wall may become adherent to the intimal shelf, producing stenosis
at the entry into the sinus of Valsalva, thereby obstructing coronary flow. This is more common in the left sinus but can occur in the right. When extreme, the proliferative process of the intimal ridge may extend into and narrow or even obstruct the ostium of the left coronary sinus. Stamm and colleagues found partial adhesion of the leaflets to the stenosing ridge in 54% of patients with supravalvar aortic stenosis. In 30%, the valve leaflets were thickened and less mobile than normal. The sinuses of Valsalva were enlarged in 75% of cases. Coronary angiography demonstrated evidence of coronary ostial stenosis in 45%. The authors concluded that the entire valvular apparatus is always affected in patients with supravalvar aortic stenosis.

In the absence of obstruction to inflow into the sinus of Valsalva or of ostial stenosis, the coronary arteries are exposed to a high pressure and show dilatation, tortuosity, medial hypertrophy, and early onset of arteriosclerosis.

Other Cardiac Anomalies

The most common associated anomaly consists of multiple stenoses in the peripheral pulmonary arteries, which may be severe enough to produce right ventricular hypertension and hypertrophy. Pulmonary valve stenosis occurs infrequently. Diffuse hypoplasia of the pulmonary trunk may be associated with diffuse hypoplasia of the aorta with both arteries showing marked wall thickening and fibromuscular dysplasia histologically in association with disorganization and replacement of the elastic tissue of the media. These patients usually give a familial history, and sudden death in infancy is common.

Less common anomalies include stenosis of the origins of subclavian and carotid and rarely other major systemic arteries, coarctation of the aorta (with or without patent ductus arteriosus), and VSD. Mitral regurgitation occurs rarely, although the mitral valve may be thickened and redundant. The patient reported by Denie and Verheugt in 1958 had Marfan syndrome, which has been noted subsequently in about 5% of patients with supravalvar aortic stenosis.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Symptoms

Symptoms rarely develop in infancy, but appear frequently in childhood, and may appear as late as the second or third decade. They are similar to those of other types of congenital aortic stenosis, although angina may occur more often because of early-onset coronary arteriosclerosis.

Signs

Auscultatory findings are similar to those of congenital valvar aortic stenosis, and the correct diagnosis may not be possible from physical signs. An ejection click is absent, however, and the murmur and thrill tend to be situated higher than in valvar stenosis. An aortic diastolic murmur is uncommon. Blood pressure may be lower in the left arm than in the right, resulting from stenosis at the origin of the left subclavian artery or from a jet effect. Similarly, the left carotid pulse may be diminished.

A diagnostic clinical feature may be elfin facies, combined with reduced intelligence quotient and failure to thrive. These retarded children are characteristically small, friendly, and loquacious. Each component of the syndrome varies in severity, however, and the supravalvar stenosis may be mild or occasionally absent in patients with the typical facies. The disease in this form is always sporadic and the facies identical to severe infantile hypercalcemia. Hypercalcemia has been documented in less than 5% of these infants, although it is more common when the elfin facies is not present. Less than half of patients with congenital supravalvar aortic stenosis have elfin facies and mental retardation. In the remainder without elfin facies, the disease may be sporadic or familial.

Echocardiography

Diagnosis and definition of severity can be made with two-dimensional echocardiography and color flow Doppler examination (Fig. 47-26).

Cardiac Catheterization and Angiography

The site of pressure change can be localized on withdrawal of a catheter from LV to aorta. Morphology of the supravalvar stenosis can be outlined on angiography (Fig. 47-26, C, and Fig. 47-27), and coexisting anomalies can be identified (Fig. 47-28). For these last reasons, cardiac catheterization and angiocardiography are usually indicated.
60% of children with the anomaly. Some of the children with elfin facies and the severe form of infantile hypercalcemia die from complications of hypercalcemia. However, a longitudinal study by Hickey and colleagues indicates a more favorable prognosis for children with moderate (mean LV outflow tract systolic gradient 30 mmHg) supravalvar aortic stenosis. Many such children, particularly those with Williams syndrome, show gradual regression of gradient without intervention. Kitchiner and colleagues followed 81 patients with supravalvar aortic stenosis from 1 to 29 years (median 8.3 years); 40 patients (49%) had Williams syndrome, 19 (23%) had additional levels of LV outflow tract obstruction, and 47 (58%) had surgical intervention, 20% in the first year after diagnosis. The data indicated that 88% of the patients would be operated on within 30 years. Predicted survival at 30 years after presentation was 66%.

**NATURAL HISTORY**

The supravalvar form is the least common type of congenital aortic stenosis. Genders are equally affected.

In infants with elfin facies, mental retardation, and combined congenital supravalvar aortic stenosis and pulmonary stenoses of the diffuse variety, sudden death is common early in life. Sudden death can occur in all age groups, presumably from severe LV outflow tract obstruction and coronary artery disease.

Progression of supravalvar aortic stenosis may be more rapid and severe than in congenital valvar aortic stenosis. Because the lesion is uncommon in adults, most untreated patients probably die before reaching adult life. Death before adult life is particularly likely to occur in those with elfin facies, because they constitute only 11% of adults but...
Figure 47-27  Left ventriculogram and aortogram in diffuse supravalvar aortic stenosis. **A,** Ascending aorta becomes diffusely narrow at the level of the aortic valve commissures, just beyond area of right and left coronary arteries. Narrowing extends into transverse arch. **B,** In this patient, diffuse supravalvar stenosis extends through aortic arch. Origin of left carotid artery is stenotic, and left subclavian artery is occluded.

Figure 47-28  Cineangiograms of localized supravalvar aortic stenosis with coexisting diffuse right and left pulmonary artery narrowing. **A,** Left ventriculogram and aortogram in lateral projection in long-axial position. **B,** Right ventriculogram in posteroanterior projection.
valvotomy for congenital valvar aortic stenosis in Section I of this chapter. After occluding the aorta and infusing cold cardioplegic solution, the aortotomy is made.

The aorta is opened above the valve and the incision carried into the noncoronary sinus of Valsalva. The aortic valve and subvalvar areas are examined to exclude obstruction at those levels. The intimal shelf is resected (Fig. 47-29, B), in part to ensure adequate inflow into the sinuses of Valsalva. A diamond-shaped patch of pericardium or collagen-coated knitted polyester or polytetrafluoroethylene (PTFE) is then incorporated into the incision with a running polypropylene suture (Fig. 47-29, C). The patch must be of sufficient size

Interestingly, the peripheral pulmonary stenosis seems to decrease in severity as patients age.\textsuperscript{G8, W9}

**Figure 47-29** Repair of congenital supravalvar aortic stenosis. **A,** External hourglass deformity of aorta is usually less prominent than internal narrowing. **B,** When prominent, as usually occurs, this ridge is excised. **C,** Supravalvar narrowing is eliminated by incorporating an enlarging patch of pericardium (or polyester) into closure of incision.

**TECHNIQUE OF OPERATION**

**Repair of Localized Type**

**Classic Repair**

The external hourglass deformity of the aorta is usually less prominent than the internal narrowing caused by the thick ridge of the sinutubular junction (Fig. 47-29, A). The operation is begun exactly as described for the procedure of
to enlarge the aortic diameter to normal. The remainder of the procedure is completed as usual (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Pressure is measured in the LV and ascending aorta to determine whether there is any residual gradient across the repair. Intraoperative echocardiography with color flow Doppler examination should be done to assess the degree of turbulence over the repair and determine whether aortic valve regurgitation is present.

**Extended Aortoplasty (Doty)**

The operation is performed on cardiopulmonary bypass (CPB) using a single two-stage venous uptake cannula, with oxygenated blood returned to a cannula in the ascending aorta (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). The aorta is occluded and cold cardioplegia infused through a cannula in the coronary sinus (see “Technique of Retrograde Infusion” in Chapter 3). A vent catheter is placed in the right superior pulmonary vein.

An oblique incision is made in the aorta, extending it across the obstructing ridge at the sinutubular junction and into the middle of the noncoronary sinus. The primary incision is also extended to the left to cross the sinutubular junction into the right sinus of Valsalva just anterior to the commissure between the left and right coronary cusps of the aortic valve (Fig. 47-30, A). The incisions into the aortic root are nearly directly opposite each other at the sinutubular junction, allowing the aorta to be divided into almost equal portions. The anterior portion of the aortic root that contains the origin of the right coronary artery may move forward (anterior) to widen the space at the sinutubular junction. Buckling of the aortic valve leaflets is relieved as the halves of the aorta are separated anteriorly and posteriorly. The thick ridge of the supravalvar stenosis located above the left coronary sinus is excised (Fig. 47-30, B). A crimped tubular polyester graft whose diameter approximates that of the ascending aorta is used for reconstruction. About half of the circumference of the graft is used, and the length should be sufficient to place enough graft into the aortotomy to prevent the anterior portion of the aortic root from being pulled down into the plane of the aorta. A wedge is removed from the graft to accommodate the portion of the aorta containing the right coronary artery. The resulting two limbs of the graft are used to widen both the right and noncoronary sinuses of Valsalva (see Fig. 47-30, B) partially closing the aortotomy; the distal end of the graft fills the aortotomy in the ascending aorta.

Entrapment of the left coronary cusp of the aortic valve may be treated not only by resection of the supravalvar thickened rim but also by incision into the left sinus of Valsalva to the left of the left coronary ostium (Fig. 47-30, C). This incision mobilizes the commissure between the left and the right coronary cusps and allows the commissure to be moved anteriorly for greater symmetry of the position of the three commissures. The pantaloon-shaped patch is attached to the adventitia of the aorta behind the commissure between the left and right cusps at the anular level. The commissure is attached directly to the patch to achieve equal distance between the three commissures at the sinutubular junction relative to the aortic anulus is difficult to accomplish.

**Three-Patch Repair (Brom)**

The operation is performed on CPB using a single two-stage venous uptake cannula and an arterial cannula in the ascending aorta (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). The aorta is occluded and cold cardioplegia infused (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3).

The aorta is divided above the sinutubular junction. Three longitudinal incisions are made through the area of stenosis into the aortic root (Fig. 47-31, A). The first is placed in the middle of the noncoronary sinus of Valsalva. The other two are determined by position of the coronary arteries. Incision into the left coronary sinus is usually to the right of the left coronary ostium, and incision into the right sinus is usually to the left of the right coronary ostium. The incisions end about halfway into the sinus aorta, but may go deeper if necessary to achieve good separation of the edges of the aorta at the stenosing ridge. Three triangular patches of autologous pericardium are inserted (Fig. 47-31, B). Width of the patch at the sinutubular junction should restore correct dimensions. The diameter at the sinutubular junction should be 10% to 15% less than the diameter at the ventriculoaortic junction (“anulus”). Larger patches achieve a greater diameter but carry the risk of reducing the coaptation area of the aortic valve by lateral displacement of commissural attachments of the valve, possibly resulting in aortic regurgitation.

The reconstructed aortic root is anastomosed to the ascending aorta.

**Sliding Aortoplasty (Myers-Waldhausen)**

The operation is performed on CPB. The aorta is divided above the supravalvar obstruction. Three longitudinal incisions are made through the area of stenosis into the three sinuses of Valsalva as described for the “Three-Patch Repair (Brom)” in the preceding text. Incisions are made into the ascending aorta distally and correspond exactly to the commissures of the aortic valve (Fig. 47-32, A). The ascending aorta is mobilized extensively to allow it to be displaced inferiorly so as to slide the flaps of the ascending aorta into the incisions in the aortic root in a “V-Y” pattern. A continuous stitch of monofilament suture is started at the nadir of each incision in the sinus aorta. The corresponding flap of ascending aorta is attached to the edges of the incision in the sinus aorta by sewing from the nadir to the top of the commissural attachment of the aortic valve (Fig. 47-32, B). The diameter of the aortic root at the sinutubular junction will be determined by the diameter of the ascending aorta and should approximate normal dimensions (see “Dimensions of Normal Cardiac and Great Artery Pathways” in Chapter 1). No prosthetic material is employed in this repair.

**Repair of Diffuse Type**

The operation proceeds as described for the localized type, except that the skin incision is carried about 2 cm more superiorly than usual. The femoral artery is exposed for arterial cannulation. Origins of the brachiocephalic, left common carotid, and left subclavian arteries and the transverse portion
Figure 47-30 Repair of supravalvar aortic stenosis by extended aortoplasty (Doty). A, Oblique incision is made in aorta extending across supravalvar ridge into middle of noncoronary sinus of Valsalva. A second incision is made as an inverted “Y” into right sinus, just anterior to commissure between left and right coronary cusps. This divides the stenosing ring at two points almost directly opposite on circumference of ring. B, Supravalvar ridge is removed from above left coronary sinus of Valsalva. A patch is fashioned from a tubular polyester graft approximately the diameter of aorta. A wedge is removed to create two limbs on the patch and accommodate position of right coronary ostium (pantaloon patch). Patch is attached to edges of aortotomy in right and noncoronary sinuses of Valsalva and to primary incision in aorta. Sufficient length of graft must be placed into aortotomy to allow portion of aorta containing right coronary ostium to separate anteriorly from primary aortic incision.

of the aortic arch are dissected below and above the left brachiocephalic vein.

CPB is established with arterial inflow to the patient through the femoral artery, and body temperature is taken to 18°C. The operating table is placed with the patient in moderate Trendelenburg position. The aorta is occluded while cold cardioplegia is infused. Aortic reconstruction is done with hypothermic circulatory arrest (see Section IV of Chapter 2).

A longitudinal incision is made in the ascending aorta and carried well down into one or two sinuses of Valsalva, as in repair of the localized form. Any intimal ridge above each sinus of Valsalva is excised as described for the localized type. The incision is carried up the ascending aorta, which is usually thick walled and has a small lumen, and around onto the aortic arch, then if necessary into the upper descending thoracic aorta (Fig. 47-33, A). Incisions are made across any stenosis present at the origin of the brachiocephalic and left common carotid arteries, and intimal proliferations dissected away. Thickened interna and media is dissected away from the aortic adventitia by endarterectomy (Fig. 47-33, B). A patch of double-velour collagen-coated polyester or PTFE is
Figure 47-31, cont’d  C, Greater symmetry of the repair may be accomplished by a third incision into left coronary sinus of Valsalva just posterior to commissure between right and left sinuses. This incision mobilizes the commissure so that it can move anteriorly to achieve better spacing between commissures of aortic valve and to achieve better configuration of left cusp. Pantaloon patch is attached to adventitia of aorta behind commissure at level of “anulus.” Commissure is attached directly to inside of patch.

Figure 47-31  Repair of supravalvar aortic stenosis by three-patch technique (Brom). A, Aorta is divided above supravalvar stenosing ridge. Three longitudinal incisions are made through the area of stenosis. First is made into middle of noncoronary sinus of Valsalva; second is into left coronary sinus to the right of left coronary ostium; third is into right sinus to the left of right coronary ostium. B, Three triangular patches of autologous pericardium are fashioned for insertion to each incision. Width of patches at the top should restore correct dimensions of the sinutubular junction, or 10% to 15% less than the diameter of the ventriculooaortic junction (“anulus”). These patches are attached to aorta by continuous stitches of fine polypropylene suture. Ends of aorta are reanastomosed.
Figure 47-32  Repair of supravalvar aortic stenosis by sliding aortoplasty (Myers-Waldhausen). A, Aorta is divided above supravalvar ridge. Three incisions are made in proximal aorta through the stenosing ring into sinuses of Valsalva (see Fig. 47-31). Three incisions are made into distal ascending aorta at points corresponding exactly to position of commissures of aortic valve. Ascending aorta is mobilized to allow it to be displaced inferiorly, sliding the flaps of ascending aorta into the incisions in aortic root in “V-Y” fashion. B, Continuous stitch of fine polypropylene suture is started at nadir of each incision in aortic root. Corresponding flap of ascending aorta is attached to edges of incision in aortic sinus by sewing from nadir to top of commissural attachment of aortic valve.

Figure 47-33  Repair of diffuse supravalvar aortic stenosis. A, Operation is performed with hypothermic circulatory arrest. Incision is made in ascending aorta extending deep into noncoronary sinus of Valsalva. It is extended distally into aortic arch or even into proximal descending thoracic aorta. B, Thickened intima and media is dissected away from aortic adventitia by endarterectomy. C, Patch of collagen-coated polyester or polytetrafluoroethylene is used to widen aorta as it is attached to edges of aortotomy.
fashioned to an appropriate size and shape (Fig. 47-33, C). In young patients, an allograft of ascending aorta and arch can be used, as in the Norwood operation. Beginning distally, the patch is sutured into place with continuous 4-0 or 5-0 polypropylene. An ear or projection is fashioned into the patch to go across the orifices of the left common carotid and brachiocephalic arteries. Once the arch reconstruction suture lines are into the ascending aorta proximal to origin of the brachiocephalic artery, CPB is reestablished.

A right-angled cannula is inserted through a purse-string suture into the superior vena cava. The vena cava is occluded between the cannula and the right atrium, the cannula is attached to the arterial tubing, and retrograde cerebral perfusion is begun at about 25 mmHg pressure. When air and blood have been flushed out, perfusion through the systemic arterial cannula is reestablished, air is extruded from beneath the patch graft, and the clamp is repositioned on the ascending aorta just proximal to the brachiocephalic artery. Reconstruction of the ascending aorta is continued into the aortic root, attaching the patch to the edges of the aortotomy. Rewarming is accomplished during reconstruction of the ascending aorta and aortic root.

RESULTS

Early (Hospital) Death

Primary repair of isolated localized congenital supravalvar aortic stenosis has a low hospital mortality. Early risks are greater in patients with diffuse congenital supravalvar aortic stenosis. Sharma and colleagues reported the total experience with operative treatment of supravalvar aortic stenosis at the Texas Heart Institute, an experience that spanned 29 years and involved 73 patients. Twenty-four patients (32%) had isolated localized supravalvar aortic stenosis and were treated by patch aortoplasty. The results were good, with only one death (4%; CL 0.5%-13%).

Time-Related Survival

Late survival is good. In analyses of 30 to 100 patients, 10-year survival after repair was 88% to 98%, with 20-year survival of 60% to 90%. Similar findings in support of the progressive nature of supravalvar stenosis, operation was advisable in patients with localized or diffuse congenital supravalvar aortic stenosis in 75 patients. A single patch in the noncoronary sinus was used in 34 patients, an extended aortoplasty to two sinuses of Valsalva in 35 patients, and three-sinus reconstruction in six patients. Multiple-sinus reconstructions (two or three) resulted in superior hemodynamics (lower gradients) and were associated with fewer reoperations (P = .007). The only independent risk factor for reoperation was type of operation (P < .001): risk was higher when a single sinus repair was used (approximately 50% by 15 years) compared with two-sinus repair (approximately 15% by 15 years). Similar findings in support of multiple-sinus aortoplasty were reported by Kaushal and colleagues.

No long-term data are available for the sliding aortoplasty, but the method may retain more of the elastic properties of the aortic root than other repair methods. However, this technique is not suitable for patients with diffuse disease.

INDICATIONS FOR OPERATION

Operation is advisable in patients with localized or diffuse congenital supravalvar aortic stenosis when peak pressure gradient across the stenosis is 50 mmHg or more. Because of the progressive nature of supravalvar stenosis, operation should be performed without delay at whatever age the criteria for surgery are met. It can be inferred from the experience reported by Sharma and colleagues that about one third of patients have a simple anomaly that can be treated with a simple operation. However, nearly half (45% in Sharma and colleagues’ experience) have a localized form of supravalvar aortic stenosis plus another obstructive lesion of the LV outflow tract that
requires patch aortoplasty plus aortic valvotomy, aortic valve replacement, or subvalvar resection. Therefore, about half of patients with supravalvar aortic stenosis classified as having only localized lesions actually have a complex LV outflow tract anomaly.

Patients with a diffuse form of the defect or with associated cardiac anomalies or infection do less well, with results commensurate with severity and complexity of the defects. Therefore, coexisting diffuse right and left pulmonary arterial stenoses should probably not be approached surgically, because the stenoses usually extend into branches. The possibility of their improvement by percutaneous balloon dilatation\textsuperscript{[12]} and the tendency for their physiologic effect to decrease as patients age indicate that, in general, their presence should not be a contraindication to surgical relief of supravalvar aortic stenosis.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Choice of Patch Material**

Inserting a patch of prosthetic material or pericardium to enlarge the aortic diameter, combined with resection of the intimal shelf, is a safe and effective procedure.\textsuperscript{[14],[16]} Theoretically, a false aneurysm may develop at the edge of a polyester onlay patch, similar to when a polyester patch is used in repair of coarctation (see “Late Aneurysm Formation” in Section I of Chapter 48). Polyester graft may also stimulate overgrowth of fibrous tissue (pannus). Pericardium is a more desirable material but might be constrictive, although it does not seem to constrict when applied in the aorta. Tanning with a short exposure to glutaraldehyde may reduce the tendency of pericardium to constrict and makes handling easier during the repair. Glutaraldehyde-fixed bovine pericardium may also have a place in this repair if autologous pericardium is not available. PTFE graft may also be useful.

Al-Halees and colleagues reported using autologous pulmonary artery for the patch in an extended aortoplasty.\textsuperscript{[21]} The pulmonary trunk above the valve and below the bifurcation was removed and fashioned to provide a pantaloon-shaped patch for reconstructing two aortic sinuses and extending the aorta after resecting the obstructing rim. They suggested that this patch material would grow with the patient.

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Section I: Coarctation of the Aorta

DEFINITION

Coarctation of the aorta is a congenital narrowing of the upper descending thoracic aorta adjacent to the site of attachment of the ductus arteriosus. The aortic lumen may be atretic in the most severe form of this defect, but aortic walls above and below the atresia are in continuity, as distinguished from aortic arch interruption, in which a short distance separates the aortic ends (see Section II). Uncommonly, coarctation occurs more proximally, between the left common carotid and subclavian arteries. Occasional examples of coarctation of the lower thoracic and abdominal aorta are not considered in this chapter.

Coarctation with or without patent ductus arteriosus but without other major associated cardiac anomalies is termed primary, pure, or isolated coarctation.

HISTORICAL NOTE

Morgagni is credited in 1760 with the first description of an aortic coarctation found at autopsy, and Paris some 30 years later was the first to fully describe its pathologic features. In 1903, Bonnett suggested dividing the lesion into adult (postductal) and infantile (preductal) types, a classification that has tended to persist despite its inaccuracy. Regardless of age at presentation, essentially all coarctations are periductal. By 1928, Abbott was able to review 200 autopsy cases in individuals older than 2 years of age.11 The natural history of this age group was further elucidated in a collective review of 104 autopsy cases between 1928 and 1946 by Reifenstein, Levine, and Gross.14 That coarctation was frequently a cause of death in infancy was not appreciated in these early reports; in the 1950s this aspect was adequately documented.59,61

Animal experiments designed to develop surgical treatment were published in 1944 by Blalock and Park.525 Their procedure involved turndown of the divided left subclavian artery onto the aorta, a technique they recognized would not provide complete relief. Experiments involving excision and end-to-end anastomosis were commenced in 1938 by Gross and Hufnagel.63 In their classic article published in 1945, they described the technique of end-to-end anastomosis, including the method of suturing and the design of appropriate clamps.63 They also noted that hindquarter paralysis occurring in some of their experimental animals was unlikely to be a problem in humans because of collateral circulation. It seemed to be prevented “by packing the entire back of the animal in ice.” They predicted use of aortic allografts when end-to-end anastomosis was not practical.

The first coarctation repair in a patient was performed by Crafoord and Nylin in October 1944.24 Gross’s first patient was operated on in June 1945.61 The procedure was rapidly adopted worldwide. Thus, Clagett in 1948 was able to report the first 21 patients operated on at the Mayo Clinic.6 In
eight of these, end-to-end anastomosis was not considered wise, and Blalock’s left subclavian turnaround operation was performed instead. Extending the operation to infants began in 1950 when Burford attempted unsuccessfully to reconstruct an infant aorta using an arterial graft. A successful end-to-end anastomosis in an infant was reported by Lynxwiler and colleagues in 1951 and by Kirklin and colleagues at the Mayo Clinic in a 10-week-old infant in 1952. Mustard and colleagues reported a successful result in a 12-day-old infant in 1953. Repair of coarctation in neonates became more successful after documentation in 1975 to 1977 of the favorable effect of prostaglandin E₁ (PGE₁) in these sick small babies, achieved by maintaining patency of the ductus arteriosus until time of repair.

Subsequent modifications of surgical technique included use of prosthetic onlay grafts across the coarctation site or of a simple vertical incision and its transverse closure by Vorsschulte in 1957 and subclavian patch aortoplasty by Waldhausen and Nahrwold in 1966. Use of a prosthetic tube graft as an alternative to the allograft, which was preferred by Gross, was reported by Morris, Cooley, DeBakey, and Crawford in 1960.

**MORPHOLOGY AND MORPHOGENESIS**

Coarctation

Coarctations vary in severity. When stenosis is localized, the lumen must be reduced in cross-sectional area by more than about 50% before there is a hemodynamically important pressure gradient across it, but longer tubular coarctations may be hemodynamically important with lesser narrowing.

Thirty-three percent of autopsy specimens (patients aged 2 years to adulthood) examined prior to the era in which operation was available show moderate luminal narrowing, 42% severe (pinhole) stenosis, and 25% luminal atresia. Occasionally the adult aorta may be redundant and severely kinked opposite the ligamentum arteriosum, without any pressure gradient; this is called a pseudocoarctation lesion.

The localized morphology of classic coarctation is a shelf, projection, or infolding of the aortic media into the lumen. It is most prominent in that portion of the circumference opposite the ductus arteriosus (the posterior and leftward wall). This inward projection is present also on anterior and posterior walls but absent on the ductal side (inferior or rightward wall). The shelf is usually marked externally by a localized indentation or waisting of the left aortic wall as if a string had been placed around it, pulling the aorta toward the ductus (Figs. 48-1 and 48-2). External narrowing may be absent in the young infant. The aorta beyond the narrowing usually shows poststenotic dilatation, and paradoxically the wall beyond the stricture is usually thicker than that just proximal to it where the pressure is higher. The localized shelf or curtain of media and intima lies adjacent to the ductus arteriosus in utero and to the ligamentum arteriosum if the ductus closes. The shelf may be preductal or postductal but is usually periductal. Hutchins pointed out that the histologic features of this aortic media infolding are identical to those seen at a branch point of the normal aorta.

In addition to infolding of aortic media, there is usually a localized ridge of intimal hypertrophy (intimal veil) that extends the shelf circumferentially and further narrows the lumen. This, and perhaps other portions of the coarctation area, consists of ductal tissue. It forms a sling that completely surrounds the periductal aorta, which may progressively proliferate after birth and cause restenoses after repair of coarctation in neonates and young infants. It is well documented that use of PGE₁ can result in symptomatic relief of a critical coarctation in some young infants by relaxing the coarctation site without reopening the ductus.

Rodbard has presented experimental and theoretical evidence that lowering of lateral pressure on the aortic wall secondary to the increase in velocity that occurs across a site of narrowing (according to the Bernoulli principle) allows the intimal cells to multiply until probe patency is reached. Resistance to flow across this stenosis then lowers the velocity so that ingrowth usually stops.

Rudolph and colleagues postulated that prevalence and type of coarctation are related to fetal flow patterns through the ductus and aorta. These investigators have shown that flow through that portion of the arch between origins of the left common carotid and left subclavian arteries in the normal fetal lamb is approximately half that across the ductus, explaining the normally smaller diameter of the arch compared with the ascending and descending aorta in the normal human newborn. A localized shelf opposite the ductus may...
result from a reorientation of the angle at which the ductus meets the aorta, which results in abnormal fetal flow patterns in some types of cardiac anomalies. The tendency for a shelf to develop is present when ductal flow is increased more than usual relative to isthmus flow; for example, with a ventricular septal defect (VSD). However, intrauterine events that account for the relatively frequent association of coarctation with lesions that produce left-to-right shunts postpartum are not fully identified.

Coarctation, as well as isthmus hypoplasia, is more common than usual when ascending aorta flow is diminished during fetal life (and ductal flow is relatively increased) by lesions such as aortic stenosis or atresia (see Chapters 47 and 49), and mitral stenosis or regurgitation (see Chapter 50). Conversely, prevalence of coarctation is severely reduced and size of the isthmus increased when pulmonary flow and thus right-to-left ductal flow is decreased by lesions such as pulmonary stenosis or atresia, tetralogy of Fallot, and tricuspid atresia. Coarctation is uncommon when the aortic arch is right sided, presumably because of alteration of ductal and isthmus flow patterns in this situation.

Distal Aortic Arch Narrowing

Narrowing of the isthmus—the segment of aorta between a discrete coarctation and the left subclavian artery—commonly exists with coarctation. Narrowing of the distal aortic arch between the left subclavian and left common carotid arteries also coexists commonly, particularly in neonates and infants. This narrowing appears in some cases to be a transient finding related to prenatal flow pattern (excessive ductal flow extending proximally in the aorta and out the left subclavian artery), which reduces flow in the distal aortic arch between the left subclavian and left common carotid arteries (PDA). Large left vertebral artery arises separately from arch proximal to left subclavian artery (LSCA). This neonate also had perimembranous and muscular ventricular septal defects and mild mitral valve hypoplasia. Key: Asc Ao, Ascending aorta; Desc Ao, descending aorta; PT, pulmonary trunk; RCC, right common carotid; RSC, right subclavian artery.

Figure 48-3 Autopsy specimen from 5-day-old neonate with coarctation, demonstrating tubular hypoplasia of aortic arch between left common carotid artery (LCC) and patent ductus arteriosus (PDA). Large left vertebral artery arises separately from arch proximal to left subclavian artery (LSCA). This neonate also had perimembranous and muscular ventricular septal defects and mild mitral valve hypoplasia. Key: Asc Ao, Ascending aorta; Desc Ao, descending aorta; PT, pulmonary trunk; RCC, right common carotid; RSC, right subclavian artery.
Collateral Circulation

Collateral circulation between aorta proximal to the coarctation and that distal to it is one of the striking features of coarctation. When well developed, it is responsible for some of the classic signs of the malformation, such as parascapular pulsations and rib notching. It is usually present to some extent in newborns but increases in size and extensiveness as the patient ages (Fig. 48-4).

Inflow into the collateral circulation is widespread, but is primarily from branches of both subclavian arteries, particularly internal thoracic, vertebral, costocervical, and thyrocervical trunks. Outflow from the collateral system is primarily into the upper descending thoracic aorta. The largest vessels participating in this outflow are usually the first two pairs of intercostal arteries distal to the coarctation. These are the third and fourth intercostal arteries, and they are greatly enlarged by the large reversed flow (outflow from collateral circulation). This reversed flow into the aorta can be documented by magnetic resonance imaging (MRI) and has been demonstrated at operation by directional Doppler velocity detector probes. Flow returns to a normal direction immediately after coarctation repair. Only the intercostals carrying this large reversed flow are sufficiently enlarged to participate in this outflow.

Degenerative changes occur in the peripheral arterial vasculature proximal to the coarctation, and these changes persist after coarctation repair and can be identified in children. Surrogate markers of arteriosclerosis, such as impaired flow-mediated vasodilatation and increased intima media thickness, were apparent in a study group with a mean age of 12 years.

The abnormalities extend out to all major arteries supplied by the aorta proximal to the coarctation.

These abnormalities may be primary ones that have developed in utero. Coarctation has been documented by fetal echocardiography in utero as early as 21 weeks of gestation, but it likely exists much earlier. Hypoplasia of the isthmus and, in some patients at least, the distal aortic arch develops during intrauterine development. It is hypothesized that either the coarctation was present very early in development and the hypoplasia is secondary, or the hypoplasia is related to a primary aortic wall abnormality rather than to the coarctation. Or the hypoplasia and coarctation are a result of altered patterns of blood flow caused by intracardiac abnormalities that lead to decreased flow to the arch and increased flow to the ductus during fetal development.

Degenerative changes occur in the peripheral arterial vasculature proximal to the coarctation, and these changes persist after coarctation repair and can be identified in children. Surrogate markers of arteriosclerosis, such as impaired flow-mediated vasodilatation and increased intima media thickness, were apparent in a study group with a mean age of 12 years.

Figure 48-4 Major collateral channels in coarctation of the aorta. (From Edwards and colleagues.)
produce rib notching, which explains lack of notching of the first and second ribs, whose intercostals arise above the coarctation. The lower intercostal arteries provide less outflow from the collateral circulation, as do the inferior epigastric artery and other branches of the abdominal aorta.

Collateral circulation and its clinical manifestations are altered by anatomic variations associated with classic coarctation. Associated stenosis at the origin of the left subclavian artery excludes this artery as an important source of inflow into the collateral circulation; thus, rib notching occurs only on the right side. When the right subclavian artery arises as the fourth aortic branch (see Morphology in Section I of Chapter 51) and distal to the coarctation, it does not serve as a source of inflow, and rib notching occurs only on the left side.

Aneurysm Formation

Enlarged, tortuous third and fourth intercostal arteries may become aneurysmal, but this is rare before about age 10 years. Resulting thin-walled aneurysms are usually saccular and are most likely to occur at the aortic origin of intercostal arteries. This is a weak point of surgical importance; if an enlarged intercostal artery must be ligated, the ligation should be placed a few millimeters beyond its aortic origin.

The aorta itself may become aneurysmal adjacent to the site of maximal narrowing as a result of hemodynamic effects, aortic dissection, or mycotic aneurysm. This is uncommon in young children. Prevalence of aneurysm is about 10% by the end of the second decade of life, 20% by the end of the third decade, and probably even higher in older patients.

Coronary Arteries

Left ventricular hypertrophy occurring in untreated patients is accompanied by histologic changes in coronary arteries. In young patients, nonarteriosclerotic lesions are conspicuous in the intimal layer. These consist of degenerative and proliferative changes of the elastic fibers and excess collagens tissue. The media thickens to about twice normal with a rich elastic fiber network and often hyaline changes. Mean total area of the coronary arteries is increased, so they have greater than normal capacity, presumably in response to increased metabolic requirements of the left ventricle. As a result of prolonged hypertension, arteriosclerotic changes are apt to occur more often and at a younger age. In adolescents and young adults, reduced myocardial perfusion reserve is apparent.

Atria

In newborn infants it is common for the “valve” of the foramen ovale to be prolapsed, causing left-to-right shunting. This prolapse often resolves after coarctation repair. A true secundum atrial septal defect (ASD) may also occur with coarctation. Moderate to large ASDs appear to show the same tendency to close when coarctation is present and when it is not. In about 10% of patients with ASD, however, intractable heart failure will develop in infancy following coarctation repair, requiring ASD closure. The best predictor of development of heart failure when ASD coexists with coarctation is small mitral valve diameter, not the size of the ASD itself.

Left Ventricle

Left ventricular hypertrophy without volume increase is present in most patients with coarctation within a few days of birth. This progresses as the patient ages and may be aggravated by associated cardiac anomalies.

The left ventricular outflow tract may be abnormal in patients with arch obstruction, particularly when a VSD coexists. The left ventricular papillary muscles may be abnormally positioned, typically with a reduced interpapillary distance.

Aortic Valve

A bicuspid aortic valve is common, although its exact prevalence is uncertain. In two autopsy series, it was 46% and 27%, with an additional 6% and 7%, respectively, with congenital valvar stenosis. Tawes and colleagues report that among 250 living children with long-term follow-up, 32 (13%) had clinical evidence of aortic valve disease (mainly stenosis but also regurgitation). When aortic regurgitation appears in coarctation, it is usually based on a bicuspid aortic valve combined with persistent hypertension. Bicuspid aortic valve is known to be associated with dilatation of the ascending aorta. In one study, presence of coarctation in this setting was not associated with increased magnitude or rate of ascending aortic dilatation. Another study indicates that patients with coarctation and bicuspid aortic valve have greater aortic root dilatation than those with coarctation and tricuspid aortic valves. In the presurgical era, aortic dissection was noted to occur in 19% of coarctation patients without bicuspid aortic valve, but in 50% of those with bicuspid aortic valve.

Intracranial Aneurysm

Coarctation and berry-type intracranial aneurysm coexist in some patients. Some instances of sudden death in untreated as well as treated coarctation are from rupture of the intracranial aneurysm. That coarctation, bicuspid aortic valve, and intracranial aneurysm are associated leads to the inference that coarctation is only one manifestation of a diffuse arteriopathy.

Coarctation as Part of Hypoplastic Left Heart Physiology

Coarctation (with or without a patent ductus arteriosus, and with or without hypoplasia of the isthmus or distal aortic arch between left common carotid and left subclavian arteries) sometimes coexists with anomalies that also affect left ventricular function and structure directly (see Morphogenesis and Morphology in Chapter 49). This is particularly a problem in symptomatic neonates and infants. These anomalies include:

- Hypoplasia of ascending aorta
- Supravalvar, valvar, subvalvar, and anular aortic stenosis or hypoplasia
- Aortic atresia
- Left ventricular hypoplasia or hypertrophy
- Endocardial fibroelastosis
Two congenital anomalies affecting left ventricular outflow

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Data from Quaegebeur and colleagues.57

*Univentricular atrioventricular connection (double inlet left ventricle in 12, double inlet right ventricle in one, mitral atresia in 13, tricuspid atresia in 5, common ventricle in 1).*

*Intact ventricular septum in 3, VSD in 24.*

*Complete in 14, partial in 2.*

Key: AV, Atrioventricular; CCTGA, congenitally corrected transposition of the great arteries; DORV, double outlet right ventricle; LCA, left coronary artery; PAPVC, partial anomalous pulmonary venous connection; PT, pulmonary trunk; TAPVC, total anomalous pulmonary venous connection; TGA, transposition of the great arteries; VSD, ventricular septal defect.

Coexisting Cardiac Anomalies

When coarctation first presents in older children and young adults (as it did in the early years of cardiac surgery, but uncommonly now), coexisting cardiac anomalies are uncommon. When it presents in neonates, and to some extent in infants, coexisting cardiac anomalies are common (Table 48-2). These associations are explained by the fact that survival beyond infancy is much less likely when coexisting anomalies are present; thus, long-term survivors tend to have simple lesions. Because in the current era most coarctations are diagnosed in neonates or infants, it follows that prevalence of associated anomalies found in neonates with coarctation closely approximates true prevalence.

Patent ductus arteriosus is present in almost 100% of neonates and in most infants with a preductal type of coarctation.26 This is considered part of isolated coarctation rather than an additional anomaly. Tubular hypoplasia of the distal aortic arch is also considered to be part of the anomaly of coarctation rather than an associated anomaly. ASD is not considered as an additional anomaly unless large enough to need closure. This excludes the fairly numerous examples of infants presenting with a left-to-right shunt through a stretched patent foramen ovale that may subsequently close. Anomalous right subclavian artery occurs in about 1% of cases of coarctation and may be proximal or distal to the coarctation.26 This variation does not appear to affect the collateral circulation that develops in any clinically significant way.26

Approximately 82% of individuals born with coarctation have it as an isolated lesion (with or without continuing patency of the ductus arteriosus). About 11% have an important coexisting VSD, and approximately 7% have other important coexisting cardiac anomalies. These prevalences are different from those in patients who become symptomatic during neonatal life or infancy and require early intervention (see Table 48-2).

Prevalence of isolated coarctation in patients with an otherwise normal heart appears to be about 40 per 100,000 live births. Persons with pulmonary stenosis or atresia, tetralogy of Fallot, and tricuspid atresia with concordant ventriculoarterial connection have a prevalence of coarctation close to 0 per 100,000. Patients with aortic stenosis and mitral stenosis or regurgitation have a considerably higher prevalence than patients with otherwise normal hearts. Patients with VSD and other lesions such as transposition, double outlet right ventricle, truncus arteriosus, atrioventricular septal defect, and single ventricle who have associated VSD also appear to have a relatively high prevalence of coexisting coarctation. This may relate to altered blood flow patterns within the heart that result in less flow across the aortic isthmus during fetal development.
CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Mode of presentation and diagnostic criteria depend to a considerable degree on prevalence and severity of coexisting cardiac anomalies, and thus on the patient’s age at presentation.

Neonates and Infants

Severe heart failure in a neonate or infant requires that coarctation be considered, especially when a favorable response to medical treatment does not occur promptly. It may be unsuspected in complex lesions when the baby is in extremis, because even when the ductus is closed, a large left-to-right shunt proximal to the aorta can decrease manifestation of hypertension in the arms. Severe proximal obstructing lesions (aortic or mitral stenosis) can have a similar effect. Control of heart failure and tachycardia in these situations frequently unmask differential pressures in upper and lower extremities as cardiac output improves.

Signs and symptoms of coarctation presenting in the neonate are those of heart failure. After a variable period of well-being, tachypnea, feeding problems, and sweating develop. On examination, there is a gallop rhythm and a systolic murmur along the left sternal edge and usually posteriorly over the coarctation site. Femoral pulses are absent or reduced in volume and delayed compared with radial or brachial pulses, although in small, sick infants with tachycardia, pulse delay may be difficult to detect. Blood pressure is higher in the arms than in the legs (by >20 mmHg). Delay in onset of heart failure is probably related, at least in isolated coarctation, to the variable time it takes for the ductus to close. Ductal closure usually commences at the pulmonary end, and generally it is not until the aortic end closes that the periductal aortic shelf produces severe obstruction (see Morphology earlier in this section). Thus, femoral pulses can be normal at birth but absent at 1 week.

When the ductus arteriosus remains widely patent and a severe coarctation lies proximal to it (predisual coarctation), there may be a right-to-left shunt into the descending aorta and, classically, cyanosis of the toes and sometimes the left hand while the right hand and lips remain pink (differential cyanosis). Femoral pulses are normal, and there is no ductus murmur. In fact, differential cyanosis is uncommon, either because flow through the coarctation is large or because PO₂ of the pulmonary artery blood is high from an additional intracardiac shunt through a VSD, an interatrial communication, or both. Moreover, despite presence of a severe coarctation proximal to a patent ductus arteriosus, systemic vascular resistance in the lower compartment usually exceeds pulmonary vascular resistance, so the ductal shunt is left to right or bidirectional.

In infancy, hypertension may be present but is seldom severe, and a collateral circulation is not palpable, although it is usually present angiographically (Fig. 48-5). Marked cardiomegaly is almost invariable on chest radiograph. The electrocardiogram (ECG) usually shows right ventricular hypertrophy in the first few months of life, even with isolated coarctation. About two thirds of infants operated on in the first year of life have right ventricular hypertrophy or combined hypertrophy, and fewer than 25% have pure left ventricular hypertrophy.

Left-to-right shunt through a stretched patent foramen ovale is common in infants with severe coarctation in heart failure. When heart failure disappears, so does the atrial shunt. Congenital aortic stenosis may not be evident clinically (or by catheter withdrawal pressure differential) in infancy, and yet it may be severe enough to require surgical relief at age 2 to 5 years, particularly when it is subvalvar (see Section II in Chapter 47).

Childhood (Age 1 to 14 Years)

Almost all patients who first present at age 1 to 14 years are asymptomatic unless they have important associated anomalies. Tawes and colleagues noted that children with associated anomalies may present in heart failure up to age 3 years, and Patel and colleagues noted heart failure in 7 of 65 children (11%) age 1 to 14 years. Subarachnoid hemorrhage from rupture of a berry aneurysm occurs occasionally but is rare in children younger than 7 years, and spontaneous paresis or paraplegia caused by dilated intercostal arteries compressing the anterior spinal artery or by epidural hemorrhage is even less common. Hypertension occurs in almost 90% of patients.

The chest radiograph shows cardiomegaly in 33% and rib notching in about 15% (Fig. 48-6), but this feature does not occur before age 3 years. ECG shows predominantly left ventricular hypertrophy, with right ventricular hypertrophy present only when there is pulmonary hypertension with elevated pulmonary vascular resistance. ECG is normal in about one third of children.

Adolescence (Beyond 14 Years) and Adult Life

Many adolescent and young adult patients remain asymptomatic and are diagnosed at routine examination because femoral pulses are noted to be absent or reduced and delayed in the presence of a cardiac murmur, hypertension, or an abnormal chest radiograph. Hypertension is common and more severe than in younger patients, and heart failure may occur after about age 30 years. Heart failure is preceded by effort dyspnea, cardiomegaly, and important left ventricular hypertrophy on ECG. Headache, nose bleeds, fatigue, and calf claudication occasionally occur. Collaterals are usually palpable or audible posteriorly. Radiographic findings include a “figure-3” sign in the left upper mediastinal shadow (Fig. 48-7) and, almost always, rib notching. (Absence of rib notching in the right chest suggests an anomalous origin of the right subclavian artery and in the left chest a stenosis of the left subclavian artery origin.)

Associated Syndromes

There is an association between Turner syndrome and von Recklinghausen disease and coarctation. Rarely, patients with coarctation have Noonan syndrome or congenital rubella.

Special Diagnostic Methods

Two-dimensional echocardiography can visualize coarctation in neonates and small infants (Fig. 48-8) and is usually the definitive study. Associated intracardiac defects can also be defined in detail. Severity of coarctation can often be assessed...
Figure 48-5  Cineangiograms in left anterior oblique view with injection into left ventricle of a severe coarctation 5 mm in length in a 7-week-old infant without other associated anomalies. **A**, Aortic arch and branches are outlined proximal to coarctation, but distal aorta is not opacified. Collateral vessels are visible. **B**, Dense collateral network is visible in this later frame, with contrast in descending aorta below coarctation. **C**, Descending aorta is well outlined, most of its filling coming from collaterals, although a tiny lumen about 5 mm long could be identified connecting the two ends. Key: LCA, Left coronary artery.
by characterizing intracardiac and great artery blood flow patterns using color Doppler signaling. Fetopatologically, measurements of the z value of the aortic isthmus and the isthmus-to-ductus ratio are sensitive indicators of postnatal coarctation.\textsuperscript{M15} Outside infancy, echocardiography may still be helpful but is usually not definitive. In moderate or mild coarctation, presence of an open ductus may obscure a coarctation at echocardiographic examination. This is due partly to altered blood flow patterns associated with the patent ductus, but more importantly to the fact that the coarctation itself may evolve as the ductus closes.

MRI and computed tomography (CT) are currently the imaging modalities of choice for coarctation in patients beyond infancy.\textsuperscript{B15,C11,G10,R11,R18,S6,S33} Excellent detailed imaging of pertinent vascular structures can be obtained, often exceeding the detail seen with aortography (Fig. 48-9). Three-dimensional rendering can be particularly informative (Fig. 48-10). Post-surgical changes also can be defined in detail (Fig. 48-11). Hemodynamic data can be assessed by MRI and may be particularly useful in older patients with well-developed collaterals, or in patients with restenosis, in whom there may be little or no gradient across the

**Figure 48-6** Portion of chest radiograph showing severe rib notch-
ing in patient with coarctation of the aorta. Note that changes are not present in first two ribs and are typically less severe below the fifth rib.

**Figure 48-7** Radiographic studies in patient with coarctation, demonstrating classic figure-3 sign present in some patients with coarctation of the aorta. **A**, Chest radiograph. Upper convexity of sign is formed by the aortic isthmus and left subclavian artery, lower convexity by the upper descending aorta at site of poststenotic dilatation. **B**, Barium esophagogram. Note how the two shadows overlap. Isthmus and descending aorta produce upper and lower indentations on leftward margin of barium-filled esophagus.
Figure 48-8  Echocardiographic images of neonatal aortic coarctation. A, Parasternal view showing small-diameter ascending aorta with origins of brachiocephalic and left carotid arteries, severe hypoplasia of distal aortic arch between left carotid and subclavian arteries, discrete coarctation, and descending aorta. B, Color imaging showing discrete narrowing at coarctation site.

Continued
Figure 48-8, cont’d  C. Image details hypoplasia of distal arch and isthmus, and a large ductus arteriosus entering descending aorta. A discrete coarctation, which was also present in this case, is not seen well in this image. Key: AA, Ascending aorta; AI, aortic isthmus; BA, brachiocephalic artery; CO, coarctation; DA, distal aortic arch; DES, descending aorta; LCA, left carotid artery; LSCA, left subclavian artery; PDA, patent ductus arteriosus.

Figure 48-9  Magnetic resonance imaging of coarctation. A, Lateral projection (using contrast-enhanced imaging and cardiac gating) of native coarctation in 20-year-old man. Isthmic hypoplasia and collateral vessels are also present. B, Lateral projection (using T1-weighted imaging) of recurrent coarctation in 35-year-old woman.
Figure 48-9, cont’d  C, Three-dimensional rendering of patient shown in B.  D, Lateral projection (using contrast-enhanced magnetic resonance imaging) of 40-year-old man with recurrent obstruction following childhood creation of left subclavian artery–to–descending aortic synthetic graft bypass of aortic coarctation.  E, Three-dimensional rendering of recurrent obstruction shown in D.  Key:  AI, Aortic isthmus;  CO, coarctation;  CV, collateral vessels;  LSCA, left subclavian artery;  SCB, subclavian-to–descending aortic bypass.
Isolated coarctation is slightly more than twice as common in males as in females, but there is no gender difference in those with important coexisting cardiac anomalies.\textsuperscript{522}

**Isolated Coarctation**

This category includes patients with or without associated patent ductus arteriosus.

**Survival**

Coarctation has been surgically correctable since 1944. As a result, information on natural history is difficult to find. Postmortem data from series and case reports published before the era of surgical correction indicate that the median age of death is 31 years, with 76% of deaths attributable to complications of the coarctation.\textsuperscript{A1,B,1,R14} These reports did not include patients under age 2 years, and therefore neonatal and infant mortality are not accounted for. Among babies born with isolated coarctation, about 10% may be expected to die of acute cardiac failure during the first month of life if untreated. Another 20% may be expected to die later during the first year of life of heart failure or its sequelae. Thus, the true median age of death may be closer to 10 years.

Antemortem series prior to the era of surgical correction indicate that mortality after infancy is about 1.6% per year during the first 2 decades, and then gradually rises to 6.7% per year by the sixth decade.\textsuperscript{15} The most common causes of death, in decreasing order, are heart failure, aortic rupture, infective endocarditis, and intracranial hemorrhage.\textsuperscript{15} The few individuals who survive to age 60 years are usually women, because of their lesser tendency to develop hypertension and arteriosclerosis.\textsuperscript{14}

**Heart Failure in Infancy**

A number of factors act singly or in combination to produce heart failure in infants with isolated coarctation. *First*, ductal closure, as it progresses from pulmonary to aortic end during the first 7 to 10 days of life, increases the degree of aortic narrowing,\textsuperscript{R26,T2} which prior to this event may have been mild and of little functional importance. Consequent development of severe coarctation precipitates left ventricular failure at age 1 to 2 weeks. If the coarctation does not become severe, heart failure does not occur. *Second*, the degree to which collateral circulation is present at birth may also be important. Mathew and colleagues found that all infants with isolated coarctation had collaterals on angiography performed at age 8 days to 15 months, indicating that collaterals developed either during fetal life or, more likely, soon after.\textsuperscript{M14} Presumably, collateral development is absent or inadequate as long as the ductus is widely patent and there is pulmonary hypertension.\textsuperscript{R6} *Third*, presence of major noncardiac anomalies contributes. Thus, of 46 autopsied infants reported by Malm and colleagues in 1963,\textsuperscript{R6} 12 died in the first week of life from major noncardiac anomalies (prematurity, tracheoesophageal fistula), and in the New England Regional Study,\textsuperscript{R15} 26% of the infants had extracardiac anomalies that, when severe, contributed to mortality.

Sequence of pathophysiologic events leading to severe heart failure that develops in the first few weeks of life has been further elucidated by Graham and colleagues.\textsuperscript{G8} They found that left ventricular wall mass was normal and left ventricular stroke volume and ejection fraction severely
depressed. Because left ventricular systolic function as reflected in stroke volume and ejection fraction returned to normal after coarctation repair, the mechanism of its preoperative reduction is clearly afterload mismatch (see “Increased Ventricular Afterload” in Section I of Chapter 5 and Natural History in Chapter 12) brought about by sudden increase in left ventricular afterload from the rapidly developing coarctation as the ductus closes in the presence of a nonhypertrophied left ventricle. Severe cardiomegaly is present, but it is the result of markedly increased right ventricular end-diastolic volume; left ventricular end-diastolic volume is normal. Right ventricular enlargement usually is associated with left-to-right shunting through the stretched foramen ovale.

Graham and colleagues reported somewhat different findings in the 10% of patients with isolated coarctation presenting with mild or moderate heart failure at 1 to 6 months of age. Left ventricular wall mass was increased in this group (as it is in older children with coarctation), and left ventricular ejection fraction and stroke volume were only mildly decreased. Increased left ventricular thickness had reduced left ventricular afterload (see “Ventricular Afterload” in Section I of Chapter 5); that is, “afterload mismatch” had largely been overcome.

Apart from incidental causes, death after infancy in patients with isolated coarctation is generally due to heart failure, infective endocarditis, aortic rupture or dissection (each in

Figure 48-11 Magnetic resonance (MRA) and computed tomographic (CTA) angiograms of previously repaired coarctation. A, Maximal-intensity projection image from contrast-enhanced MRA of a 25-year-old man who had a remote childhood repair of coarctation. Image demonstrates an eccentric filling defect (arrow) that nearly occludes repaired segment of the aorta. It may represent thrombus and fibrous scar. B, Maximal-intensity projection image from cardiac gated CTA of an 18-year-old man who had a focal periductal coarctation distended by a stent. C, Maximal-intensity projection image from contrast-enhanced MRA of a 27-year-old woman who developed an aneurysm at site of repaired coarctation.
Heart Failure in Childhood and Adult Life

In Reifenstein’s series of adolescents and adults, there was only one death from heart failure in a patient younger than 20 years of age; most such deaths occurred in the fourth and fifth decades. In most instances, there was associated valvar heart disease, usually aortic but occasionally mitral, that combined with hypertension to produce heart failure. Congenitally abnormal aortic valve (bicuspid valves were present in 42% of the hearts) was the usual cause of stenosis or regurgitation. Heart failure occurs at the extremes of age; about two thirds occurs in infancy. It is uncommon between age 1 and about age 30 and reappears in about two thirds of patients who survive beyond 40 years.

Infected Endocarditis or Endarteritis

Infected endocarditis or endarteritis causes death at an average age of 29 years and is equally common in the first 5 decades of life. Infection usually occurs on a bicuspid aortic valve and rarely on a mitral valve or in relationship to a VSD. Endarteritis is less common and usually occurs in the poststenotic segment in relationship to the jet lesion on the aortic wall. Mycotic aneurysms can result.

Aortic Rupture

Rupture occurs at an average age of 27 years and is most common in the second and third decades. It usually involves the ascending aorta and often occurs into the pericardium with tamponade; less often, the aorta immediately beyond the coarctation ruptures at the site of poststenotic dilatation where the wall is dilated and thin. Many of these ruptures are probably true dissecting aneurysms, but pathologic details of the aortic wall are scarce.

Intracranial Lesions

Intracranial lesions caused death at an average age of 28 years in Reifenstein’s series and at 30 years in Abbott’s series. Among the 35 patients younger than age 21 years with coarctation and cerebrovascular disease reported in the literature and reviewed by Shearer and colleagues, only three were younger than age 7 years at the time, and in most the incident was fatal. In the majority of cases, there is a subarachnoid hemorrhage from rupture of a congenital berry aneurysm on the circle of Willis arteries. These lesions are considerably more common in patients with coarctation than in the general population and are more likely to rupture because of associated hypertension. Other causes of cerebrovascular accidents are arteriosclerosis, particularly in older patients, and emboli, particularly in the presence of infective endocarditis. In the treated series reported by Liberthson and colleagues, a cerebrovascular accident had occurred in only 1 of 91 patients (1.1%; CL 0.1%-3.7%) younger than age 11 years at the time of diagnosis and in 12 of 143 (8%; CL 6%-12%) age 11 to 39 years. However, in those older than 40 years, 21% (5 of 24; CL 12%-33%) had had a cerebrovascular accident.

Coarctation Associated with Ventricular Septal Defect

Most infants born with a large VSD and coarctation develop severe heart failure in the first month. By contrast, presentation so early is uncommon in patients with isolated large VSD (see under Natural History in Section I of Chapter 35). Unless the VSD rapidly diminishes in size, most of these babies die within a few months without surgical treatment. However, in many the VSD rapidly becomes small (see Fig. 35-21 in Chapter 35), and the natural history then becomes essentially that of isolated coarctation.

Coarctation Associated with Other Major Cardiac Anomalies

The combination of coarctation with other major cardiac anomalies nearly always produces severe heart failure during the early weeks of life. Without surgical treatment, from 80% to 100% of such babies die in their first year of life.

All reported series show a high proportion of associated cardiovascular anomalies in patients with coarctation presenting in infancy (see Table 48-2). In such infants, isthmus and arch hypoplasia is almost constant as a consequence of disturbed fetal blood flow patterns (see Morphology earlier in this section). In many of these infants, particularly those with complex and severe intracardiac anomalies, the natural history is primarily that of the associated anomaly. However, associated severe coarctation undoubtedly precipitates early heart failure.

TECHNIQUE OF OPERATION

In general, resection of the coarctation and reconstruction of the aorta should be considered the ideal method of repairing coarctation. For a number of reasons, however, this cannot always be achieved, and alternative methods must be used. The technique of each operation is described in this section.

Preparation, Incision, and Dissection

Neonates and Infants

After anesthetic induction, body temperature is allowed to drift down to a nasopharyngeal temperature of about 35°C. This downward drift is helped by reducing the operating room temperature to about 18°C (65°F) and by using the cooling mode in the heating-cooling pad under the child. Blood pressure in the right arm is monitored by an indwelling radial or brachial artery catheter. Near-infrared spectroscopy can be used to monitor tissue oxygenation both proximal and distal to the coarctation. Substantial changes in tissue oxygen values both above and below the coarctation have been documented with varying technical maneuvers; however, these changes have not yet been correlated with clinical adverse events.

The patient is positioned in full lateral position, secured with strapping across the hip and onto the operating table, with a sandbag tucked against the front of the chest. Approach is made through a left posterolateral thoracotomy, with the entry through the fourth intercostal space. For this, the intercostal muscles may be incised in the center of the interspace or entry made via the fifth rib bed, elevating the periosteum from the superior half of this rib and incising the rib bed rather than the intercostal muscles. Care is required posteriorly because careless elevation of the periosteum too far in this direction or attempts to dislocate the costotransverse joint will result in excessive bleeding from
collaterals. In most cases, the trapezius muscle need not be incised. Scoliosis is well documented following left thoracotomy in infants and children\(^4\); however, it is not known whether minimizing trauma to chest wall muscles and ribs will reduce this late development.

The rib spreader is inserted and opened in stages to avoid rib fractures (Fig. 48-12, B). The lung is retracted anteriorly, and the mediastinal pleura is opened over the aorta downward for several centimeters below the coarctation site and upward to include the distal arch and subclavian artery and, if necessary for arch hypoplasia, all the brachiocephalic arteries. Numerous closely placed stay sutures are placed along each side of the pleural incision, and the ends are gathered into clamps for exposure (Fig. 48-12, C). No other retractors are then required. The left superior intercostal vein is ligated and divided.

Keeping dissection in the areolar tissue just superficial to the adventitial aortic coat, the proximal left subclavian artery, the distal transverse arch, and the aortic isthmus are dissected. All dissection is kept close to the aorta, in part because this is the best plane of dissection and in part to minimize the possibility of damage to the thoracic duct. “The Abbott
artery occasionally arises from the medial aspect of the isthmus and, when present, should be ligated and divided. Next, with great care to avoid damaging the intercostals and bronchial arteries, the aorta beyond the coarctation is dissected. It is occasionally necessary to divide one or more bronchial arteries medially. Finally, the ductus arteriosus or ligamentum arteriosum is dissected. If the nasopharyngeal temperature has not decreased to about 35°C, and especially if the patient is hyperthermic, the left pleural space is lavaged with ice-cold saline for the few minutes required to accomplish the repair (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24).

Children
The operation is technically more demanding in children than in neonates and infants because collateral circulation is much larger. A long posterolateral thoracotomy incision is made, cutting 1 to 4 cm of the trapezius muscle posteriorly and carrying the incision to the nipple line anteriorly. The pleural space is entered through the top of the bed of the nonresected fifth rib and the rib spreader is opened gradually until a wide exposure is obtained. The mediastinal pleura is opened widely over the upper half of the descending thoracic aorta and subclavian artery. Numerous stay sutures are applied as described for infants (see previous text).

The aortic dissection then proceeds as described for infants; however, it must be done with particular accuracy and precision because of the large intercostal arteries. Even the smallest subadventitial dissection must be scrupulously avoided by keeping dissection in the areolar tissue just superficial to the adventitia. In most cases, after incising the pleura over the aorta and brachiocephalic arteries and dividing the superior intercostal vein, dissection is carried around the aorta just proximal to the coarctation and a tape placed around it. A similarly sharp dissection is made just distal to the coarctation, taking care to avoid damage to a hidden Abbott artery above or an enlarged intercostal artery below. Further dissection is facilitated by gentle traction on the tapes.

The ligamentum arteriosum, the third and sometimes fourth pair of intercostal arteries, Abbott artery if present, and left subclavian and carotid arteries are now completely dissected. The Abbott artery requires ligation and division, as may a bronchial (or esophageal) artery beyond the stricture. All dissection details described for infants are important here as well.

Immediate Post-Repair Management
Following repair by any technique, the distal clamp is removed first. After the proximal clamp has been slowly opened, great care is taken to maintain proper ventilation and baseline systemic blood pressure for at least the next 5 minutes as a precaution against sudden development of intractable ventricular fibrillation 3 to 4 minutes after release of the clamp (de-clamping syndrome). It may be necessary for the anesthesiologist to give sodium bicarbonate or an infusion of a pure peripheral vasoconstrictor (or both) just before clamp removal in particularly unstable infants or in those with prolonged clamp times.

After repair, pressures are measured proximal and distal to the repair with fine needles. If there is a systolic gradient of greater than 10 mmHg, clamps are reapplied, sutures removed, and the repair refashioned. In neonates, the residual gradient may reside in the hypoplastic distal aortic arch between left carotid and subclavian arteries. Other causes may be inadequate excision of the intimal flap combined with failure to carry the incision in the aorta far enough distally if the subclavian flap technique is used (see following text), or a poorly formed anastomosis using resection and end-to-end anastomosis.

After the clamps are removed, the heating blanket, warming lamps, a warmed operating room, and warmed and humidified inspired gases are used to warm the infant. Usually the suture line is hemostatic, and the mediastinal pleura can soon be closed over it. A small chest tube is placed through a lateral and inferior stab wound. Incision through the interspace is closed with a few interrupted sutures. Muscles and subcuticular layers are closed with a continuous suture. The chest tube may be removed in the operating room in neonates and infants after closing the incision. The baby is usually returned to the intensive care unit still intubated.
Resection and Primary Anastomosis

**Neonates and Infants**

Some form of this operation is currently the preferred technique for young patients. Preparations for operation, incision, and dissection are described previously under “Preparation, Incision, and Dissection.” Once the coarctation is resected, there are various options for reconstruction, each of which is described in this section.

When the coarctation is well beyond the origin of the left subclavian artery, the proximal clamp is usually placed across the aorta to include the origin of the left subclavian artery. The distal clamp is placed on the aorta below the third and fourth set of intercostal arteries. The ligamentum arteriosum or ductus arteriosus, which has been tied at its pulmonary end, is transected at its aortic insertion. The aorta is transected proximal to the coarctation at a level that ensures removal of any narrowed portion of the isthmus as well as the coarctation (Fig. 48-13, A). Similar transection of the aorta is made beyond the coarctation, where the aortic diameter is usually ample.

The suture line is made with a continuous simple suture of 6-0 or 7-0 absorbable monofilament suture, sewing “from within” for the posterior wall (Fig. 48-13, B). After the posterior row of sutures has been placed, the ends of the aorta are approximated by the assistant and the sutures are pulled up snugly. The remainder of the anastomosis is completed by sutureing the anterior wall using the other end (Fig. 48-13, B).

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**Figure 48-13**  Resection and end-to-end anastomosis for repair of coarctation. **A,** With patient in right lateral decubitus position, a curving incision is made around the angle of the scapula, the chest opened, and stay sutures placed on the edges of the mediastinal pleura and held under tension to aid exposure (as shown in Fig. 48-12, but eliminated here for simplicity). After sharply dissecting out the coarctation and contiguous structures, tapes are placed around aorta just above and below coarctation site. Traction on tapes elevates aorta anteriorly or posteriorly to provide exposure that facilitates dissection. Dashed lines show levels of aortic transection above and below coarctation site. **B,** Ductus arteriosus (or ligamentum arteriosum) has been ligated and divided, and small bulldog clamps (clips) have been placed on third and fourth pairs of intercostal arteries. Proximal clamp is positioned across aorta and base of subclavian artery to leave ample length for the proximal cuff. Coarctation is excised, getting back to a wide orifice proximally and distally. Running monofilament absorbable suture line is begun at far end of the circumference and progresses along posterior aspect of anastomosis.

*Continued*
Finally, the clamps are removed as described under “Immediate Post-Repair Management” and the operation completed similarly (Fig. 48-13, D).

When the coarctation is near the takeoff of the left subclavian artery, or when the segment between it and the subclavian artery is importantly hypoplastic, proximal transection is begun just beyond the origin of the left subclavian artery.

When the distal portion of the aortic arch between the left common carotid and subclavian arteries is hypoplastic, as it often is in neonates and young infants, the operation may be modified so as to enlarge this area. In young patients, end-to-end anastomosis is easily accomplished after extended resection, and the distal transverse arch and aorta proximal to the coarctation are widened by the procedure. Alternatively, hypoplasia in the distal arch and even the proximal arch can be managed by placing the curved proximal side-biting clamp to occlude the proximal arch just distal to the brachiocephalic artery origin, occluding both the left carotid and left subclavian arteries, in preparation for performing an end-to-side distal aorta to arch reconstruction (see Fig. 48-14, A). After resecting the discrete coarctation, the isthmus is ligated with a 5-0 polypropylene ligature, and the undersurface of the proximal arch is incised opposite the left carotid artery origin and extended to the point opposite the left subclavian artery origin. The cut end of the descending aorta, trimmed of all ductal tissue, is connected to the incision in the undersurface of the arch with an end-to-side anastomosis using a running suture technique with 6-0 or 7-0 absorbable monofilament suture (Fig. 48-14, B and C).

Resection with end-to-end anastomosis can be combined with subclavian flap aortoplasty (see “Subclavian Flap Aortoplasty” in text that follows) if there is concern about the size of the aorta just beyond the subclavian artery. This problem is better managed by resection with extended end-to-end anastomosis or resection with end-to-side anastomosis, as described earlier; however, the combined operation will be briefly described for completeness. After preparing the subclavian artery and placing clamps as for the standard subclavian flap repair, the coarctation area is excised as described for standard end-to-end anastomosis. The proximal and distal aortic segments are reconstructed with an end-to-end anastomosis, with the exception that the posterior wall and anterior wall continuous suture lines are not tied to each other posterolaterally after their completion. Rather, each suture line is tied to itself posterolaterally, leaving a small posterolateral gap. The subclavian artery is split open longitudinally, and incision is extended into the proximal aortic segment, then carried through the small suture line gap onto the distal aortic segment. The subclavian flap is sewn into position as described previously in the standard subclavian flap method, straddling across the end-to-end anastomosis.

Children and Adults
Operation is carried out in the same steps as in very young patients. However, the vessels are much more friable, intercostal arteries larger and more easily damaged, and the dissection potentially more hazardous. Use of controlled hypotension by the anesthesiologist (see “Coarctation of the Aorta” in Section II of Chapter 4) during dissection is important because it allows dissection to be done more safely and expeditiously. Once the aortic clamps are in place, upper body blood pressure is allowed to increase to moderately hypertensive levels (to promote collateral blood flow, see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24). It is helpful to monitor left ventricular function by transesophageal echocardiography during the aortic clamping. Vasodilatory agents must be withdrawn before the clamps are removed.

Hemorrhage from intercostal arteries or from the Abbott artery can be massive and difficult to control, especially if one of these vessels is damaged early in the dissection before adequate exposure is obtained. Therefore, no effort is made...
tucked against the aorta, the tapes swung to the other side, and dissection continued.

It is safer to control the intercostals temporarily with small metal bulldog clamps during resection and anastomosis than it is to ligate and divide them, because delayed hemorrhage can occur from slippage of such a ligature.

Occasionally, because of immobility of the aortic structures in an older patient or because of a long-segment coarctation, end-to-end anastomosis is not possible, and either an interposed polyester tube graft or an augmentation patch is necessary.

Figure 48-14  Resection and end-to-side aortic anastomosis for aortic coarctation with hypoplasia of isthmus and aortic arch. A, Incision and dissection are similar to that described in Fig. 48-12. Dashed lines show transection sites on distal aspect of isthmus, ductus arteriosus, and descending aorta, and incision site on undersurface of proximal aortic arch. B, Proximal aortic clamp is placed on aortic arch to include bases of left subclavian and left carotid arteries, with tip of the clamp angled precisely to extend as far proximally as possible without causing obstruction of flow to brachiocephalic artery. Distal aortic clamp is placed between third and fourth sets of intercostal vessels, and the third set of intercostal vessels is controlled with clips. Aortic isthmus is ligated. Ductus arteriosus is ligated at its pulmonary artery end, and coarctation site, including aortic end of ductus, distal aspect of aortic isthmus, and first portion of descending aorta beyond coarctation site, is completely resected along the lines shown in A. Incision in undersurface of aortic arch is made such that the length of the incision accommodates entire circumference of the normal aspect of descending aorta. Suture line is begun at far end of the circumference with a running monofilament absorbable suture. C, Anastomosis is performed essentially identically as described in the end-to-end anastomosis (see Fig. 48-13), proceeding along the posterior aspect of the circumference and then the anterior aspect. Completed end-to-side distal aorta to arch anastomosis is shown. Key: BA, Brachiocephalic artery; LCA, left common carotid artery; LSCA, left subclavian artery; PDA, patent ductus arteriosus.
Subclavian Flap Aortoplasty

Currently this technique is most frequently used selectively in neonates, when circumstances make resection and reconstruction inappropriate—for example, when it is advantageous to preserve the ductus in the setting of a borderline left ventricle (see Indications for Operation later in this section). PGE1 infusion is maintained throughout the procedure (see Fig. 48-12, A and B, which illustrate the exposure). To begin the subclavian flap aortoplasty, dissection of the subclavian artery is carried distally to expose the branches. It is ligated and divided proximal to all branches, none of which are ligated (Fig. 48-15, A). The ductus arteriosus is dissected, and a delicate vascular clamp, such as a temporary neurovascular clip, is placed across the ductus. A delicate vascular clamp is placed across the aortic arch between the left common carotid and left subclavian arteries, and a second clamp is placed well distal to the coarctation but proximal to the intercostal arteries, allowing space above and below the coarctation for the incision, as shown by the dotted line in Fig. 48-15, A. Uncommonly, it must be placed beyond the third pair of intercostal arteries (the first set beyond the coarctation), which are then controlled with removable metal clips or vessel loops made from heavy suture material.

The subclavian artery, before its transection, is split open longitudinally along its posterior margin, carrying this incision across the coarctation into the dilated distal aorta for at least 1 cm. Stay sutures are placed on either side at the level of the coarctation. The subclavian artery is transected just proximal to the ligature. Sharp corners at the end of the opened subclavian artery are trimmed; if the subclavian flap is unusually wide, the lateral edge is trimmed so that its width is about 1.5 times the diameter of the aorta. The turned-down subclavian flap may be tacked to the distal opened aorta using a double-ended 6-0 or 7-0 absorbable monofilament suture, which is then carried proximally as a continuous stitch (Fig. 48-15, B). Alternatively, the suture line may be started proximally on the medial side and carried just beyond the inferior angle of the aortic incision; another suture line is then started proximally on the lateral side and carried down to the previous one. Absorbable monofilament suture material 6-0 or 7-0 is used. Angles at either end of the turned-down subclavian flap must lie beyond the level of the coarctation, achieving this when necessary by sliding the flap distally in the process of suturing. In this manner, a proper “cobra head” is achieved. Following completion, the aortic clamps and the neurovascular clamp on the ductus are removed (Fig. 48-15, C).

Modifications of the subclavian flap repair have been used successfully.

Repair of Coarctation Proximal to Left Subclavian Artery

When hypoplasia occurs proximal to the left subclavian artery, the usual methods of repair can be unsatisfactory. When the situation is encountered in infants, a reversed subclavian flap aortoplasty may be used, or resection with end-to-side anastomosis as described earlier in this section and shown in Fig. 48-14 can be performed. The reverse subclavian flap combined with end-to-end anastomosis is illustrated in Fig. 48-16. After usual exposure and dissection, the left common carotid artery and aortic arch between this and the subclavian artery are completely dissected. Clamps are placed on the left common carotid artery and on the aorta just distal to this vessel and on the aorta distal to the left subclavian artery. The subclavian artery is ligated and divided distally. The subclavian artery is split down its medial side and the incision extended proximally onto the arch and the origin of the left common carotid artery (Fig. 48-16, A). The subclavian artery is turned down, in reverse to the classic subclavian flap operation, and sewn into place (Fig. 48-16, B and C). Alternatively, the end-to-side anastomosis of the descending aorta to the arch, as described earlier in this section under “Resection and Primary Anastomosis,” can be used. In addition, when an anomalous right subclavian artery is present, it can be used in the reconstruction to address arch hypoplasia.

In older patients, replacement of the coarcted area with an interposed tube graft may be done when the coarctation is severe, but techniques for aneurysms of the distal portion of the transverse aortic arch are necessary (see “Replacement of Aortic Arch” under Technique of Operation in Chapter 26). The simpler palliative placement of a bypassing polyester tube graft between the ascending aorta and lower descending thoracic aorta via a right thoracotomy may be used, but is less satisfactory and should be reserved for particularly complex recurrent arch obstructive problems (see Special Situations and Controversies later in this section for further discussion).

Repair When Aneurysm Is Present

When an aneurysm is present, either in the intercostal arteries (single or multiple) or aorta (see Morphology earlier in this section), resecting the segment of aorta involved along with the coarctation is required, and continuity is reestablished with an interposed tubular polyester graft. This procedure can be hazardous, particularly in regard to hemostatic control of the large intercostal artery feeding into the aneurysm. Pharmacologically induced hypotension is helpful to dissection. Early placement of the proximal aortic clamp and then ligation and division of the ligamentum arteriosum and placement of a clamp across the coarctation itself allows transection of the aorta proximal to the coarctation. Then gentle forward traction on the clamp across the coarctation allows the distal aorta and posteriorly placed intercostal artery aneurysm to be brought into better view for dissection and management.

Postrepair paraplegia is a greater hazard than usual because of the need to sacrifice intercostal arteries (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24). Special precautions required for all aneurysm surgery in this area are used (see “Replacement of Descending Thoracic Aorta” under Technique of Operation in Chapter 26).

Repair of Persistent or Recurrent Coarctation

Several options are open to the surgeon. The choice is partly determined by morphologic details of the obstruction and partly by surgeon preference. Resection and primary anastomosis, subclavian flap repair with or without resection, patch aortoplasty, and placing an interposition graft can all be considered. Repeat left thoracotomy is feasible in selected cases with discrete obstruction that does not involve the arch;
Figure 48-15  Subclavian flap repair for coarctation with preservation of patent ductus arteriosus. Exposure is shown in Fig. 48-12, A and B. A, Mediastinal pleura has been opened and stay sutures placed on the edges for exposure. After dissection is completed (see text) and after left subclavian artery has been ligated just proximal to vertebral artery, a vascular clamp is placed across aortic arch between left common carotid and left subclavian arteries. Distal aortic clamp is placed on descending aorta and may be positioned proximal to the third set of intercostal arteries, or as far distally as just distal to the fourth set of intercostal arteries (see text). A delicate temporary neurovascular clip is placed across the ductus arteriosus. Dashed line indicates proposed aortic incision. B, Subclavian artery has been divided distally and turned down for the flap. C, Flap sewn into place and aortic clamps and ductal clip removed (see text). Key: ICA, Intercostal artery; LCA, left common carotid artery; LPA, left pulmonary artery; LSCA, left subclavian artery; PDA, ductus arteriosus; RLN, recurrent laryngeal nerve.
bypass graft, is contraindicated because of the rupture risk. Standardized management techniques have not been established, but they include surgical, interventional, and hybrid techniques. Optimal outcomes will be achieved with a multidisciplinary team including a cardiac surgeon, interventional cardiologist, and radiologist. The variables that influence treatment strategy include the severity of residual stenosis or hypoplasia, location of the aneurysm relative to the obstruction, suitability of "landing zones" for transcatheter devices, patient age and comorbidity, and likelihood of exclusion of the left subclavian artery or other brachiocephalic artery. Surgical management can vary but typically requires CPB, either via median sternotomy or left thoracotomy. Results are excellent. In particularly difficult technical situations in older patients, a bypassing polyester tube graft on the left or right side may be all that is possible. This is most conveniently performed through a right thoracotomy. The end of a properly prepared polyester tube is anastomosed to the side of the intrapericardial portion of the ascending aorta using a side-biting clamp on the aorta. A side-biting clamp is placed on the descending aorta, just above the diaphragm, the tube graft is routed posterior to the right pulmonary hilum, and end-to-side anastomosis is performed. Intermediate-term results are generally good. Alternative extra-anatomical approaches have been described.

**Repair of Persistent or Recurrent Coarctation with Aneurysm**

Aneurysm following coarctation repair is more likely when transverse arch hypoplasia is present. The aneurysm may be very large and thin walled, with rupture almost a certainty over a 15-year period. These cases represent a major challenge and must be addressed directly. The option of "indirect management," such as by an extra-anatomical bypass graft, is contraindicated because of the rupture risk. Standardized management techniques have not been established, but they include surgical, interventional, and hybrid techniques. Optimal outcomes will be achieved with a multidisciplinary team including a cardiac surgeon, interventional cardiologist, and radiologist. The variables that influence treatment strategy include the severity of residual stenosis or hypoplasia, location of the aneurysm relative to the obstruction, suitability of "landing zones" for transcatheter devices, patient age and comorbidity, and likelihood of exclusion of the left subclavian artery or other brachiocephalic artery. Surgical management can vary but typically requires CPB, either via median sternotomy or left thoracotomy, with resection of the aneurysm and obstructive segment and interposition graft insertion. These procedures carry a mortality risk of 14% to 23%, and therefore endovascular management should be considered when anatomic details are favorable.

**Repair from an Anterior Midline Approach**

Particularly in neonates and young infants, coarctation of the aorta can be well repaired from an anterior midline approach using CPB. Although use of hypothermic circulatory arrest is
advocated by some, \textsuperscript{95,91,719,171,275} continuous CPB with antegrade cerebral perfusion can be used routinely for this repair.\textsuperscript{13,24,11,12,21} (Fig. 48-17). The midline approach is particularly useful when concomitant repair of intracardiac defects is contemplated, but it can also be used to advantage when coarctation is accompanied by severe hypoplasia of the proximal transverse arch, or when there is no proximal arch segment because the left carotid and brachiocephalic arteries share a common origin (“bovine” trunk) in association with hypoplasia of the segment between this common brachiocephalic trunk and the left subclavian artery.

Technical and CPB considerations are similar to those involved with repair of interrupted aortic arch (see Section II). The anterior midline approach has also been described for both children and adults with coarctation and other complex arch problems using interposition conduits.\textsuperscript{99,14}

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

**General**

Generally, care of patients after coarctation repair is simple and similar to that accorded any patient after thoracotomy. In neonates and young infants, usual care accorded to small babies who have been critically ill preoperatively is used (see Section IV of Chapter 5).

**Managing Systemic Arterial Hypertension**

Systemic arterial hypertension is usually present after operation, and its management is controversial. In older patients, mean arterial blood pressure is lowered to about 110 mmHg with nitroprusside for the first 24 hours, and the drug is then rapidly tapered and discontinued (see Appendix 5A in Chapter 5). Thereafter, if systolic blood pressure is greater than 150 mmHg, a \( \beta \)-adrenergic receptor blocking agent or captopril is administered for a few weeks. Care must be taken to avoid a dose that leads to hypotension.

In infants and young children, treatment is given less routinely for postoperative hypertension. Intravenous nitroprusside is the treatment of choice; however, esmolol is also effective.\textsuperscript{99}

**Abdominal Pain**

Careful interrogation and observation of older patients postoperatively indicate that most have mild abdominal discomfort for a few postoperative days. In 5% to 10% of cases, this is prominent, and abdominal distention with hypoactive bowel sounds may develop.

Treatment consists of bowel decompression via a nasogastric tube and antihypertensive drugs. Antihypertensive therapy is begun and continued until symptoms subside. Intravenous fluids may be required for a day or two. In a study from 1972, Ho and Moss\textsuperscript{122} reported that routine treatment with antihypertensive drugs resulted in fewer (no) instances of laparotomy for abdominal pain than did nontreatment. In current practice, the need for laparotomy for abdominal crisis is rare.

**Chylothorax**

The nature of chest tube drainage should be observed. Copious serous or milky drainage is probably chyle, a finding in about 5% of patients. The chest tube should be left in place until this stops. If it continues profusely until the sixth or seventh postoperative day, reoperation is indicated.

A chest radiograph is obtained about 7 days after coarctation repair, because chylothorax may develop late and be initially manifested as an unexpected pleural effusion. If present, it should be aspirated. Occasionally, repeated aspirations are required; if the chyle reaccumulates after the third aspiration, reoperation is indicated (see “Chylothorax” under Special Considerations after Cardiac Surgery in Section II of Chapter 5).

**RESULTS**

**Repair of Isolated Coarctation**

**Survival**

**Early (Hospital) Death** Hospital mortality over the last 20 years has been low (2%-10%) in neonates undergoing operation with or without persisting patency of the ductus arteriosus\textsuperscript{718,82} (Table 48-3). In recent years it is not unusual for reports to show early mortality of 0% to 2%.\textsuperscript{80,81,12,83,84,25,29,124,125,23,713,718,913} When repair of coarctation is performed in older infants, children, adolescents, and young adults, early mortality is about 1%.

**Time-Related Survival** In a heterogeneous group of neonates reported by the Congenital Heart Surgeons Society (CHSS), 12- and 24-month survivals were both 95%.\textsuperscript{91} In a single-institution study of 191 heterogeneous patients, survival at 2, 5, and 10 years was 92%, 88%, and 88%, respectively. Survival was better at all time points for patients with isolated coarctation\textsuperscript{28} (Fig. 48-18).

**Modes of Death** When repair is performed in the first few months of life, the few deaths that occur result from continuing heart failure, management errors, or poor preoperative status. Persisting or recurrent hypertension, rupture of intracranial or other aneurysms, acute aortic dissection, acute myocardial infarction, and complications of late-appearing aortic valve disease (related to congenitally bicuspid aortic valve) account for most of these.\textsuperscript{82,83,84}

**Incremental Risk Factors for Death after Repair** There are few well-established risk factors for death except older age at operation. Although low birth weight is likely to increase morbidity when repair is performed in the neonatal period,\textsuperscript{82} this has not been extensively evaluated. Coarctation repair has been successfully performed in neonates weighing less than 1 kg.\textsuperscript{81,82} In one single-institution study, presence of transverse arch hypoplasia was a risk factor for death.\textsuperscript{92}

**Hypoplastic left heart class** (see Table 48-1) also seems to be related to survival, although most patients with isolated coarctation are in hypoplastic left heart class I (Fig. 48-19; see also Table 48-3). A single-institution study of 55 isolated coarctation repairs with at least one hypoplastic intracardiac left heart structure indicates that outcomes, both early and midterm, are equal to outcomes of patients without associated left heart hypoplasia, and that the hypoplastic intracardiac structures demonstrate somatic growth over time.\textsuperscript{91,111}

Whether technique of repair is a risk factor for death is arguable.\textsuperscript{92,711,914,915}

**Late Postoperative Exercise Capacity**

Exercise capacity is lower than normal (80% of predicted) at late follow-up in patients who have had coarctation repair.
Figure 48-17  Coarctation repair through median sternotomy using cardiopulmonary bypass (CPB). This approach is used when proximal aortic arch obstruction is severe or when an intracardiac procedure (usually a ventricular septal defect) is also repaired. A, A standard median sternotomy incision is shown, and great vessels are dissected extensively, similar to that required for neonatal repair of hypoplastic left heart (see Technique of Operation in Chapter 49). After standard preparation for CPB, cannulation is performed with the arterial cannula placed into brachiocephalic artery through a standard purse string, and superior and inferior venae cavae cannulated individually. At institution of CPB, left and right branch pulmonary arteries are temporarily ligated. (See text for details of CPB management.) Dashed lines show incision in proximal aortic arch and transection sites at the distal aspect of hypoplastic aortic isthmus, at the descending aorta, and at the ductus arteriosus. B, Cardioplegia needle is placed into mid-ascending aorta, and after clamping the ascending aorta cephalad to the needle, cardioplegic solution is administered (see text for details). After achieving adequate cardiac arrest, the original aortic clamp is moved to base of brachiocephalic and left carotid arteries as shown, allowing continued perfusion into these arteries. The distal aorta is clamped and coarctation site resected along the dashed lines shown in A. Aortic isthmus and ductus arteriosus are both ligated, and temporary branch pulmonary artery ligatures are removed. An incision is made in undersurface of proximal aortic arch, and anastomosis is begun at midpoint of posterior aspect of the circumference of descending aorta as shown. A running monofilament absorbable suture is used. C, Anastomosis is shown in its completed form, aortic clamps have been removed, and patient is separated from CPB (see Technique of Operation in Section 1 of Chapter 35, and details in text of this chapter for approaches to closure of the ventricular septal defect). Key: BA, Brachiocephalic artery; IVC, inferior vena cava; LCA, left common carotid artery; LPA, left pulmonary artery; LSCA, left subclavian artery; PDA, patent ductus arteriosus; RPA, right pulmonary artery; SVC, superior vena cava; VSD, ventricular septal defect.
Table 48-3  Hospital and Total Deaths after Repair of Isolated Coarctation in Neonates

<table>
<thead>
<tr>
<th>Method of Repair</th>
<th>Class I</th>
<th>Class II</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subclavian flap aortoplasty</td>
<td>27</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Resection with end-to-end anastomosis</td>
<td>18</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Resection with end-to-end anastomosis + subclavian aortoplasty</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Patch-graft aortoplasty</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Unknown type of repair</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>No repair</td>
<td>2</td>
<td>1</td>
<td>50</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>57</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Data from multiinstitutional study of the Congenital Heart Surgeons Society, 1990 to 1991.

Figure 48-18  Survival of 191 patients undergoing coarctation repair. Group 1 = isolated coarctation. Group 2 = coarctation with ventricular septal defect. Group 3 = coarctation with complex intracardiac anatomy. (From Kaushal and colleagues.

This is independent of type or success of repair, age at repair, and presence or absence of upper-lower body blood pressure gradient.

Late Postoperative Upper Body Hypertension at Rest and during Exercise

Resting Values  About 50% of patients who have undergone coarctation repair have an upper body resting systolic blood pressure higher than the mean value for normal individuals. The two groups behave differently with exercise as well, with the coarctation group demonstrating exercise-induced hypertension, even in some patients whose blood pressure is normal at rest (Fig. 48-20). It is important to recall that systolic hypertension portends the same prevalence of unfavorable outcome events as diastolic or mean blood pressure hypertension.

Time course of upper body blood pressure may be generalized as follows. It is often considerably elevated early postoperatively. Thereafter it tends progressively to normalize in most patients such that by 5 years after repair, 80% to 90% of patients have normal upper body systolic and diastolic blood pressures at rest (Fig. 48-21). After 5 years, prevalence of patients with normal blood pressure begins to decline, and by 20 years after operation, only 40% to 50% have normal blood pressure (Fig. 48-22). Prevalence declines still further after that.

The younger the patient is at operation, the longer the period of normotension, or the greater the prevalence of normotension at any given interval after operation (see Figs. 48-21 and 48-22). However, the differences appear
Evidence is beginning to emerge that late hypertension is less prevalent in patients who undergo coarctation repair preoperatively. In patients undergoing coarctation repair as adults to be small so long as repair is done before about age 10 years. In patients undergoing coarctation repair as adults (age ≥ 16 years), generally more than half are normotensive; the remainder are on antihypertensive medication, but blood pressure is improved and medication reduced compared with preoperatively.

Values with Exercise Patients who have undergone coarctation repair experience a considerable increase in upper body blood pressure during exercise, although variability in response is even greater than that at rest (Fig. 48-23; also see Fig. 48-20) and is more variable than that of normal persons, who also experience some increase during exercise (Fig. 48-24; see also Fig. 48-23). The increase with exercise in postcoarctectomy patients with upper body hypertension is similar to that of hypertensive patients without coarctation (see Fig. 48-20). There appears to be an age-related association, with patients operated on after age 1 year having a greater chance of developing exercise-induced hypertension.

Correlates (Risk Factors) of Upper Body Hypertension Possible basic correlates of an excessive upper body tension and compliance of the systemic arterial system a decade or more after coarctation repair, patients undergoing primary resection and end-to-end anastomosis had less hypertension and better vascular compliance than those undergoing subclavian flap aortoplasty. Additionally, method of repair may influence the likelihood of developing hypertension. In two studies evaluating hypertension and compliance of the systemic arterial system a decade or more after coarctation repair, patients undergoing primary resection and end-to-end anastomosis had less hypertension and better vascular compliance than those undergoing subclavian flap aortoplasty.

Figure 48-20 Increase (Δ) in upper body systolic blood pressure during standardized exercise testing in patients who have undergone repair of coarctation, and in other patients. (Three asterisks indicate columns that are different from normotensive patients [P < .01].) Key: HE, Hypertensive patients without coarctation; HPC, postcoarctation repair patients with upper body resting hypertension; NN, normotensive patients without resting hypertension; NPC, postcoarctation repair patients with upper body resting normotension. (From Simsolo and colleagues.)

Figure 48-21 Stack plots depicting percent of patients with resting normal blood pressure and with resting hypertension (systolic or diastolic) at various intervals related to age at repair of coarctation. Numbers across top are number of years after repair of coarctation, and numbers beneath bars are number of patients at risk. A, Patients 5 to 9 years old at coarctation repair. B, Patients 10 to 19 years old at coarctation repair. Key: DH, Diastolic hypertension; Dis, after discharge from hospital after coarctation repair; Pre, preoperatively; SH, systolic hypertension. (From Clarkson and colleagues.)

Figure 48-22 Percentage of patients normotensive at various intervals after repair of coarctation, according to age at repair. Dashed line represents all cases combined. Numbers at risk are shown above baseline. (Modified from Clarkson and colleagues.)

Figure 48-23 Arm systolic blood pressure at rest and during and after exercise in 15 control subjects and 15 patients before and after coarctectomy. Open circles represent preoperative; triangles, postoperative; and closed circles, control subjects. Bars indicate ± 1 SD. * = P < .01 postoperative vs. control values. Key: BP, Blood pressure; Post, post-exercise; sys, systolic. (From Pelech and colleagues.)

within the first year of life rather than at an older age. Additionally, method of repair may influence the likelihood of developing hypertension. In two studies evaluating hypertension and compliance of the systemic arterial system a decade or more after coarctation repair, patients undergoing primary resection and end-to-end anastomosis had less hypertension and better vascular compliance than those undergoing subclavian flap aortoplasty.
Older age at operation (i.e., >20 years or so) increases prevalence of upper body hypertension after repair of coarctation (described in preceding text), but its effect is probably mediated by one or more basic factors. It is not known whether this prevalence is decreased by operation in very early life.

After repair of coarctation, a positive correlation exists between resting upper body systolic blood pressure (and magnitude of increase with exercise) and the systolic blood pressure gradient between the upper and lower body \( M33,Z2 \) (Fig. 48-25). A positive correlation also exists between resting pulse pressure and development of an upper body–lower body gradient with exercise in repaired coarctation patients who have no resting gradient \( M10 \). There is no such correlation in controls. This does not identify the cause of the gradient—that is, whether it is true morphologic residual or recurrent coarctation, or whether it is stiffness in the upper body blood vessels. In general, no correlation has been found between width of the anastomosis as determined by aortography and excessive hypertensive tendency. Thus, it is problematic as to whether a true morphologic narrowing at the surgical site (persistent or recurrent coarctation) can be diagnosed without imaging the operative area to identify or exclude an anatomic narrowing. This is because non-compliance in large-diameter portions of the upper body arterial tree can result not only in hypertension but also in gradients between upper and lower body blood pressure.

Urschel and colleagues showed long ago that diversion of

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Figure 48-24  Systolic blood pressure before and after exercise in patients after coarctectomy and end-to-end anastomosis and in 20 control subjects. A, Arm systolic pressure increased in both groups but more so in coarctectomy patients. B, Systolic blood pressure gradient between arm and leg increased, often to high levels, in postcoarctectomy group. Key: θ, Average values. (From Freed and colleagues.)

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Figure 48-25  Relationship of systolic ascending aortic blood pressure to ascending-to-descending aortic systolic pressure gradient observed at follow-up catheterization 3 months to 9 years after neonatal coarctation surgery. Key: \( \Delta p \), Systolic pressure gradient across repair; E-E, end-to-end anastomosis; SF, subclavian flap repair. (From Ziemer and colleagues.)

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blood pressure response to rest or exercise in persons who have undergone coarctation repair include:

- Endocrine factors
- Abnormal compliance or reactivity of upper body small blood vessels
- Poorly compliant aorta proximal to coarctation repair
- Morphologically persistent or recurrent coarctation
- Presence of an angulated or “gothic-shaped” arch \( ^{13} \)
left ventricular output into a rigid tube resulted in increased systolic pressure.\textsuperscript{25,26}

Poorly compliant upper body aorta and large and small arteries, as discussed earlier in this chapter under Morphology, probably explain these tendencies to hypertension and to developing upper body–lower body systolic pressure gradients during exercise and hypertension of a greater magnitude than in normal individuals.\textsuperscript{35} However, any explanation must account for the fact that upper body hypertension and an exaggerated response to exercise are usually less after coarctation repair. The persisting hypertensive tendency probably explains the persistence of left ventricular hypertrophy in some patients.\textsuperscript{78}

Upper body systolic hypertension appears to be more marked and its exacerbation by exercise greater when a long bypassing tube graft is used for the repair than when end-to-end anastomosis is accomplished.\textsuperscript{52} This may, again, be the effect of a poorly compliant “aortic” segment between the upper and lower body arterial trees.

Studies by Peleck and colleagues, as well as by others, indicate that differences in elaboration of hormones with vasomotor activity or in sensitivity to them do not explain differences in resting and exercise blood pressure in postcoarctectomy patients or between them and normal persons.\textsuperscript{78}

Persisting Upper Body Vascular Abnormalities
Numerous studies in patients many years after coarctation repair have provided convincing evidence for persisting upper body arterial and arteriolar wall abnormalities that produce increased stiffness unrelieved by vasodilating agents.\textsuperscript{54} Whether performing repair in neonates or infants will change this situation is not known. One study suggests that vascular abnormalities are reduced in the postcoarctation arteries, but not in the precoarctation arteries, when repair is performed in infancy, supporting the concept that there is a diffuse developmental defect in the proximal arterial tree.\textsuperscript{82,19}

Other studies have shown increased reactivity to norepinephrine compared with normal in the blood vessels of the upper body of patients who had received adequate repairs of their coarctation, at least among those with persisting hypertension.\textsuperscript{52}

Persistent or Recurrent Coarctation
Arm/leg gradients commonly develop with exercise in postcoarctation repair patients who have no resting gradient (see Fig. 48-26), but it is uncertain whether this represents a persistent or recurrent coarctation.\textsuperscript{516} The previous discussions make it clear that persistent or recurrent coarctation can be identified with any degree of certainty only by imaging or by examining the repair itself. Reliable information of this type is not widely available.

Many have defined persistent or recurrent coarctation as a postoperative condition characterized by a resting peak pressure gradient exceeding 20 mmHg across the repair area.\textsuperscript{537} Usefulness of this criterion is limited. Freedom from recoarctation is not a satisfactory surrogate for known absence of a resting gradient or imaging of the area of repair. It may overestimate or underestimate prevalence of persistent or recurrent coarctation. A ratio of the aortic diameter at the repair site to the aortic diameter at the diaphragm of less than 0.7 has been suggested as a criterion for more than mild aortic narrowing; however, even patients with a higher ratio may exhibit elevated blood pressure and vascular abnormalities.\textsuperscript{523}

It is probable that many early “recoarctations” with luminal narrowings are in fact persistent coarctations.\textsuperscript{514,51,18} True recurrent recoarctation probably occurs, although its demonstration by serial aortography has been infrequent. True recoarctation after end-to-end anastomosis has been attributed to lack of growth of the suture line and presence of abnormal mesodermal tissue that proliferates and produces marked intimal and medial hypertrophy.\textsuperscript{511,11,51,13,84,54,55,101,20}

Remnants of ductal tissue behave in this same way.\textsuperscript{82} Damage to the aorta from the vascular clamps used at repair has also been implicated.\textsuperscript{34} Also, aortic wall mucopolysaccharides in coarctation have an increased chondroitin sulfate fraction, more marked in recoarctation specimens,\textsuperscript{82} a difference that leads to increased wall rigidity (decreased distensibility) that predisposes to or mimics restenosis.\textsuperscript{523}

Technical factors are no doubt responsible for persistent coarctation—for example, insufficient resection of a long, narrow segment followed by end-to-end anastomosis, or excessive tension on the suture line due to inadequate mobilization of the aorta above and below the coarctation. Other technical causes include incorrect fashioning of a subclavian flap or polyester onlay patch, failure to resect an obstructing intimal ridge, use of a too-small tube graft in a child, or kinking of such a graft particularly when used as a bypass.

A residual hypoplastic segment of aortic arch, usually between the left subclavian and common carotid arteries (tubular hypoplasia), can possibly contribute to a residual gradient. However, serial aortograms have shown progressive growth of this segment in many cases after coarctectomy, no doubt secondary to restoring normal arch blood flow.\textsuperscript{533,515} This has been corroborated by Brouwer and colleagues in a well-controlled study; they found that even severely hypoplastic arch segments between the left common carotid and left subclavian arteries substantially increased in size within 6 months of simple repair of coarctation in young infants. Despite the increase, however, $z$ values sometimes remain as low as −3, and one early recoarctation has been documented\textsuperscript{536} (Fig. 48-27). To further cloud the picture, in an MRI follow-up evaluation of 65 coarctation repairs, 47% of patients had hypoplasia of the isthmus and arch, and clinical evidence of recoarctation was related to this finding.\textsuperscript{12} Finally, in follow-up of 191 isolated coarctation patients extending to 30 years, recurrent coarctation was noted to

![Figure 48-26 Relation between pulse pressure at rest and exercise arm/leg gradient. Coarctation group is represented by triangles, and normal group by circles. (From Markham and colleagues.\textsuperscript{516})](image-url)
Develop even as late as several decades after repair and was correlated with arch hypoplasia.531

Experimental animal data showing that normal growth of an artery can occur after end-to-end anastomosis843,524 are not necessarily relevant to the situation after coarctectomy if indeed the tissue left behind is abnormal and tends to proliferate and produces excessive scar tissue. Experimental data do not conclusively demonstrate superiority of one suture technique over another for end-to-end anastomosis.

Recoarctation in children and adults is considerably more common when anatomy of the coarctation is unsuitable for direct end-to-end anastomosis because of a long narrowing or aneurysm formation, necessitating some other type of repair.

Prevalence after End-To-End Anastomosis Prevalence of persisting coarctation or recoarctation after the end-to-end anastomosis technique has been reported as high as about 20% in patients operated on before age 2 years and appears to be related smaller size (weight) at time of repair.2,37,126 One study indicates that presence of anomalous right subclavian artery is a risk factor for recurrence.312 Other studies suggest that prevalence of persistent or recurrent coarctation is much lower, about 2% to 6%, but they have used reoperation-free data as evidence.16,126,37,128,113 Harlan and colleagues interpret their data to indicate a lower prevalence when 7-0 polypropylene rather than silk sutures are used, but they also used reoperation-free data rather than measurement of gradient as their criterion.512 Lack of imaging information handicaps drawing appropriate inferences.

More recent studies of infants and neonates in whom more aggressive resection and primary anastomosis techniques were used54,55 indicate a reduction in recurrence, suggesting that eliminating abnormal tissue, rather than suture technique or some other factor, may be the predominant reason for achieving a sustainable unobstructed anastomosis. Prevalence of persistent or recurrent coarctation (a resting postoperative gradient <20 mmHg) of less than 5% has been demonstrated in neonates and infants younger than age 3 months using the technique described by Hanley and colleagues of resection with end-to-side primary anastomosis of the descending aorta to the aortic arch.54 Midterm follow-up of 88 patients from this series revealed that at 2 years after operation, 2 of 54 neonatal repairs required reintervention, and none of the non-neonatal repairs did.511 End-to-side repair using median sternotomy has also been reported, and outcomes compare favorably with the extended end-to-end technique.576

Prevalence after Subclavian Flap Aortoplasty The subclavian flap operation may have low prevalence of persistent coarctation in infants.151,13,111 Hamilton and colleagues reported that of 34 infants younger than age 6 months, none (0%; CL 0%-6%) had residual or recurrent coarctation when followed up to 6 years postoperatively118,119. The report of Waldhausen and colleagues also indicates zero occurrence (0%; CL 0%-8%) within 6 or more months of operation in 23 infants younger than age 14 months.911 Campbell and colleagues reported small gradients (15 and 20 mmHg) in two of four patients studied an average of 42 months after repair in infancy using continuous nonabsorbable suture, and no gradients in seven patients in whom a subclavian flap aortoplasty was made using interrupted or absorbable sutures (P = .1).49,58 Penkoske and colleagues at the Toronto Hospital for Sick Children found persisting or recoarctation in 6% (CL 3%-10%) of 81 infants repaired by the subclavian flap, in contrast to 27% using end-to-end anastomosis.711 In eight patients studied 4 years after subclavian flap aortoplasty, Fripp and colleagues found a normal arm/leg blood pressure response to exercise.516 Growth of the subclavian flap has been demonstrated by Moulton and colleagues.434

The favorable experience reported by Campbell and colleagues included 45 neonates and infants younger than age 8 weeks, as did that of Hamilton and colleagues.2,148 In contrast, Metzdorff and colleagues inferred from their experience that occurrence of persistent or recurrent coarctation is excessive when subclavian flap angioplasty is performed in patients younger than age 8 weeks.525 They reported only 75% 2-year freedom from reoperation after subclavian flap aortoplasty in infants younger than age 8 weeks, compared with 100% in older patients.

Finally, Cobanoglu and colleagues reported equally low prevalence of recurrence at 5- and 10-year follow-up using either subclavian flap aortoplasty or resection.337 Differences in results in the various series cannot be reconciled, but lack of imaging information probably explains most of them.

Prevalence after End-To-End Anastomosis with Subclavian Flap Aortoplasty Dietl and colleagues reported a lower prevalence of recoarctation in neonates and infants repaired by the combined resection-flap procedure than in those repaired with a subclavian flap or a patchgraft aortoplasty.477 This has been confirmed by others using this combined technique.426

Prevalence after Patch Aortoplasty Late results of poly-}

ester or polytetrafluoroethylene (PTFE) patch aortoplasty have been variable. Sade and colleagues reported persisting coarctation (mean arm/leg systolic blood pressure difference 33 ± 7.5 mmHg) after end-to-end anastomosis in infants but not after PTFE patch aortoplasty (difference was 5.1 ± 2.3 mmHg).52 They also reported growth of both the preoperatively hypoplastic isthmus and the intact posterior aortic wall at the site of repair.511 Similar findings were reported by Connor and Baker.521 Smith and colleagues found arm/leg pressure gradient during exercise to be only mildly increased over the minimal resting gradient when patch aortoplasty had
been used, but it was importantly increased when end-to-end anastomosis was used.\(^{52}\) However, Hesslein and colleagues from Houston reported a prevalence of persistent or recoarctation (by the criteria used in this chapter) of 18% with no difference for end-to-end anastomosis vs. patch aortoplasty.\(^{117}\) Younger patients had a higher prevalence with either operation. Again, the lack of imaging information makes interpretation difficult.

**Paraplegia after Repair**

A collective review by Brewer and colleagues\(^{834}\) identified 51 instances of paraplegia (0.41%; CL 0.35%-0.48%) among 12,532 coarctectomies.

Enough knowledge of the incremental risk factors for paraplegia and their neutralization (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24) is currently available to make it possible for occurrence of paraplegia after coarctectomy to approach zero. Wherever the collateral circulation typical of coarctation has not developed, risk of paraplegia is increased. This is probably because blood pressure in the distal aorta is lower during aortic clamping when collaterals are poorly developed.\(^{521}\)

Situations that may fail to stimulate development of the usual amount of collateral circulation include:

- Coarctation in infants
- Coarctation proximal to the left subclavian artery
- Coarctation with patent ductus arteriosus supplying the descending thoracic aorta
- Coarctation associated with stenosis at the origin of the left subclavian artery
- Coarctation with the right subclavian artery arising as the fourth branch distal to the coarctation
- Something less than severe narrowing at the coarcted area
- Re-repair\(^{834}\)

**Early Postoperative Hypertension and Abdominal Pain**

Nearly all patients, including infants, have some systolic and diastolic hypertension for a variable period after coarctation repair. Many patients, if observed carefully, have mild abdominal discomfort and distention during the first 5 or 6 postoperative days.\(^{122,87}\) In 10% to 20% of cases, this becomes sufficient to produce important discomfort and distention. Then there may be abdominal tenderness, fever, ileus, and leukocytosis. Management should be nonsurgical in virtually all cases (see “Abdominal Pain” under Special Features of Postoperative Care earlier in this section for treatment).

Further discussion of this syndrome is difficult because in the early years of coarctation surgery, many complications that are currently rare were reported as examples of the syndrome. Also, “paradoxic” hypertension is the rule after coarctation repair rather than the hallmark of a special syndrome. However, the syndrome was first described in a single case report by Sealy in 1953.\(^{51}\) At laparotomy on the tenth postoperative day, the jejunum and proximal ileum were “edematous and cyanotic but the superior mesenteric arteries and veins were patent.” At autopsy, “inflammation of the small arteries and arterioles was confined to the body area below the coarctation,” and there were infarcts in liver, spleen, kidney, and intestines. Lober and Lillehei added two cases in 1954,\(^{114}\) and Perez-Alvarez and Oudkerk another in 1956.\(^{817}\) Ring and Lewis in 1956\(^{817}\) considered that the lesion justified the term syndrome and that it was due to sudden increase in pulsatile pressures in vessels distal to the coarctation, with acute overdistention of these vessels. In 1957, Sealy and colleagues\(^{112}\) linked onset of abdominal pain with presence of paradoxical hypertension, which they described in detail. They noted that following successful coarctectomy, an early systolic hypertension could develop within the first 36 postoperative hours or a more delayed mainly diastolic hypertension could develop after 48 hours that lasted 7 to 14 days. This delayed phase was associated with abdominal pain in 6 of 14 of his patients. This observation was confirmed by many others.\(^{122,111}\) Sealy suggested that the hypertension might be due to an altered baroreceptor response plus an increased excretion of epinephrine or norepinephrine.\(^{67,312}\) Rocchi and colleagues\(^{8,20}\) suggest that the sympathetic nervous system is responsible for the early phase and that the renin-angiotensin system plays a major role in the later phase, although more recent information would indicate that the renin-angiotensin system also plays a role in the early phase.\(^{73}\)

Pathologic findings have been described in small arteries and arterioles in vessels below the repaired coarctation\(^{111}\) in these patients, and they probably are present to some degree routinely after coarctation repair. They include thrombosis, inflammatory cell infiltration of the entire wall, fragmentation of the internal elastic lamina, and fibroelastic proliferation, as well as marked mesenteric lymphadenitis in the jejunum and proximal ileum.\(^{910}\) Rarely there may be infarcts in liver, spleen, and kidneys, and rupture of aneurysms that may have formed on large intraabdominal arteries.\(^{114}\)

In a review of the literature up to 1970, Ho and Moss\(^{122}\) found the syndrome was reported in 9% (107 of 1193) of patients surviving coarctectomy. It is said to be rare in children younger than age 2 years,\(^{114,17,117,111}\) but this is questionable because it is difficult to be sure of its presence or absence in young infants.

**Left Arm Function after Subclavian Flap Aortoplasty**

Long experience with the Blalock-Taussig shunt showed considerable variability in arm function late after coarctation repair. They include thrombosis, inflammatory cell infiltration of the entire wall, fragmentation of the internal elastic lamina, and fibroelastic proliferation, as well as marked mesenteric lymphadenitis in the jejunum and proximal ileum.\(^{910}\) Rarely there may be infarcts in liver, spleen, and kidneys, and rupture of aneurysms that may have formed on large intraabdominal arteries.\(^{114}\)

In a review of the literature up to 1970, Ho and Moss\(^{122}\) found the syndrome was reported in 9% (107 of 1193) of patients surviving coarctectomy. It is said to be rare in children younger than age 2 years,\(^{114,17,117,111}\) but this is questionable because it is difficult to be sure of its presence or absence in young infants.

**Late Aneurysm Formation**

A true or false aneurysm may occur late postoperatively. A true aneurysm from progressive deterioration of the aortic wall opposite a prosthetic onlay patch has been reported on long follow-up by Knyshtov and colleagues,\(^{114}\) Vosschulte,\(^{117}\) Bergdahl and colleagues,\(^{819}\) Olsson and colleagues,\(^{83}\) and Rheuban and colleagues.\(^{816}\) Ala-Kulju and colleagues found this to develop in 27% (CL 21%-34%) of 62 patients followed up 2 to 14 years.\(^{84}\) Others report a much lower occurrence, 1% to 3% with up to 30 years of follow-up.\(^{819}\) One study identifies arch hypoplasia as a risk factor for late aneurysm formation after patch aortoplasty for coarctation.\(^{85}\) Another
identifies concomitant ridge resection at the time of patch placement. Presumably, the stiff patch transmits additional tension to the adjacent elastic aortic wall, which thus bears the total burden of the pulse wave and dilates. This makes the polyester onlay patch technique undesirable in most circumstances. An interposed aortic allograft tube may become aneurysmal, but this is not common on long follow-up.

A dissection may occur occasionally, either in the ascending or descending aorta, proximal or distal to the coarctation repair site. This may lead to late aneurysm formation.

False (suture line) aneurysms can be mycotic when they occur early postoperatively, but they are usually uninfected and have an etiology similar to the false femoral aneurysm that occurs at the distal anastomosis of an aortofemoral prosthetic graft. They may complicate prosthetic tubular grafts as well as prosthetic onlay patches. In the former instance, they are said to be more common at the proximal anastomosis of a bypass tube graft, where the suture line is more oblique in relationship to the transverse forces in the aortic lumen. They are rare with end-to-end tubular grafts, unless mycotic.

Aneurysms of uncertain type but in the region of the repair have been reported after the subclavian flap repair. Prevalence of this problem is uncertain.

Valvar Heart Disease
Valvar heart disease may complicate long-term management of patients who have undergone coarctation repair and occasionally prevents a good result. No doubt a larger number with bicuspid valves will require surgery for calcific aortic stenosis when they reach their fifth and sixth decades of life. Thus, among the 23 patients in Crafoord’s original series followed by Bjork and colleagues for more than 26 years, definite aortic valve disease developed in 11 (48%), although operation had not yet been required in four.

Congenital mitral valve disease has been thought to be infrequent in this setting. Celano and colleagues found coexisting mitral valve anomalies in 12 of 56 (21%) patients with coarctation studied by two-dimensional echocardiography.

Other Events
Heart failure may occasionally persist postoperatively in older patients who have had bicuspid valves requiring surgery for calcific aortic stenosis when they reach age 50. Maron and colleagues noted a high prevalence of conduction defects in ECGs of their patients. Bjork and colleagues found degenerative disease of the hip joints present in 20% of their 25 patients who had been followed up for 27 to 32 years and who were age 7 to 31 years at coarctectomy. Pregnancy is reasonably well tolerated after coarctation repair, and is even well tolerated in women with unrepaired coarctation. Hypertension, cardiovascular complications, miscarriage, and premature delivery rates are elevated, however. Late aortic root and ascending aortic complications including rupture, dissection, aneurysm, and perforation occur more frequently in patients with repaired coarctation and bicuspid aortic valve than in patients with isolated bicuspid aortic valve or isolated coarctation (Fig. 48-28).

Repair of Coarctation and Coexisting Ventricular Septal Defect
Little specific information other than survival is available in this group of patients. The information suggests that similar VSDs have the same tendency to close as when coarctation is not present (see “Spontaneous Closure” under Natural History in Section I of Chapter 35). VSD in patients with coarctation, however, is more likely to be malaligned posteriorly, and malalignment VSDs are less likely to close than those without malalignment. In one study following 23 infants with coarctation and VSDs of various sizes in whom coarctation repair alone was initially performed before 3 months of age, 14 of 23 required subsequent VSD closure, and importantly, size of VSD was not correlated with need for closure. Other studies indicate that VSD size, as well as other characteristics of the VSD, are important predictors that surgical closure will be required (see Indications for Surgery for an in-depth discussion of surgical decision making for coarctation with VSD). Among neonates with large VSD undergoing only coarctation repair, by age 12 months 12% of VSDs had become small, and by 24 months 19% had done so in the multi-institutional study of the CHSS. Results of repair of coarctation when VSD coexists, with regard to early, intermediate-term, and late upper body blood pressure, are presumably the same as when the coarctation is isolated, but this has not been confirmed by specific study.

Figure 48-28 Freedom from aortic root or ascending aorta complications for patients with isolated bicuspid aortic valve (244 patients) and patients with associated bicuspid aortic valve and coarctation (97 patients). Numbers in brackets indicate numbers of patients remaining in each period. Key: BAV, Bicuspid aortic valve; COA, coarctation. (From Ciotti and colleagues.)
Figure 48-29 Early survival after repair of coarctation of aorta in neonates (n = 127) with no other hypoplastic left heart components (hypoplastic left heart class I), according to whether the coarctation is isolated, or with coexisting ventricular septal defect (VSD), or with other important coexisting cardiac anomalies. A, Survival. B, Hazard function. (From multinstitutional study of the Congenital Heart Surgeons Society, 1990 to 1991.)

Table 48-4 Hospital and Total Deaths after Repair of Coarctation Coexisting with Ventricular Septal Defect and Presenting in Neonatal Life

<table>
<thead>
<tr>
<th>Method of Repair</th>
<th>Class I</th>
<th></th>
<th>Class II</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hospital Deaths</td>
<td>Total Deaths</td>
<td>Hospital Deaths</td>
<td>Total Deaths</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>No.</td>
<td>%</td>
<td>CL (%)</td>
</tr>
<tr>
<td>Coarctation alone</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>0-7</td>
</tr>
<tr>
<td>One-stage coarctation + VSD</td>
<td>7</td>
<td>3</td>
<td>43</td>
<td>20-68</td>
</tr>
<tr>
<td>Coarctation + PT band with later VSD closure</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0-47</td>
</tr>
<tr>
<td>Coarctation + PT band</td>
<td>7</td>
<td>1</td>
<td>14</td>
<td>2-41</td>
</tr>
<tr>
<td>Coarctation with later PT band</td>
<td>1</td>
<td>1</td>
<td>100</td>
<td>15-100</td>
</tr>
<tr>
<td>Coarctation with later VSD closure</td>
<td>4</td>
<td>1</td>
<td>25</td>
<td>3-63</td>
</tr>
<tr>
<td>Coarctation + aortic valve commissurotomy</td>
<td>0</td>
<td>1</td>
<td>100</td>
<td>15-100</td>
</tr>
<tr>
<td>Coarctation with later VSD closure + aortic valve commissurotomy</td>
<td>0</td>
<td>1</td>
<td>100</td>
<td>15-100</td>
</tr>
<tr>
<td>Balloon aortoplasty with later PT band + coarctation resection</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0-85</td>
</tr>
<tr>
<td>No repair</td>
<td>1</td>
<td>1</td>
<td>100</td>
<td>15-100</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>7</td>
<td>14</td>
<td>9-21</td>
</tr>
</tbody>
</table>

*Data from multiinstitutional study of the Congenital Heart Surgeons Society, 1990 to 1991.

Again, some single-institution studies indicate that presence of a VSD has no effect on either early or late risk, with excellent early and midterm outcomes reported.\textsuperscript{1,13,15,22}

A higher proportion of patients with coarctation and VSD may be in hypoplastic left heart class II than is the case in those with isolated coarctation, and survival may be less in those in class II than in class I (Table 48-4).

Current information does not permit comparison of outcomes with different management protocols in a risk-adjusted fashion, although in contrast with interrupted aortic arch and VSD,\textsuperscript{10} the multienstitutional study of the CHSS found staged repair gave a survival advantage.\textsuperscript{21} Options include repair of coarctation via thoracotomy with medical management of the VSD, repair of coarctation via thoracotomy with pulmonary trunk banding, and coarctation repair via median sternotomy with VSD closure, using either hypothermic circulatory arrest or continuous perfusion. Excellent results using the midline approach have been reported, employing either continuous perfusion\textsuperscript{15} or hypothermic circulatory arrest.\textsuperscript{21} Although natural history of VSD associated with coarctation is not established, attempts have been made to predict in early infancy the likelihood a VSD associated with coarctation will require surgical closure.\textsuperscript{538} Another approach involves coarctation repair with pulmonary trunk banding using absorbable material (polydioxanone).\textsuperscript{827} Band reabsorption occurred over approximately 6 months in an experience with
11 selected patients. VSD closure was necessary in only one patient following band reabsorption.

Repair of Coarctation and Other Major Coexisting Intracardiac Anomalies

Early and intermediate-term survival is less good in this group than in others (see Fig. 48-29), particularly when patients are in hypoplastic left heart classes II and III. This was a highly heterogeneous group of patients (see Table 48-2), and experience with any one group is small. Individual institutions have recently demonstrated substantially better outcomes in these patient groups, with 5-year survival of more than 70% for the milder hypoplastic left heart classes and even better outcome for other complex lesions such as transposition, truncus, and other conotruncal lesions (87% hospital survival and 83% survival at 7 years).

Difficulties in prospectively (preoperatively) defining a left heart as hypoplastic is discussed in detail in the introductory remarks to Chapter 49 and the footnote to Table 48-1. These difficulties are underscored by the experience of Tani and colleagues, who performed coarctation repair only in 20 neonates, without mortality, who were designated preoperatively as having a degree of left heart hypoplasia too severe to survive with two-ventricle physiology as judged by a widely used grading system. One confounding factor was that immediate changes in left ventricular cavity size can occur with change in loading conditions after coarctation repair.

INDICATIONS FOR OPERATION

Isolated Coarctation

Diagnosis of isolated coarctation is an indication for operation, because the probability of survival and a resting upper body normotensive state is greater after repair than in the natural history of the condition.

In the first few months of life, resection with reanastomosis is indicated. Need for enlarging or bypassing a hypoplastic segment of arch between the left common carotid and left subclavian arteries (distal arch) remains arguable, although good results have been reported. If no arch hypoplasia is present, end-to-end anastomosis is the choice for aortic reconstruction. If distal aortic arch hypoplasia is present, this may be addressed using either a reverse subclavian flap, an extended end-to-end anastomosis, or an end-to-side anastomosis of the descending aorta to the segment of arch between the brachiocephalic and left carotid arteries (proximal arch).

In critically ill neonates with coarctation, intravenous PGE$_1$ (0.1 mg · kg$^{-1}$ · min$^{-1}$) is begun immediately and continued until the situation is remedied at operation. (For more details about use of PGE$_1$, see Indications for Operation in Chapter 41.) Response is dramatic in about 80% of infants, with reappearance of femoral pulses and disappearance of metabolic acidosis from hypoperfusion of the lower body. Operation is then delayed 6 to 12 hours or more until the baby’s condition has stabilized in this improved state (for more details, see Indications for Operation in Section II).

Operation (after proper preparation) is indicated when diagnosis is made in neonates and young infants who present in important cardiac failure. If cardiac failure or failure to thrive is not present, urgency of the operation is less; however, surgery should still be considered at the time of presentation, although some prefer to delay it for 3 to 6 months. Argument to proceed at diagnosis is based on recent studies showing a prevalence of persistent or recurrent coarctation that is no different between neonates and older infants. Argument to delay is based on older information showing an apparently higher prevalence of persistent or recurrent coarctation when repair is performed in the first few months of life, and on the absence of any demonstrated lesser probability of long-term survival and a resting upper body normotensive state after repair in neonates than after repair in infants.

In occasional patients with a mild to moderate degree of left heart hypoplasia in whom it may not be clear that the left heart is adequate to sustain the systemic circulation, the subclavian flap operation can be particularly useful. With this operation, the ductus arteriosus can be preserved, and the PGE$_1$ can then be weaned slowly to test the adequacy of the left heart once the coarctation is repaired.

In patients presenting beyond early infancy, coarctation resection and aortic reconstruction is also the procedure of
choice if there is no proximal hypoplasia. If important proximal hypoplasia is present, the options available for neonates and young infants are generally not applicable for older patients. The older the patient, the less mobile the aortic tissue becomes, making extensive mobilization of the aorta impossible. If proximal hypoplasia is moderate in severity, patch augmentation of the arch and coarctation site, or graft interposition, are the options of choice. If proximal hypoplasia is severe, graft interposition in indicated.

Coarctation and Coexisting Ventricular Septal Defect

When coarctation coexists with a VSD in a neonate or infant with heart failure, the probability of the VSD closing spontaneously is the major determinant of the treatment protocol. Some have found that if the VSD is larger than small, VSD size is not particularly predictive of spontaneous closure. Others have found that the likelihood of spontaneous VSD closure is correlated inversely with VSD size. This same study also suggests that only muscular-type VSDs are likely to close, not perimembranous, outlet, or malalignment types. Thus, it is reasonable to assume that if the VSD is a large conoventricular one, is large in the outlet portion of the right ventricle, or is posteriorly malaligned, the probability that it will spontaneously narrow appreciably or close is very small. One-stage repair of the coarctation (by end-to-end anastomosis) and the VSD through a median sternotomy is the procedure of choice for such situations. There are, however, alternative practices. Coarctation repair alone may be performed, with later VSD closure if it remains large or the infant has failure to thrive. Also, coarctation repair with concomitant banding of the pulmonary trunk can be performed, with later removal of the band and VSD closure. Finally, a single-stage repair with two incisions has been described. The arch is repaired using a thoracotomy; the patient is then repositioned, and a median sternotomy is performed for VSD closure using standard CPB techniques. When the VSD is small or moderate in size, and particularly if it is muscular and occasionally perimembranous, spontaneous reduction in size, and closure, are real possibilities. In this situation the option of coarctation repair alone, with subsequent observation of the VSD and patient, is the preferred treatment protocol.

Whatever the initial procedure, if heart failure persists and the VSD remains large, it is repaired before hospital discharge (see Indications for Operation in Section I of Chapter 35).

Coarctation and Other Major Coexisting Intracardiac Anomalies

When coarctation coexists with other major intracardiac anomalies, the decision to proceed with one-stage repair of both, or to address the coarctation only, is a complex one. This is especially true in cases of single-ventricle physiology in which either a complex cardiac repair or a pulmonary trunk band must accompany coarctation repair. (See Chapter 41 for a more complete discussion of this issue.) With coarctation and truncus arteriosus, both are repaired. With coarctation and transposition, the preferred approach is to repair both, although a staged coarctation repair with subsequent arterial switch can be performed. With coarctation and atrioventricular septal defect, the preferred approach in most cases is to repair the coarctation and defer intracardiac repair for several months.

SPECIAL SITUATIONS AND CONTROVERSIES

Coarctation Proximal to Left Subclavian Artery

Coarctation proximal to the left subclavian artery is rare (=1% of all cases). Stenosis is localized, and femoral pulses are usually only slightly decreased and systolic pressure gradient across the coarctation mild (<20 mmHg) or moderate. Coarctation is often not detected until young adult life, at which time upper body hypertension is often present. A collateral circulation is generally not well developed.

The natural history of this lesion and its prognosis with antihypertensive medication is not clear, so neither are indications for operation. However, when upper body systolic and diastolic hypertension are severe during moderate exercise, operation is advisable.

A reverse subclavian flap or resection with end-to-side anastomosis is optimal treatment in infants and young children (see Technique of Operation earlier in this section). When a resection and anastomosis is used in older children and adults, either directly or with interposition of a tubular polyester graft, risk of hospital death or a major complication is probably less than 5%.

When an operation is performed in this subset of patients, particular attention must be paid to preventing paraplegia (see “Repair of Coarctation Proximal to Left Subclavian Artery” under Technique of Operation earlier in this section).

Some controversy remains regarding the importance of proximal hypoplasia in the aortic arch in association with coarctation (see Morphology earlier in this section). When it is considered important in association with coarctation, end-to-side reconstruction or reverse subclavian flap plus coarctation resection and anastomosis are effective solutions.

Mild and Moderate Coarctation in Classic Position

Uncommonly in infants and older patients, moderate coarctation is present in the classic position. Collateral vessels are absent. The natural history of this entity is not clear and thus neither are indications for operation. Degenerative changes are, however, prone to occur in the region of the coarctation, and when calcification is apparent, resection and replacement of this area with a tube graft may be recommended. Surgical techniques are the same as for thoracic aneurysms in this area (see “Replacement of Descending Thoracic Aorta” in Chapter 26).

When coarctation is so mild that there is no gradient across the area, in which case the lesion is usually found because of the buckled appearance of the aorta on chest radiography (pseudocoarctation), operation is advised only when degenerative changes have developed and thus an increased risk of aneurysm formation.

Preventing Paraplegia as a Complication of Repair

Paraplegia does not occur as an operative complication in classic coarctation of the aorta with well-developed collateral circulation. Thus, in preventing paraplegia, great importance attaches to preoperative identification of patients with potentially inadequate collateral circulation. In children and adults
with periductal coarctation, absence of rib notching on the chest radiograph or of palpable parascapular pulsations suggests that collateral circulation is not well developed. Only mildly diminished femoral pulsations in such patients are often associated with a poorly developed collateral circulation, as are a diminished left radial pulse (usually caused by involvement of the origin of the left subclavian artery in the coarctation) or a diminished right radial pulse (present when the right subclavian artery arises distal to the coarctation). Aortography or CT angiography is indicated under these circumstances, and when adequate collateral arteries are not present, special measures are taken at operation (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24). If uncertainty remains, pressure can be measured at thoracotomy in the descending aorta with the proximal aortic clamp temporarily in place; if this pressure is less than 50 mmHg, special measures are needed.

Likelihood of paraplegia in very young patients is uncertain, because some collateral circulation is present at birth. However, use of mild hypothermia (35°C nasopharyngeal or tympanic membrane temperature) is a good precaution. This probably allows 30 minutes of safe aortic clamping (see “Subclavian Flap Aortoplasty in Infants” under Technique of Operation earlier in this section). This degree of hypothermia is as protective in older patients as in infants, and a similar technique may be used when the collateral circulation is not well developed. Ice-cold saline lavage may need to be prolonged to about 10 minutes. Instead, a temporary bypass shunt, usually from left subclavian to descending thoracic aorta, or femorofemoral CPB (see “Cardiopulmonary Bypass Established by Peripheral Cannulation” in Section III of Chapter 2) may be used during the period of aortic clamping (see “Paraplegia after Aortic Clamping” under Special Situations and Controversies in Chapter 24). Another alternative is placing a large bypass graft as a permanent method of repair.

Reintervention for Persistent or Recurrent Coarctation

Current indication for reintervention is demonstrating a reduced luminal diameter of greater than 50% at the anastomosis. Under this circumstance, heart failure or upper body hypertension (systolic pressure greater than 140 mmHg in infants and children) is an indication for reintervention. Currently, percutaneous balloon aortoplasty is generally the treatment of choice (see text that follows), but surgical measures also provide good results.

Balloon Aortoplasty and Stenting for Coarctation

Percutaneous balloon aortoplasty is controversial as a method of primary treatment for aortic coarctation, particularly in small patients. For neonates and young infants, balloon aortoplasty appears to have the same disadvantages as subclavian flap aortoplasty, in that the sling of ducral tissue at the coarctated site is not removed.

Aneurysmal dilatation has developed in some patients treated by balloon angioplasty. This is not surprising, because the mechanism of gradient relief appears to be tearing of the intima and media. This process is confirmed in clinical studies by contrast extravasation in 25% of patients at the time of balloon dilatation. However, some interventional cardiologists have observed no aneurysms, even when an intimal tear is noted acutely, whereas others have observed aneurysms in 10% to 20% of patients. An immediate reduction in gradient across the coarctation is usually observed (a decrease from 48 ± 21 to 10 ± 7.3 mmHg was obtained by Rao and colleagues and usually persists during the intermediate term).

The question remains as to whether this result is similar to that obtained by optimal surgical techniques. Several studies directly address this question, although it is acknowledged that there are important difficulties in properly comparing surgical and catheter-based outcomes. In a recent multicenter study that retrospectively evaluated 80 patients older than age 1 year who were treated either by surgery or transcatheter intervention (balloon angioplasty or stenting), initial relief of the obstruction was similar in the two groups; however, reintervention (32% vs. 0%, P < .001) and aneurysm formation (24% vs. 0%, P < .01) were both higher after transcatheter therapy. In a comparison of 57 neonates, retrospective analysis showed that surgery resulted in fewer recurrences and aneurysms, better arch growth, and less need for antihypertensive therapy than did balloon angioplasty. In a randomized clinical trial of 36 patients between age 3 and 10 years, Shaddy and colleagues showed equal initial outcomes in the surgical and balloon groups, but a significantly greater rate of recurrence and aneurysm formation in the balloon group.

Arterial occlusion at the site of catheter insertion occurs in some small patients. This is not a trivial complication and can lead to underdevelopment of the ipsilateral leg and claudication, despite good collateral flow.

A detailed multivariable study of risk factors for a poor result from primary balloon dilatation emphasized that age younger than 1 year was particularly associated with a poor result; recoarctation developed in 71% (CL 45%-90%) of infants. Highest prevalence of recurrence (83%) is found in neonates. Small size of the aorta between the left subclavian artery and coarctation also was found to predispose patients to a poor result.

Recurrent aortic obstruction after surgical treatment is a more favorable situation than primary coarctation for percutaneous balloon angioplasty. Angioplasty may be most effective for recurrent postsurgical coarctation when it is performed in infancy. Both surgery-free survival and reintervention-free survival after angioplasty for recurrence are higher if the angioplasty occurs beyond infancy (Fig. 48-31). Excellent initial and intermediate-term results, without aneurysm formation in most patients, appear to be the rule after percutaneous balloon aortoplasty in this setting, as well as in the setting of recurrent aortic obstruction after repair of interrupted arch and hypoplastic left heart (see “Persistent or Recurrent Aortic Arch Obstruction” under Results in Section II). Newer data from the Valvuloplasty and Angioplasty of Congenital Anomalies (VACA) Registry, however, indicate that acute suboptimal outcome was present in 25% of recurrent obstruction but only 19% of primary lesions. On the other hand, arguments have been made that surgical reintervention is preferable to balloon angioplasty for recurrent coarctation, particularly in patients beyond the infancy period and in those with arch hypoplasia.

Percutaneous stenting of both native and recurrent coarctation is currently well established, particularly in older
Figure 48-31 Survival and event-free survival in 99 consecutive patients undergoing balloon angioplasty for recurrent coarctation following initial surgical coarctation repair. Outcomes are shown for (A) all patients undergoing angioplasty, (B) those younger than age 1 year, and (C) those older than age 1 year. (From Shaddy and colleagues.)

Short-term evaluation shows effective relief of obstruction and favorable effects on the myocardium and peripheral vasculature, but longer-term outcome is lacking. Intimal thickening and luminal reduction were observed in young patients at follow-up, and aneurysm formation was identified in 7%. In selected adults, complications have generally been lower, and follow-up at 5 years revealed no recurrent obstruction in 46 native and recurrent coarctation patients in one series. In the 17-institution study of 565 patients (mean age 15 years, all over age 4 years) reported by Forbes and colleagues, 98% had effective relief of obstruction. Acute complications including dissection, intimal tears, aneurysms, cerebrovascular events, and peripheral vascular problems at the insertion site occurred in 14%, and there were two deaths. A subsequent intermediate-term outcome report on this same multistitutional cohort showed that 25% of patients undergoing aortic imaging at a mean follow-up of 19 months had abnormal studies, consisting of dissection, reobstruction, stent fracture, or aneurysm. Dissection risk may be higher in elderly patients. Studies examining post-stent hypertension and peripheral vascular abnormalities indicate that similar persistence of these problems occurs as in patients treated surgically.

Some have taken the position that interventional management is the treatment of choice for native coarctation in older children and adults. The acute and very early midterm complications noted in the previous paragraph bring into question the validity of this position, because they do not compare favorably with current-era surgical outcomes in similar populations. Furthermore, the truly long-term fate of the aorta after ballooning and stenting is unknown. Interventional management is not considered the procedure of choice in neonates and infants because of the well-documented extremely high recurrence rate; however, it may be of benefit as a temporizing maneuver in selected circumstances, such as the presence of profoundly depressed left ventricular function. Some have recommended temporary stenting in premature infants, but this is not recommended. Several studies demonstrate that low birth weight is not a risk factor for death or recurrence following surgical repair and that catch-up growth of the arch occurs.

Finally, the engineering of stents continues to evolve. Covered stents, growth stents, and self-expanding nitinol stents have recently been introduced into clinical practice for coarctation management.

Coarctation in Adults

Native coarctation diagnosed in adulthood should be treated regardless of age (see Section X in Chapter 29). Excellent results have been achieved with operation in patients older
Section II  Interrupted Aortic Arch

DEFINITION

Interrupted aortic arch is complete luminal and anatomic discontinuity between two segments of the aortic arch. Those rare specimens that exhibit a fibrous strand connecting two widely separated ends are also included under aortic arch interruption rather than coarctation.

HISTORICAL NOTE

The first description of interrupted aortic arch is attributed to Steidele in 1778. In this case, the aortic isthmus was absent, so morphology was similar to preductal coarctation. Description of the absence of more proximal portions of the arch occurred later, for the segment between the left subclavian and left common carotid arteries in 1818 by Siedel and for that between the left common carotid and brachiocephalic arteries by Weisman and Kesten in 1948. By 1959, Celoria and Patton were able to collect 28 cases that they classified according to the site of obstruction into types A, B, and C (see Morphology and Morphogenesis later in this section).

The first patient to have successful surgical treatment was a 3-year-old girl operated on by Samson in 1955. The aortic isthmus was absent between the left subclavian artery and a widely patent ductus arteriosus, but both structures were adjacent, and it was possible to join the divided ductus to the undersurface of the proximal left subclavian artery; the two VSDs were closed 4 years later. Mustard apparently performed a similar successful procedure in a similar patient age 7 months in 1957. Villalobos and colleagues and Blake and colleagues each reported a successful case during the early 1960s, using a prosthetic graft to bridge the gap. Sirak and colleagues were the first to use the turned-down arch branches successfully (left subclavian or left common carotid artery, or both) for end-to-end anastomosis to the descending aorta (combined with pulmonary trunk banding for the VSD), although this type of operation was attempted as early as 1959. Sirak’s patient was also the first neonate to survive operation, followed by an 18-hour-old boy reported by Norton and colleagues and an 11-day-old infant operated on in Houston in 1970. In 1970, a palliative operation consisting of a polyester graft between the pulmonary trunk and descending aorta, combined with pulmonary trunk banding, was used successfully by Litwin and colleagues in an 11-day-old infant, but this procedure is no longer advocated.

The first simultaneous repair of both interrupted arch and all intracardiac lesions was performed successfully in 1970 in an 8-day-old infant with an interruption distal to the left subclavian artery, a VSD, and total anomalous pulmonary venous connection through a left thoracotomy. The distal end of a 12-mm polyester conduit was anastomosed to the descending aorta; then, through a median sternotomy, the proximal end was anastomosed to the ascending aorta and both intracardiac lesions repaired. The procedure demonstrated that circulatory arrest techniques made an anastomosis to the ascending aorta feasible. In 1973, Murphy and colleagues reported a successful complete repair in a 3-day-old infant of an aortic interruption proximal to the left subclavian artery and a VSD, using circulatory arrest. They used a segment of the father’s basilic vein as the graft between descending and ascending aorta and approached the heart and descending aorta through a median sternotomy with an extension into the third left intercostal space. In 1975, Trusler and Izuwaka demonstrated that a median sternotomy alone provided adequate exposure for this procedure in small infants; using circulatory arrest techniques, after excising ductus tissue, they were able to anastomose successfully the descending aorta end to side to the ascending and transverse arch without interposing a graft. The VSD was also closed. Finally, primary repair via median sternotomy using continuous perfusion cardiopulmonary bypass (CPB) techniques was reported by Asou and colleagues in 1996 and by McElhinney and colleagues in 1997.

In 1976, the remarkable immediate preoperative improvement produced by the ductus-opening effect of PGE was reported as part of the treatment plan for interrupted aortic arch.

MORPHOLOGY AND MORPHOGENESIS

Types

The aortic arch may be interrupted at one of three sites (Table 48-5). It may be interrupted just distal to the left subclavian artery (type A of Celoria and Patton), with blood flowing into the descending aorta from the ductus arteriosus. All forms of interrupted aortic arch display this latter feature, except in rare cases in which the ductus is absent or closes during fetal life. About 40% of cases are type A. The most common site of interruption (55% of cases) is between the left subclavian and left common carotid arteries (type B). In

<table>
<thead>
<tr>
<th>Type</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Interruption located just distal to left subclavian artery</td>
</tr>
<tr>
<td>B</td>
<td>Interruption located between left subclavian and left common carotid arteries</td>
</tr>
<tr>
<td>C</td>
<td>Interruption located between left common carotid and brachiocephalic artery</td>
</tr>
</tbody>
</table>
only about 5% of cases is the interruption between the left common carotid and brachiocephalic arteries (type C).\textsuperscript{11}

**Aortic Arch**

Anomalies of the origins of brachiocephalic vessels are frequent in interrupted aortic arch.\textsuperscript{19} Thus, an aberrant right subclavian artery, usually originating as a fourth brachiocephalic branch from the upper descending thoracic aorta, is common in type B but can also occur in type A.\textsuperscript{8} The right subclavian artery may arise high in the neck from the right common carotid artery (cervical origin of right subclavian artery).\textsuperscript{24} A right-sided ductus may persist from the right pulmonary artery and give origin to the right subclavian artery, and the right pulmonary artery may arise from the ascending aorta (see “Anomalous Origin of Right Pulmonary Artery” in Chapter 48). Rarely, interrupted arch occurs with a right aortic arch, and in this instance both the left and right ducts may remain patent and give origin to the subclavian arteries.\textsuperscript{25}

Characteristically, the ascending aorta is about half normal diameter and is straight, dividing into two branches of about equal size (the V sign), and the pulmonary trunk is huge. The descending aorta is a direct continuation of the ductus arteriosus, as in the fetus, and is usually a little larger than the ascending aorta.

In the newborn, there is usually a gap of variable width between the aortic ends, although when the interruption is beyond the left subclavian artery (type A), the gap tends to be wider. Rarely, a fibrous strand connects the two ends. In this situation, the “interruption” should be viewed as a case of severe coarctation and may be distinctly different embryologically. “Interrupted” aortic arch diagnosed beyond infancy as an isolated lesion almost certainly represents coarctation that has progressed to luminal closure.\textsuperscript{22,21}

**Left Ventricular Outflow Anomalies**

The aortic valve is bicuspid in 30% to 50% of patients, analogous to coarctation (see Morphology in Section I). Congenital valvar aortic stenosis may be present occasionally, and subaortic stenosis may be present or develop.\textsuperscript{11,13,22,23} Generalized narrowing of the left ventricular outflow tract, conal septal posterior malalignment, the muscle of Moulaert, small aortic anulus, and aortic hypoplasia occur to some degree in most patients with interrupted arch.\textsuperscript{24,27,28,29,30}

As discussed in Section I for coarctation, interrupted aortic arch may be part of the complex of lesions that constitute hypoplastic left heart physiology.

**Coexisting Cardiac Anomalies**

A large VSD is present in over 95% of patients, and frequently the infundibular (conal) septum is malaligned and displaced posteriorly and leftward (Figs. 48-32 and 48-33). Most of the VSDs are conoventricular in type, although virtually all types may occur. Some conoventricular defects are also perimembranous, although some may be only juxtratricuspid in position. The malaligned and displaced infundibular septum usually produces subaortic obstruction of variable severity.\textsuperscript{13,14,24,31} This is an important complicating feature. When there are two structurally normal ventricles and inlet valves but no VSD, an aortopulmonary window is typically present. In a multicenter retrospective study of 472 patients with interrupted aortic arch, 4.2% had aortopulmonary window.\textsuperscript{22} Aortopulmonary window may occur with either type A or type B interruption (Fig. 48-34).

Other coexisting lesions are shown in Table 48-6. Pulmonary stenosis rarely if ever occurs as a coexisting lesion. Coexisting lesions occur with equal frequency and with a similar spectrum for interrupted arch types A and B.\textsuperscript{14} Coexisting lesions have been documented with type C as well.\textsuperscript{17}

**Morphogenesis and Associated Syndromes**

Microdeletion of the q11 segment of chromosome 22 and variable manifestations of velocardiofacial syndrome are common.\textsuperscript{1,2,3,19,11,20,27,28} Absence of thymic tissue (DiGeorge syndrome) is frequent\textsuperscript{24,27,28} and should be sought routinely. Van Mierop and Kutsche found this association only in type B interrupted arch, and they believe this finding has pathogenetic significance.\textsuperscript{27} Up to half of type B cases have DiGeorge syndrome.\textsuperscript{12,19} However, a population-based regional study indicates that although DiGeorge syndrome is more common in type B interruption, it occurs in type A as
Figure 48-33 Intracardiac image of neonate with interrupted aortic arch and posteriorly malaligned ventricular septal defect. Aortic anulus is mildly hypoplastic, and aortic valve is bicuspid. Infundibular (conal) septum protrudes into left ventricular outflow tract just below aortic valve, narrowing outflow tract substantially.

Key: AA, Ascending aorta; AV, aortic valve; IS, infundibular septum; LA, left atrium; LV, left ventricle; MS, muscular septum; RV, right ventricle; VSD, ventricular septal defect.

Table 48-6 Coexisting Cardiac Anomalies (Exclusive of Other Important Levels of Obstruction in the Left Heart–Aorta Complex) in Interrupted Aortic Arch

<table>
<thead>
<tr>
<th>Coexisting Cardiac Anomalies</th>
<th>n</th>
<th>% of 250</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSD</td>
<td>183</td>
<td>73</td>
</tr>
<tr>
<td>Truncus arteriosus</td>
<td>25</td>
<td>10</td>
</tr>
<tr>
<td>AP window</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Univentricular AV connection</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>TGA with VSD</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>DORV</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Taussig-Bing DORV</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Complete AV septal defect</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Corrected transposition</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>None</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>250</td>
<td>100</td>
</tr>
</tbody>
</table>

Data from Jonas and colleagues.18

*Double inlet left ventricle in three, mitral atresia in four, tricuspid atresia in two.

Key: AP, Aortopulmonary; AV, atrioventricular; DORV, double-outlet right ventricle; TGA, transposition of the great arteries; VSD, ventricular septal defect.

Figure 48-34 Morphologic subtypes of aortopulmonary window and interrupted aortic arch when they occur together. Numbers in parentheses are numbers of patients in each category. (From Akdemir and colleagues.45)
Figure 48-35  Echocardiographic images of neonatal interrupted aortic arch. **A,** Type B interruption. Origin of brachiocephalic artery from ascending aorta is seen, as is origin and entire length of left carotid artery. Interrupted segment is clearly visualized. Ductus arteriosus and descending aorta are also seen, with origin of left subclavian artery arising from descending aorta. **B,** Color-flow imaging of view similar to that seen in **A** helps define length of interrupted segment. Key: **AA,** Ascending aorta; **BA,** brachiocephalic artery; **DES,** descending thoracic aorta; **IN,** interrupted aortic arch; **LCA,** left common carotid artery; **LSCA,** left subclavian artery; **PDA,** patent ductus arteriosus.

well\textsuperscript{G6} and has also been reported with type C interruption.\textsuperscript{V14} When DiGeorge syndrome is present, hypocalcemia requires treatment,\textsuperscript{N5} as do immunologic problems.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Almost all patients with aortic interruption present as critically ill neonates in severe heart failure as a result of the combined effects of volume overload from left-to-right intracardiac shunting and the high afterload imposed by the closing ductus. Metabolic acidosis and anuria develop rapidly.\textsuperscript{S15} Femoral pulses become diminished and then impalpable as the ductus closes, and may vary in volume from hour to hour.\textsuperscript{H19} When the ductus closes, flow reverses in the vessels distal to the interruption (left subclavian and left common carotid) without recognizable neurologic symptoms developing.\textsuperscript{H19} With the ductus still shunting, the expected differential cyanosis between arms and legs is usually not visible, in part because the intracardiac bidirectional shunt minimizes oxygen saturation differences between ascending and descending aorta. Reversed differential cyanosis (blue arms and pink legs) can be obvious, however, when there is associated transposition of the great arteries (see Clinical Features and Diagnostic Criteria in Chapter 52).

Cardiac murmurs are not specific, nor is ECG. The chest radiograph shows gross cardiomegaly and pulmonary plethora. Cardiac catheterization with cineangiography were required for diagnosis in the past.\textsuperscript{B8} Currently, enhanced echocardiography usually provides all the necessary diagnostic information relating to both the aortic arch and intracardiac structures.\textsuperscript{G3,T21} (Fig. 48-35; see also Fig. 48-33). Increasingly, interrupted arch is being diagnosed by fetal echocardiography.\textsuperscript{G3} In the unusual case that echocardiography does not provide all the pertinent information, CT angiography provides excellent spatial resolution (Fig. 48-36); thus, cardiac catheterization and contrast studies are unnecessary and disadvantageous.

**NATURAL HISTORY**

Interrupted aortic arch accounts for 1% to 4% of autopsy cases of congenital heart disease and 1.3% of infants presenting with critical congenital heart disease.\textsuperscript{C18,V2} Estimated prevalence is 0.06 per 1000 births.\textsuperscript{G3} There is male predominance, and the ratio of type B to type A is 11:4.\textsuperscript{G3}
This uncommon anomaly is highly lethal, with median age of death 4 to 10 days; 75% of such babies die within 1 month of birth.\textsuperscript{19,20} Because the ductus arteriosus is almost always widely patent at birth, collateral circulation does not develop, and death occurs when the ductus closes soon after birth. When the ductus is obliterated in fetal life, collateral circulation is already present at birth\textsuperscript{199} and survival is usual. If the ductus arteriosus stays open, longer survival is possible, but even then, 90% of babies die by age 1 year. In those unusual circumstances in which major associated cardiac anomalies are absent, natural history is similar to that of coarctation without major associated cardiac anomalies.\textsuperscript{199,200}

**TECHNIQUE OF OPERATION**

**Repair of Interrupted Arch and Ventricular Septal Defect**

One-stage repair is considered optimal by some\textsuperscript{19,20,23,25,71} and in the multinstitutional study of the CHSS, one-stage repair gave the best 5-year survival.\textsuperscript{198} Others indicate that little advantage is gained using this technique when compared with staged repair in which the arch is repaired via left thoracotomy, and the VSD is managed by either a concomitant pulmonary trunk band or by subsequent intracardiac closure at a separate operation.\textsuperscript{195} Nevertheless, in institutions experienced with complex neonatal surgery, one-stage repair provides the benefits of immediate normalization of physiology, a single operation, and avoidance of involving the right side of the heart with iatrogenic problems (pulmonary artery stenosis) while achieving good outcomes.

Traditionally, interrupted aortic arch has been repaired using hypothermic circulatory arrest. Recently, CPB techniques have been developed that allow repair to proceed using moderate hypothermia and continuous perfusion.\textsuperscript{201,202} In a single-institution analysis of 50 patients, mortality using continuous perfusion in 25 patients was 8% (CL 2.8%-18%), and using deep hypothermic circulatory arrest in 25 patients, 32% (CL 21%-44%). By multivariable analysis, however, the difference did not achieve significance.\textsuperscript{185} Another analysis showed that continuous perfusion, when compared with hypothermic circulatory arrest, was an independent factor protecting against death.\textsuperscript{187} In a study of 26 cases focusing on neurodevelopmental outcome at 18 to 24 months following repair, longer hypothermic circulatory arrest time was associated with worse neurodevelopmental outcome.\textsuperscript{189} Both techniques are described in the text that follows.

**Repair Using Continuous Perfusion**

Operation for a patient with type B interruption and VSD with posteriorly displaced and deficient infundibular septum is described (Fig. 48-37, A). Following standard preoperative stabilization and preparation in the operating room, a median sternotomy with slight superior extension is made. The thymus gland is removed except for a small remnant in the neck, and the pericardium is widely opened. The anterior pericardium is removed and fixed in glutaraldehyde. The ascending aorta, pulmonary trunk, ductus arteriosus, all arch vessels, and both venae cavae are dissected. The arch vessels are dissected and mobilized superior to the brachiocephalic vein. A purse-string suture is placed on the brachiocephalic artery midway between its origin and bifurcation; another is placed on the pulmonary trunk. Venous purse strings are placed on the superior and inferior venae cavae. A purse string is placed on the right superior pulmonary vein as it merges with the left atrium. After heparin is given, a side-biting clamp is placed on the brachiocephalic artery and a careful arteriotomy is made inside the purse-string suture. A 6F or 8F cannula is then inserted, as allowed by the vessel size, taking care to position the tip of the cannula well within the vessel lumen but not against the back wall of the artery (Fig. 48-37, B). A second 8F cannula is then placed into the pulmonary trunk. These cannulae are then connected to the bifurcated arterial end of the CPB circuit. Superior and inferior venae cavae are each cannulated with angled metal-tipped 12F venous cannulae connected to the bifurcated venous end of the CPB circuit. CPB is then begun. The branch pulmonary arteries are individually snared. A 10F vent is placed through the right upper pulmonary vein purse string and guided across the mitral valve to decompress the left ventricle. The patient’s core temperature is lowered to 25°C over a 15-minute period.

During this time, the distal part of the ductus and the upper descending aorta are dissected. After the target core temperature is reached, perfusion flow rate is reduced to 40 to 50 mL · kg\textsuperscript{-1} · min\textsuperscript{-1}, and the arterial cannula in the pulmonary trunk is clamped and removed. A 5-0 polypropylene suture on the ductus arteriosus is tied to occlude the pulmonary artery end of the ductus. A small C clamp is placed on the descending aorta at approximately the second pair of intercostal vessels below the ductus insertion. The left subclavian artery is occluded temporarily with a removable neurovascular clip. The ductus arteriosus is transected near the ligature, and the remaining ductal tissue is removed from the descending aorta, using origins of the intercostal arteries as a landmark indicating normal aortic tissue. The C clamp on the descending aorta prevents backbleeding through the aorta and is also used to manipulate the descending aorta to facilitate its approximation to the ascending aorta at the time of anastomosis.

A small angled clamp is placed obliquely across the arch of the aorta at the base of the brachiocephalic and left carotid arteries, allowing continuous perfusion through the brachiocephalic artery cannula to both of these vessels (Fig. 48-37, C). Cardioplegia is introduced in standard fashion through a cannula placed into the midportion of the ascending aorta. Incision is made on the left posterolateral aspect of the distal ascending aorta onto the base of the left carotid artery over a sufficient length to match the circumference of the orifice of the descending aorta. End-to-side anastomosis between the descending and ascending aorta is performed using a running suture technique with 7-0 absorbable monofilament suture. Upon completion of the anastomosis, the obliquely placed clamp on the aortic arch and the descending aortic clamp are removed. The ascending aorta is then clamped in standard fashion, allowing perfusion to the entire systemic circulation except the coronary arteries. The perfusion flow rate is increased to 100 mL · kg\textsuperscript{-1} · min\textsuperscript{-1}. A repeat dose of cardioplegia is given about this time, and the operation proceeds with VSD closure (see Chapter 35) and, if needed, atrial septal defect (ASD) closure. In the typical case, the VSD is closed via an incision in the pulmonary trunk, and the ASD via right atriotomy. After these defects, the pulmonary trunk incision and atrial incision are closed, and standard maneuvers...
Primary repair of interrupted aortic arch using continuous cardiopulmonary bypass (CPB). **A**, Cardiac exposure is through a standard median sternotomy, and preparation and dissection are similar to that used for repair of hypoplastic left heart (see Chapter 49). This figure shows type B aortic arch interruption, with patent ductus arteriosus (PDA) and ventricular septal defect (VSD). **B**, Two separate arterial cannulae are used, one introduced into the brachiocephalic artery and the other into the pulmonary trunk. Venous cannulation is performed into superior and inferior venae cavae through standard purse strings. After beginning CPB, branch pulmonary arteries are temporarily occluded (see text for details). Moderate hypothermia and standard cardioplegic myocardial protection are used (see text for details). Dashed lines show points of transection of distal ductus arteriosus and incision in posterolateral aspect of ascending aorta.

**Repair Using Circulatory Arrest**

After proper stabilization as described under Indications for Operation later in this section, the baby is brought to the operating room, usually with an umbilical artery catheter in place. After usual preliminary steps, primary median sternotomy is made (see Preparation for Cardiopulmonary Bypass in Section III of Chapter 2). Most of the thymus gland, if present, is removed to adequately mobilize branches of the aortic arch. The pericardium is opened widely and stay sutures applied. A portion of the pericardium is prepared in case it is necessary to use it in repairing the ASD. The
Cardioplegia has been introduced through a catheter in mid-ascending aorta. Proximal aortic clamp is positioned to allow continued flow through brachiocephalic and left carotid arteries. Arterial cannula in pulmonary trunk has been removed and ductus arteriosus ligated and divided. All ductus tissue has been removed from distal aorta. Incision in posterolateral aspect of ascending aorta has been made. Running suture anastomosis is begun at posterior aspect of circumference of descending aorta. Completed arch repair. Aortic clamps have been removed and patient separated from CPB (see text for details of methodology for ventricular septal defect closure). Key: IVC, inferior vena cava; LPA, left pulmonary artery; RPA, right pulmonary artery; SVC, superior vena cava.

Figure 48-37, cont’d  C, Cardioplegia has been introduced through a catheter in mid-ascending aorta. Proximal aortic clamp is positioned to allow continued flow through brachiocephalic and left carotid arteries. Arterial cannula in pulmonary trunk has been removed and ductus arteriosus ligated and divided. All ductus tissue has been removed from distal aorta. Incision in posterolateral aspect of ascending aorta has been made. Running suture anastomosis is begun at posterior aspect of circumference of descending aorta. D, Completed arch repair. Aortic clamps have been removed and patient separated from CPB (see text for details of methodology for ventricular septal defect closure). Key: IVC, inferior vena cava; LPA, left pulmonary artery; RPA, right pulmonary artery; SVC, superior vena cava.
the aortic cannula and one arm of the arterial tubing, and the arterial tubing is carefully arranged to lie smoothly and as much as possible outside the surgical field. After inserting the aortic cannula, a round-nosed right atrial catheter of appropriate size is introduced through the right atrial appendage and positioned in the orifice of the superior vena cava. This allows the cannula and the venous tubing to sweep inferiorly and lie outside the surgical field. CPB is established with the perfusate about 34°C; a second arterial cannula is inserted into the pulmonary trunk through a purse string and is connected to the other arm of the arterial Y; the tip of the cannula remains within the pulmonary trunk. The left pulmonary artery is dissected out promptly and a snare placed and tightened around it, and the snare on the right pulmonary artery is tightened. Cooling of the patient with the perfusate then proceeds. Infusion of PGE₁ is continued during the cooling phase of CPB.

During cooling, the brachiocephalic, right subclavian, right common carotid, left common carotid, and left subclavian arteries are fully mobilized. This step is extremely important to preclude tension on the aortic suture line once it is made. The ductus arteriosus is dissected, and a tie is placed loosely around it. Elastic snare is placed around the right and left common carotid arteries, but not around the subclavian arteries. When the patient’s nasopharyngeal (or tympanic membrane) temperature reaches 16°C to 18°C, circulatory arrest is established, leaving the venous tubing open until the patient’s blood volume has been transferred to the pump-oxygenator. The aorta is clamped just distal to the aortic cannula, and cold cardioplegic solution is infused through the stopcock on the aortic cannula (see Section IV of Chapter 2). All cannulae are then removed from the surgical field, the carotid artery tourniquets tightened, and the aortic clamp removed.

The ductus arteriosus is ligated, taking care to avoid distorting the bifurcation of the pulmonary trunk, and it is transected at its junction with the aorta. As much ductal tissue as possible is removed from the opened aorta, but this cannot be performed in as satisfactory a manner as in discrete coarctation. Particularly in type B interruption, the distal aortic segment is thoroughly mobilized. If the right subclavian artery arises anomalously from the upper descending aorta, it is dissected and divided between ligatures. If the anastomosis cannot be made tension-free in any other manner, the left subclavian artery is also ligated and divided. A small delicate C clamp is placed on the descending aorta so that an assistant can bring it into apposition with the proximal aortic segment without tension. An opening for the anastomosis is made in the left posterolateral aspect of the ascending aorta, as much as possible in its midportion and approximately opposite the arterial cannulation site. An end-to-side anastomosis is made with continuous 7-0 absorbable monofilament suture, beginning along the far side of the inferior angle and sewing so that the stitching in the proximal aorta is from the inside out, because this is the most delicate structure. Five or six of the stitches should be placed before they are carefully pulled up as the aortic segments are brought together; the remainder of the suture line is then completed.

The VSD is repaired. If there is considerable infundibular (conal) septal tissue separating the superior margin of the VSD from the pulmonary valve, the VSD is repaired through the right atrium (see Technique of Operation in Chapter 35). If preliminary echocardiographic studies have shown that the infundibular septum beneath the pulmonary valve is deficient, as is often the case, the VSD is repaired through the pulmonary trunk, which is usually very large in this condition. The foramen ovale, which may have been considerably stretched by a preexisting left-to-right shunt, must be closed. This can be accomplished either primarily or by suturing into place a piece of pericardium using continuous sutures.

Saline is flushed into the left side of the heart before completing closure of the foramen ovale, to emerge through the aortic cannulation site to de-air the left heart. The right atrium is closed. Only the ascending aortic cannula is reinserted, and it is important to have blood gently coming out the cannula as it is inserted into the ascending aorta to prevent air entrapment. After reinserting the right atrial cannula, CPB is begun, the carotid artery tourniquets are released, and rewarming is accomplished. Before removing the aortic cannula, pressure in the ascending aorta can be measured by connecting to a pressure transducer to the stopcock that has previously been placed. It is compared with that recorded from the umbilical artery catheter to assess the status of the aortic anastomosis. The remainder of the procedure is completed in the usual manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Alternative Methods of Arch Repair

Occasionally, other methods of arch repair are indicated when a primary ascending-to-descending aortic anastomosis is not advisable. Methods that preserve growth potential, such as using the left carotid or subclavian artery, are preferred to interposition grafts. When an anomalous right subclavian artery is present, it can be used for the arch reconstruction.[21]

Repair of Interrupted Arch and Ventricular Septal Defect and Left Ventricular Outflow Obstruction

Left ventricular outflow tract (LVOT) obstruction occurs to varying degrees with interrupted aortic arch and VSD. The decision to perform a specific procedure to address the LVOT at the initial neonatal operation is a difficult one (see Special Situations and Controversies later in this section). When the LVOT is deemed inadequate, various techniques have been used to address this problem:

- Pulmonary trunk–to-aortic anastomosis (Damus-Kaye-Stansel [DKS] procedure) with arch repair and Rastelli septation (VSD closure and right ventricle–pulmonary trunk conduit)[71,71]
- DKS procedure with arch repair and systemic–pulmonary artery shunt, followed by staged Rastelli septation
- Direct muscular or fibromuscular LVOT resection along with arch and VSD repair[40]
- Norwood operation with Rastelli septation[15,15]
- Norwood operation, followed by staged Rastelli septation[8]
- Ross-Konno operation[12,55]

Repair of Interrupted Arch and Other Coexisting Cardiac Anomalies

In general, coexisting cardiac anomalies such as transposition of the great arteries or truncus arteriosus are repaired
concomitantly with repair of the interrupted arch, except for those in which a Fontan operation is required. For these exceptions, the procedures described under Indications for Operation in Chapters 41 and 56 are applicable. Several techniques have been described for one-stage repair of interrupted arch with aortopulmonary window.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Care is as usual (see Chapter 5). Special attention is paid to the possible occurrence of hypocalcemia if DiGeorge syndrome is present.

Because in this setting appreciable left-to-right shunting is apt to occur through a small residual VSD or ASD (presumably because of some degree of hypoplasia of the left ventricular cavity or outflow obstruction), left-to-right shunting must be carefully sought (see “Risk Factors for Low Cardiac Output” in Section I of Chapter 5). If found in patients whose hemodynamic state is not good, reoperation is indicated.

If extensive atelectasis of the left lung develops, its cause may be left bronchial compression by a directly reconstructed aortic arch. Prevalence of this complication is low when the operation has included wide mobilization as described. However, if this complication occurs, reoperation may be considered if it is believed that the vessels can be further mobilized.

Because the aortic valve is commonly small or bicuspid, and the subvalvar LVOT is small as a result of the posteriorly malaligned infundibular septum, it is common for some degree of LVOT obstruction to be present after repair once the left ventricle ejects a full cardiac output. The degree of obstruction should be assessed immediately after separation from CPB using transesophageal echocardiography. If preoperative assessment and surgical judgment are appropriate, the gradient should be less than 30 mmHg systolic. If the gradient is higher, particularly if there is left ventricular dysfunc-

**RESULTS**

**Survival**

**Early (Hospital) Death**

Most early reports were based on a small number of patients, and in these mortality ranged from 20% to 80%. However, in patients with interrupted arch and VSD, early mortality in the current era can be 10%. In the multinstitutional study of the CHSS, mortality after optimum repair for type A interruption with or without concomitant VSD was 4% at 30 days; for type B, 11%.

**Time-Related Survival**

Realizing that many patients are seriously ill, survival from time of diagnosis (birth), including deaths before operation, is the most realistic evidence of the impact of treatment on the natural history. Overall, 5-year survival after birth can be predicted to be about 45%; rate of dying (hazard function) is rather high immediately after birth but declines rapidly thereafter, reaching a low level by 12 months (Fig. 48-39).

Survival after repair of interrupted aortic arch and VSD in the CHSS multinstitutional study of a heterogeneous population was 63% at 4 years (Fig. 48-40), and optimal repair in type A interruption with or without coexisting obstructive lesions elsewhere in the left heart was associated with 5-year survival of 93%, and for type B, 83% (Fig. 48-41). Recent follow-up of this patient cohort indicates that non–risk-adjusted 16-year survival is 59%, and not unexpectedly, it improved the later the date of birth (Fig. 48-42). Single-institution studies from approximately the same era suggest similar 5-year survival of greater than 70%, Unadjusted survival for interrupted arch with aortopulmonary window (Fig. 48-43) is better than unadjusted survival for interrupted arch with VSD (see Fig. 48-40), and is similar to “optimal repair” survival for interrupted arch with VSD (see Fig. 48-41).

**Modes of Death**

Most deaths are with acute or subacute heart failure without or with multiple subsystem failure, although some are related to late reoperations for LVOT obstruction or aortic arch obstruction.
Incremental Risk Factors for Premature Death

The 2005 report on the CHSS multiinstitutional study of 472 cases of interrupted aortic arch focuses on risk factors for mortality and reintervention. A relatively cohesive picture of the risk factors for mortality can be constructed based on this study and a number of other individual institutional studies.

Nature of the coexisting cardiac anomaly has been identified as an important risk factor for death, with VSD the most favorable (see Fig. 48-41). The CHSS study confirms the presence of truncus arteriosus as a risk. Additionally, the CHSS study identifies certain VSD characteristics as risks. Small and moderate VSD and VSDs that are not malaligned are noted to be risks. Several relatively small series showed no association with survival of complexity of coexisting cardiac anomalies. Location of the interruption has its most important effect when it has been between the brachiocephalic and left common carotid artery (type C); this has been a highly lethal but rare lesion. A smaller difference in survival has been observed between interruptions distal to the left subclavian artery (type A) and those between the left

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Figure 48-39 Early and intermediate-term survival after entry into treatment institution (essentially at birth) of heterogeneous group of neonates with interrupted arch \((n = 168)\). A, Percent survival. B, Hazard function for death. (From multiinstitutional study of the Congenital Heart Surgeons Society, 1987 to 1991.)

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Figure 48-40 Early and long-term survival after repair of interrupted aortic arch in heterogeneous group of neonates with interrupted aortic arch and ventricular septal defect. Depiction is as in Fig. 48-39. A, Survival. B, Hazard function for death. (From Jonas and colleagues.)

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Figure 48-41 Risk-adjusted survival of neonate undergoing single-stage repair at age 7 days of either type A or B interrupted aortic arch (IAA) and single large ventricular septal defect. Graph represents nomograms of specific solutions of multivariable equation given in original paper. Solid lines are point estimates enclosed within 68% confidence limits. (From Jonas and colleagues.)
subclavian and left common carotid artery (type B) (see Fig. 48-41). The CHSS study confirms higher risk for types C and B; thus, type A carries the lowest risk.

Type of initial surgical procedure used to address interrupted aortic arch with VSD does not appear to importantly influence outcome, whether the approach is arch repair with VSD closure, arch repair with pulmonary trunk banding, or arch repair alone\(^{38}\) (Table 48-7). The CHSS study confirms this as well. As intimated under Technique of Operation earlier in this section, condition of the patient on entry into the operating room is important, and a low arterial pH at that time has been a strong risk factor for death (Tables 48-8 and 48-9; Fig. 48-44).

Table 48-7 Repair of Interrupted Aortic Arch and Ventricular Septal Defect in Neonates, without or with a Concomitant Procedure, and the Non–Risk-Adjusted Total Deaths in Each Group

<table>
<thead>
<tr>
<th>First Repair</th>
<th>Total Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>One-stage repair</td>
<td>116</td>
</tr>
<tr>
<td>Repair IAA + PT band</td>
<td>40</td>
</tr>
<tr>
<td>Repair only IAA</td>
<td>17</td>
</tr>
<tr>
<td>Transplant</td>
<td>1</td>
</tr>
<tr>
<td>Subtotal</td>
<td>174</td>
</tr>
<tr>
<td></td>
<td>0.6</td>
</tr>
<tr>
<td>No repair of anything</td>
<td>9</td>
</tr>
<tr>
<td>TOTAL</td>
<td>183</td>
</tr>
</tbody>
</table>

Data from Jonas and colleagues.\(^{18}\)

Subtotal 174 62 36 32-40

P(χ²) = 0.6

P(χ²) = 0.5

Seven (zero deaths) had type A interruption, 10 (four deaths) had type B interruption.

Key: CL, 70% Confidence limits; IAA, interrupted aortic arch; PT, pulmonary trunk.

Other levels of LVOT obstruction is a risk factor, and is depicted as decreasing survival as left ventricular aortic junction diameter decreases (see Table 48-8). More complex procedures designed to address this obstruction are identified as carrying greater risk, as is ignoring the obstruction and performing a simple repair of the interruption and VSD closure (see Table 48-9). The CHSS study suggests that a pulmonary trunk to aortic anastomosis (DKS anastomosis) increases risk.

Date of operation has been a powerful risk factor because of great improvements achieved over time (see Fig. 48-38). The CHSS study confirms this. Thus, data from earlier eras have little applicability in the current era in institutions prepared for neonatal cardiac surgery.

Low weight at operation is identified as a risk in the CHSS study, as is lack of augmentation of the arch at the time of initial arch repair; however, other studies seem to contradict the latter.\(^{129}\)

Left Ventricular Outflow Obstruction

Patients with interrupted aortic arch often have at least some degree of hypoplastic left heart physiology as well (see
### Table 48-8  Incremental Risk Factors for Time-Related Death at Any Time after Repair of Interrupted Aortic Arch and Ventricular Septal Defect in Neonates

<table>
<thead>
<tr>
<th>Incremental Risk Factors for Death (Patient-Specific Variables, Including Institutionally Measured Dimensions)</th>
<th>P (Single Hazard Phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
</tr>
<tr>
<td>Lower Birth weight</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Younger Age at repair</td>
<td>.04</td>
</tr>
<tr>
<td>Morphologic</td>
<td></td>
</tr>
<tr>
<td>IAA type B</td>
<td>.02</td>
</tr>
<tr>
<td>Outlet or trabecular VSD</td>
<td>.003</td>
</tr>
<tr>
<td>Smaller Size of VSD</td>
<td>.0002</td>
</tr>
<tr>
<td>Smaller Dimension (z) of LV-aortic junction</td>
<td>.03</td>
</tr>
</tbody>
</table>

Data from Jonas and colleagues.¹⁸

**Note:** For this, the obstructive levels in the left heart–aorta complex were not entered, nor were procedural or institutional variables.

Key: IAA, Interrupted aortic arch; LV, left ventricular; VSD, ventricular septal defect.

### Table 48-9  Incremental Risk Factors for Time-Related Death at Any Time after Repair, Entering Patient-Specific, Procedural, and Institutional Variables

<table>
<thead>
<tr>
<th>Incremental Risk Factors for Death (Patient-Specific, Procedural, and Institutionally Variables)</th>
<th>P (Single Hazard Phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td></td>
</tr>
<tr>
<td>Lower Birth weight</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Younger Age at repair</td>
<td>.0004</td>
</tr>
<tr>
<td>Morphologic</td>
<td></td>
</tr>
<tr>
<td>Higher Grade of subaortic obstruction (0-5)</td>
<td>.0004</td>
</tr>
<tr>
<td>IAA type B</td>
<td>.04</td>
</tr>
<tr>
<td>Smaller Size of VSD (small, moderate-sized, large)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Procedural</td>
<td></td>
</tr>
<tr>
<td>PT–Asc Ao anastomosis (DKS anastomosis)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Subaortic myotomy/myectomy and subaortic obstruction (≥grade 2) (interaction term)</td>
<td>.02</td>
</tr>
<tr>
<td>Simple repair and coexisting obstructive lesions elsewhere in the LHA complex (interaction term)</td>
<td>.02</td>
</tr>
<tr>
<td>Institutional</td>
<td></td>
</tr>
<tr>
<td>Institution B</td>
<td>.006</td>
</tr>
<tr>
<td>Institution H</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

Data from Jonas and colleagues.¹⁸

Key: Asc Ao, Ascending aorta; DKS, Damus-Kay-Stansel; IAA, interrupted aortic arch; LHA, left heart–aorta; PT, pulmonary trunk.

“Coarctation as Part of Hypoplastic Left Heart Physiology” under Morphology in Section 1. The specific features all relate to the LVOT, as pointed out several times elsewhere in this section, including:

- Posterior malalignment of infundibular septum
- Hypertrophy of anterolateral muscle bundle of the left ventricle (muscle of Moulaert)
- Bicuspid dysplastic aortic valve
- Narrowness of aortic anulus
- Hypoplasia of ascending aorta and aortic arch; occasionally this is apparent before operation, but more often it becomes evident after repair.

LVOT obstruction has important implications for both short- and long-term prognosis, and for decision making and surgical technique (see Results in following text and Special Situations and Controversies later in this section). In a minority of neonates with interrupted aortic arch and VSD, the LVOT is inadequate, and repair of the arch and VSD alone results in unacceptable obstruction. Although difficult to accomplish, it is best to identify such patients before the initial operation (see Special Situations and Controversies later in this section). In about 40% of patients with a conoventricular VSD, or with a VSD in the outlet portion of the right ventricle, evidence of LVOT obstruction develops at midterm or late follow-up, even when the LVOT was adequate after initial operation.¹⁴,¹⁵ (Fig. 48-45).

Whether the LVOT obstruction develops during or sometime after the initial operation, or whether it was present at birth and only becomes evident later is uncertain, but both probably occur. Probability that at least the anatomic basis for the obstruction was present at birth is heightened by the shape of the hazard function, which indicates that the rate of recognizing (or developing) LVOT obstruction declines to a constant hazard after about 2 years following initial repair (see Fig. 48-45).
Late Reoperation from All Causes

Late reoperation is frequent after neonatal repair of interrupted aortic arch, reflecting the complexity of the underlying lesion. There are multiple reasons for reoperation, including:

- Recurrent arch obstruction
- LVOT obstruction
- Residual VSD
- Bronchial compression
- Diaphragm palsy
- Complete heart block

In a single-institution analysis of 94 patients undergoing initial operation between 1975 and 1999, with follow-up of up to 21 years (mean 6.7 years), reoperation from all causes was 40% at 15 years. Similar prevalence of
reintervention was noted in other series from the same period.\textsuperscript{34} Reflecting the general trend that outcomes improve over time, another single-institution analysis of 65 patients undergoing initial operation between 1982 and 2005 showed that reoperation from all causes was 60\% at 15 years\textsuperscript{M5} (Fig. 48-48).

The cumulative incidence of all types (surgical or catheter-based) reinterventions after repair of interrupted aortic arch exceeds one per patient within about 3 years and approached two per patient by about 25 years (Fig. 48-49). The most common are catheter-based arch procedures (Fig. 48-50).

**INDICATIONS FOR OPERATION**

Diagnosis of interrupted aortic arch is an indication for operation, no matter what the coexisting cardiac anomaly. Severe chromosomal abnormalities may contraindicate surgical intervention.

Intensive treatment is an essential part of the therapeutic program and begins the moment the diagnosis is suspected, which should be shortly after birth. An infusion of PGE\textsubscript{1} is begun, usually in a dose of 0.05 to 0.1 µg · kg\textsuperscript{-1} · min\textsuperscript{-1}, and the infant is intubated and appropriately ventilated; high FIO\textsubscript{2} is avoided. If the infant’s condition is good in all ways, operation is undertaken at the first convenient time, but not as an emergency. If the infant’s condition is not good, then:

- Right-to-left shunting into the descending aorta for augmenting systemic blood flow is encouraged by increasing

CO\textsubscript{2} in the inspired gas mixture or mildly hypoventilating the patient so that PaO\textsubscript{2} is about 40 mmHg (to increase pulmonary vascular resistance).

- Cardiac output and renal blood flow are increased by infusing dopamine at 2.5 to 5 µg · kg\textsuperscript{-1} · min\textsuperscript{-1}.

- Acidosis is corrected by intravenous sodium bicarbonate (see Appendix 5N in Chapter 5).

Nearly always, the baby can be brought into a good clinical condition by these measures. At that point, operation is performed.

One-stage repair of the interrupted arch and the coexisting anomaly, or repair of the interruption with staged repair of the coexisting anomaly, is carried out, except when some form of single ventricle is the coexisting anomaly. An alternative plan is then necessary (see Section I of Chapter 41).

**SPECIAL SITUATIONS AND CONTROVERSIES**

Preoperative assessment of adequacy of the LVOT, including the aortic valve and subaortic region, can be challenging in patients with interrupted aortic arch. The aortic valve is frequently bicuspid with some degree of hypoplasia. The subaortic region is often narrowed by a posteriorly malaligned infundibular septum. Preoperative assessment of the LVOT is difficult because preoperative physiologic measurements are unreliable predictors of postoperative physiology. Because flow across the LVOT is typically low preoperatively from the patent ductus with right-to-left shunting, preoperative obstruction is almost never detected, even when the LVOT proves to be inadequate after repair. Therefore, other preoperative measures must be relied on to predict LVOT adequacy after repair. The most difficult assessment is of the subaortic region. Specific criteria for identifying the patient with inadequate LVOT preoperatively have not been widely accepted; currently, individual institutions use various measures to identify these patients. In many cases a subjective intraoperative decision is made by the operating surgeon regarding whether to perform a procedure that addresses the LVOT.\textsuperscript{436} Hanley and colleagues at Stanford (personal communication) have used a simple formula that permits an objectively based

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure48-47.png}
\caption{Freedom from reoperation from all causes in 94 patients undergoing initial interrupted arch repair between 1975 and 1999. (From Schreiber and colleagues.)}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure48-48.png}
\caption{Freedom from reoperation from all causes in 65 patients undergoing initial operation for interrupted aortic arch between 1982 and 2005. (From Malhotra and colleagues.)}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure48-49.png}
\caption{Cumulative hazard for subsequent procedures of any type after repair of interrupted aortic arch. Graph demonstrates cumulative number of events per patient at any given point since index procedure. Circles represent any subsequent procedure (n = 436). (From Jegatheeswaran and colleagues.)}
\end{figure}
decision preoperatively. Using echocardiography, if the smallest diameter of the subaortic region (measured in millimeters) is equal to or greater than body weight (measured in kilograms), the LVOT will be adequate, as defined by a postrepair LVOT gradient of less than 20 mmHg. (Others have described different anatomic dimensions used to predict subsequent obstruction.117,153) Thus, a 4-kg neonate must have a minimum subaortic dimension of at least 4 mm. If this criterion is met, a standard repair involving direct arch reconstruction and VSD closure is performed. If this criterion is not met, an alternative one-stage repair is performed. This involves direct arch reconstruction, DKS procedure, VSD closure allowing the LV to eject to both the aortic and pulmonary valves, and placement of a right ventricle–to–pulmonary trunk valved conduit. Although the 1994 CHSS data indicate that the DKS procedure carries elevated risk,18 several single-institution studies suggest that the DKS procedure or similar variants can be performed with low mortality.18,61,153 Others advocate directly resecting the obstruction in the LVOT at the time of the arch repair and VSD closure52,546; however, the 1994 CHSS data suggest that attempting to do this is a risk factor for death.18

Finally, the Ross-Konno operation (see Technique of Operation in Section II of Chapter 47) has been applied to this problem.112,153

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C


D


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E


F


G


5. Goldberg SJ, Gerlis LM, Ho SY, Penilla MB. Location to the left papillary muscles in juxtaaortic aortic coarctation. Am J Cardiol 1995;75:746.


H

J

K


Chapter 48 Coarctation of the Aorta and Interrupted Aortic Arch


O


T


W


Y


Z


Hypoplastic left heart syndrome is defined as inability of the left heart to sustain adequate cardiac output following birth because of underdevelopment of one or more left heart structures despite surgical or medical intervention. Box 49-1 emphasizes four important implications of this definition.

We have chosen to use the term hypoplastic left heart physiology rather than the more common and entrenched term hypoplastic left heart syndrome, because it more accurately describes the entity. In fact, both terms have important limitations when applied in the clinical setting. In practice, the exact point along the aforementioned continuum where an inadequate left heart is encountered cannot be defined with certainty. This limitation is not intrinsic to the definition of hypoplastic left heart physiology itself, but rather is due to two important factors: (1) tests designed to define morphologic and physiologic characteristics are limited in their ability to accurately predict overall left heart function, and (2) new
Box 49-1 Hypoplastic Left Heart Physiology

1. The term left heart refers to the morphologic composite or unit that includes left atrium, mitral valve, left ventricle, aortic valve, and aorta. Each of these plays an important role in determining left heart function.  

2. Definition of hypoplastic left heart is physiologic, not morphologic, despite morphologic abnormalities being the underlying cause of left heart inadequacy. A morphologic definition of the hypoplastic left heart is not possible because underdevelopment of a variable number of specific left heart structures, either alone or in various combinations, may be responsible for physiologic inadequacy of the left heart. Some morphologic constellations (e.g., aortic and mitral atresia in combination) essentially always result in hypoplastic left heart physiology, whereas others (e.g., aortic or mitral stenosis) may or may not. Nevertheless, typical morphologic abnormalities that result in hypoplastic left heart physiology can be identified. These include a constellation of atresia or marked hypoplasia of the mitral valve, left ventricle, and aortic valve, in association with hypoplasia of the ascending aorta and aortic arch, aortic coarctation, patent ductus arteriosus, and atrial septal defect. It is important, however, to reemphasize that this constellation does not define hypoplastic left heart physiology; hypoplastic left heart physiology can be present without including all morphologic abnormalities mentioned in this typical example.  

3. Hypoplastic left heart physiology is present within a relatively narrow band of the broad continuum of hypoplastic lesions of the left heart. This continuum ranges from isolated simple lesions (e.g., discrete coarctation) at one end of the spectrum to complex multilevel lesions (e.g., combination of aortic atresia, mitral atresia, and absent left ventricle) at the other end. The point along this gradually increasing continuum of left heart abnormalities where hypoplastic left heart physiology is encountered is impossible to pinpoint morphologically. Hypoplastic left heart physiology may be the result of a severe abnormality of a single left heart structure (e.g., mitral atresia) or a combination of several milder abnormalities (e.g., mitral stenosis, left ventricular hypoplasia, and aortic stenosis).  

4. Inclusion of the phrase despite surgical or medical intervention in its definition is critical to the concept of hypoplastic left heart physiology, because abnormalities such as isolated critical aortic stenosis or isolated severe aortic coarctation may meet the criteria of this physiologic definition before but not after intervention to correct the abnormality. As a result, the lesions cited in the previous sentence are not considered examples of hypoplastic left heart physiology. An important implication of the term hypoplastic left heart physiology is that the left heart is incapable of sustaining systemic cardiac output, thereby limiting therapeutic options to (1) reconstructions that use a single (right) ventricular pumping chamber (Norwood procedure, superior cavopulmonary connection, Fontan procedure) or (2) heart transplantation.

The concept of borderline hypoplastic left heart physiology, therefore, refers to a zone along this continuum in which it is currently not possible to predict with certainty whether the left heart can be salvaged with surgical reconstructive methods. This concept is of practical importance because it helps characterize the clinical dilemma faced by surgeons who must make a dichotomous decision (reconstructive surgery to salvage the left heart vs. the Norwood procedure or transplantation) in the context of a continuum of morphologic and physiologic left heart compromise. At either pole of this continuum, decision making is straightforward. However, within the zone of borderline hypoplastic left heart physiology, the appropriate management decision requires exquisite attention to many subtle details.

The various malformations that result in hypoplastic left heart physiology together represent a special example of univentricular atrioventricular connection (see Chapters 41 and 56). Because of the special clinical and surgical importance of this group of malformations, this subject is discussed separately from other forms of univentricular heart.

### HISTORICAL NOTE

The first description of aortic atresia was apparently by Canton in 1850. Although Abbott had recognized aortic and mitral atresia, Brockman in 1950 emphasized that in about 50% of cases of mitral atresia, there was coexisting aortic atresia and severe underdevelopment of the left side of the heart. In 1952, Lev further emphasized the group of congenital heart malformations associated with underdevelopment of the left-sided cardiac chambers and a small ascending aortic arch, articulating for the first time the concept that multiple left-sided structures tended to occur together. In 1958, Noonan and Nadas brought together the morphologic features of combined aortic and mitral atresia and introduced the phrase “hypoplastic left heart syndrome.” In 1976, Roberts and colleagues further organized the knowledge about this subject by emphasizing that in the presence of a large ventricular septal defect (VSD), aortic atresia can coexist with normal development of the left ventricle and mitral valve.

The history of attempted reconstructive procedures for hypoplastic left heart physiology dates back to 1970 when Cayler and colleagues described an anastomosis between right pulmonary artery and ascending aorta with placement of bilateral pulmonary artery bands. Other variations in neonatal reconstructive procedures designed to allow survival without the use of prostaglandins to maintain ductal patency were described by Doty and colleagues in 1977, Norwood and colleagues in 1980, Levitsky and colleagues in 1980, Behrendt and colleagues in 1981, and others. 

Even though some of these reports noted short-term successes, there is no documentation of long-term survival. In 1983, Norwood and colleagues described for the first time neonatal palliative surgery leading to a subsequent successful Fontan procedure. Following this report and subsequent reports that systematically documented long-term survival of patients with hypoplastic left heart physiology, it has become widely accepted that many of the technical details of the procedure as described by Norwood are critical to achieving long-term survival. These technical details ensure long-term aortic growth potential, minimize pulmonary valve distortion, address distal arch obstruction, preserve pulmonary developments and reconstructive techniques may allow previously unsalvageable left hearts to function adequately.
artery patency, balance pulmonary and systemic blood flows, and ensure adequate atrial-level mixing. Many of the procedures described before implementation of the Norwood procedure failed to address one or more of these issues critical for long-term survival.

Allograft heart transplantation for hypoplastic left heart physiology dates back to 1985, when Bailey performed the first successful cases as primary therapy in neonates. Since then, Bailey and colleagues and a limited number of other groups have considered transplantation as one option for treatment, along with reconstructive surgery.

The hybrid procedure for hypoplastic left heart physiology was first developed in 1993 in response to poor outcomes following the Norwood procedure. The hybrid procedure combines surgical placement of bilateral branch pulmonary artery bands, placement of a stent in the ductus arteriosus, and catheter-based atrial septostomy, avoiding cardiopulmonary bypass (CPB). Initially, it was not widely embraced because of poor interim outcomes; however, more recently it has been used by some programs as an alternative to the Norwood procedure in high-risk patients, and variations of the hybrid procedure have been used as a bridge to transplantation.

MORPHOGENESIS AND MORPHOLOGY

Morphogenesis

Currently, it is unclear whether the etiology of hypoplastic left heart physiology is similar in all cases. There are genetic factors involved, although these are multiple, complex, and poorly understood at the present time. Available evidence suggests that a number of primary morphologic etiologies may lead to the end result of hypoplastic left heart physiology. Primary morphologic abnormalities at the aortic valve level, mitral valve level, left ventricular myocardial level, or atrial septal level (intact atrial septum) could all in theory lead ultimately to hypoplasia of the entire left side of the heart as gestation progresses.

Fetal echocardiography has yielded much information regarding progression of hypoplastic left heart physiology. In some cases, critical aortic stenosis with documented forward flow on early fetal echocardiograms progresses to aortic atresia before birth. In such cases, the left ventricle shows evidence of progressive dysfunction and hypoplasia as stenosis proceeds to atresia. Echocardiographic evidence of fetal left ventricular dilated cardiomyopathy progressing to hypoplastic left heart physiology has been reported. Controversy remains as to whether a closed foramen ovale in utero is a cause or a result of hypoplastic left heart physiology.

Morphology

In hypoplastic left heart physiology, the heart is enlarged to about twice normal weight for age. Its shape is determined by the large right and small left heart chambers (Fig. 49-1, A). Beyond this, morphologic details vary widely. Four morphologic subtypes of hypoplastic left heart physiology can be defined based on status of the left heart valves:

- Aortic and mitral atresia
- Aortic atresia with mitral stenosis

Of these, aortic stenosis with mitral atresia is the least common subtype, representing approximately 5% of cases; aortic and mitral atresia is the most common, representing approximately two thirds of cases. Within these subtypes, the status of the atrial septum, size of the left ventricular cavity and muscle mass, ascending aorta and aortic arch, and ductus arteriosus are also important.

Aortic Valve and Ascending Aorta

In aortic atresia, the aortic valve is totally absent. Diminutive aortic sinuses of Valsalva are frequently present, giving origin to relatively normally positioned right and left coronary arteries that have a normal distribution pattern. The ascending aorta is narrow, sometimes as small as 1.5 mm in diameter. The portion of the aorta between the atretic valve and brachiocephalic artery serves only as a conduit for coronary blood flow (Fig. 49-2).

At and beyond the brachiocephalic artery, the aortic arch gradually widens and is joined beyond the origin of the left subclavian artery by a large patent ductus arteriosus. The ductus carries blood from the right ventricle into the descending aorta and retrograde to the brachiocephalic and coronary arteries. A localized aortic coarctation exists in approximately 80% of cases and is usually juxtaaortic in location (see Chapter 48). Prevalence of coarctation is highest in patients with the most severe hypoplasia of the ascending aorta. In some cases, there may be only mild infolding of the aortic media on the wall opposite the ductal insertion site, or there may be no aortic coarctation whatsoever.

When a patent but hypoplastic aortic valve is present, there may be a variable but still reduced amount of forward flow across the aortic valve (see Chapter 47). The ascending aorta and arch tend to be larger than in aortic atresia, with the diameter of the ascending aorta ranging from 2 to 6 mm. Aortic coarctation is common.

Left Ventricle and Mitral Valve

The left ventricle is severely hypoplastic in 95% of cases of aortic atresia. In this setting, the ventricular septum is intact. The mitral valve is either atretic (about one third of patients) or patent but severely hypoplastic (about two thirds of patients) (see Fig. 49-1, B and C). When the mitral valve is patent in association with aortic atresia, there may be left ventricular–coronary connections (Fig. 49-3) similar to those present in the right ventricle in cases of pulmonary atresia with intact ventricular septum (see “Right Ventricle” under Morphology in Chapter 40). It is postulated that these connections serve to decompress the left ventricular chamber. Localized thickening of coronary arteries occurs adjacent to these connections, and there is also a variable degree of endocardial thickening (endocardial fibroelastosis).

Rarely, there is focal calcification and scarring limited to the ventricular subendocardium. The hypoplastic left ventricle shows myocardial fiber disarray qualitatively similar to that present in hypertrophic obstructive cardiomyopathy (see “Left Ventricle” under Morphology in Section II of Chapter 47), and in the right ventricle in pulmonary atresia with intact ventricular septum (see “Right Ventricle” under Morphology in Chapter 40).
extremely hypoplastic with hypertrophic muscle and severe endocardial fibroelastosis to a dilated, thin-walled, poorly functioning chamber. The mitral valve is almost always hypoplastic and may be atretic when severe aortic stenosis is present.

Right Ventricle

In approximately 5% of cases of aortic atresia, the left ventricular cavity is near normal size in association with a large VSD. In such cases, there may be mitral valve atresia or a normal mitral valve. In cases of a normal mitral valve, the malformation does not represent hypoplastic left heart physiology, because such patients can undergo two-ventricle repair (see Special Situations and Controversies).

When aortic stenosis rather than atresia is present, the left ventricle tends to be larger than the typically minute, slitlike left ventricle of aortic atresia. Its size may vary widely from

Figure 49-1 Autopsy specimen of aortic atresia and hypoplastic left heart physiology from a 4-day-old neonate. A, Globular external shape of heart results from massive right ventricular (RV) hypertrophy and enlargement. Pulmonary trunk (PT) is large and ascending aorta (AscAo) small. Left ventricle (LV) is small and displaced posteriorly and does not reach cardiac apex. Arrow points to left anterior descending coronary artery. B, Interior of left atrium (LA) and partly opened LV. Septum primum (SP; fossa ovalis) is thickened and protrudes into right atrium (RA). Mitral valve (MV) is hypoplastic and stenotic, and LV wall is grossly thickened. C, Interior of fully opened LV. Its cavity is small, and there is marked endocardial fibroelastosis (EFE), which also involves rudimentary papillary muscles (PM) of small MV. Key: LAA, Left atrial appendage; PVs, pulmonary veins.

Right Ventricle

The right ventricle is enlarged, with uniform hypertrophy and a marked increase in cavity size (to approximately three times normal). Both tricuspid and pulmonary valves are larger
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than normal, and tricuspid regurgitation of variable degree is common.

Pulmonary Arteries
The pulmonary trunk is large and continues directly into the large patent ductus arteriosus. The right and left branches arise relatively posteriorly and at right angles from the short pulmonary trunk.

Atria and Atrial Septum
The left atrium is relatively small and thick walled, with its long axis directed transversely toward the right atrium. The atrial septum is also thick, making balloon atrial septostomy generally unsatisfactory. An atrial communication is usually present; in the great majority of cases, this communication is a stretched patent foramen ovale. The septum primum is thickened and stretched so that it herniates into the right atrium and allows left-to-right shunting (see Fig. 49-1, B). There may be an aneurysm of the septum primum projecting to the right. The right atrium is larger than normal, with uniform hypertrophy of its walls. When the atrial septum is intact or severely restrictive in association with mitral or aortic atresia or both, there is pulmonary venous hypertension and a variable degree of decompression of pulmonary venous return through connections to the systemic venous system. Pulmonary venous hypertension usually begins in fetal life. This may have important implications for fetal lung development. Dilated pulmonary lymphatic channels form, and these can have an important effect on postnatal lung physiology and surgical outcome.

Other Associated Cardiac Anomalies
Associated anomalies are uncommon. Structural abnormalities of the tricuspid and pulmonary valves are rare. Bicuspid pulmonary valve has been described in 4% of specimens; cleft tricuspid valve, tricuspid valve dysplasia, and double orifice tricuspid valve have also been reported. Other unusual cardiac anomalies include intact atrial septum, total anomalous pulmonary venous connection, levoatrial cardinal vein, coronary sinus atresia, atretic pulmonary veins, complete atrioventricular septal defect, transposition of the great arteries, and interrupted aortic arch. Coronary artery abnormalities are rare except in patients with aortic atresia and mitral stenosis, in which they occur in approximately 50% of cases.

Associated Noncardiac Anomalies
Other abnormalities unrelated to the cardiovascular system are found frequently with hypoplastic left heart physiology. Chromosomal abnormalities, genetic defects, and major extracardiac structural malformations, including central nervous system abnormalities, occur in 28% to 40% of patients.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA
Presentation is in the newborn period, with mild cyanosis, respiratory distress, and tachycardia. If supportive measures are not undertaken, there can be rapid deterioration, heart failure, and death due to a combination of pulmonary overcirculation and systemic obstruction from ductal closure. Ductal closure is almost inevitable, but its timing varies from

Figure 49-2 Lateral cineangiogram obtained after pressure injection of contrast medium into a brachial artery cannula in a neonate with hypoplastic left heart physiology. (This resulted in marked bradycardia and hypotension and is not a recommended technique.) Size of blind ascending aorta, which supplies large coronary arteries, and larger aortic arch and its branches are displayed. Pulmonary trunk (PT) is faintly outlined by contrast medium reaching it through the ductus arteriosus.

Figure 49-3 Postmortem coronary angiogram obtained by cannulating and injecting contrast medium into a coronary artery ostium in a heart with aortic atresia and hypoplastic left heart physiology. Small left ventricular (LV) cavity filled rapidly as contrast medium reached it through numerous coronary-LV connections. These form a prominent network within the thickened LV myocardium (arrows).
 Chapter 49  Aortic Atresia and Other Forms of Hypoplastic Left Heart Physiology

hours to weeks. This event is followed by rapid circulatory collapse.

On examination, there is a hyperactive right ventricular precordial impulse and a moderate-intensity mid-systolic murmur along the left sternal border. The second heart sound is accentuated and single. Heart failure is associated with rales and liver enlargement. In many instances, peripheral pulses and perfusion are poor and blood pressure is low.

The chest radiograph shows moderate cardiomegaly and pulmonary plethora secondary to increased pulmonary blood flow. The electrocardiogram demonstrates right axis deviation and right ventricular hypertrophy and usually no left ventricular forces. However, left ventricular voltages can be present but do not necessarily signify an adequate left ventricular cavity. Two-dimensional echocardiography is diagnostic and usually definitive. It demonstrates the large right ventricle, tricuspid valve, and ductus arteriosus and the small or absent left ventricle, aortic and mitral valves, and ascending aorta (Fig. 49-4). Status of the atrial septum is also easily determined. Doppler color flow signals indicate retrograde flow in the aortic arch and ascending aorta in cases of aortic atresia. Antegrade flow in the ascending aorta in the setting of aortic atresia strongly suggests that left ventricle-to-coronary artery fistulae are present, with left ventricular blood flowing retrograde in the coronary arteries and into the ascending aorta. When the aortic valve is not atretic, forward flow from the left ventricle across the aortic valve is normal. The amount of flow varies widely and may reach as far as the aortic arch. If Doppler color flow indicates substantial forward flow to the level of the arch or bidirectional flow in the patent ductus arteriosus, the patient should be considered to have borderline hypoplastic left heart physiology (see Special Situations and Controversies).

Cardiac catheterization is rarely indicated if it is clear by echocardiographic evaluation that the patient has unequivocal hypoplastic left heart physiology. However, in borderline hypoplastic left heart physiology, cardiac catheterization is often indicated to further characterize the physiology, especially mitral valve gradient and left ventricular end-diastolic pressure. The physiologic information obtained may help determine whether two-ventricle reconstruction is advisable. Catheterization is also indicated when a severely restrictive or intact atrial septum is present, resulting in pulmonary venous hypertension.

Rather than urgently bringing an hours-old infant to surgery under unstable conditions, the atrial septum can be opened by various interventional techniques (e.g., balloon dilatation, blade septostomy, atrial septal puncture with dilatation).

At this writing, computed tomography (CT) and magnetic resonance imaging (MRI) have a limited role in neonates with hypoplastic left heart physiology. CT angiography, however, may play an important role in follow-up, providing precise anatomic detail of aortic arch and pulmonary artery growth and development (Fig. 49-5). MRI can provide quantitative analysis of neoaortic and tricuspid valve regurgitation, and may be helpful in assessing left ventricular size in neonates with borderline left heart physiology in whom two-ventricle reconstruction is being contemplated.

NATURAL HISTORY

Various morphologic forms of hypoplastic left heart physiology constitute the fourth most common congenital cardiac defect. About 70% of cases are boys. Severe heart failure usually develops in the first week of life. Many neonates die within 1 to 2 weeks of birth; only 40% survive the neonatal period, and survival beyond 6 weeks of age is uncommon (Fig. 49-6). Hypoplastic left heart physiology accounts for 25% of cardiac deaths during the first week of life and 15% of those in the first month of life.

The ductus arteriosus typically begins to close shortly after birth. In some infants, ductal closure leads to restriction of systemic perfusion, metabolic acidosis, and circulatory collapse.

Figure 49-4  Echocardiographic findings in hypoplastic left heart physiology. A, Parasternal long-axis view of neonate with aortic atresia, severely hypoplastic ascending aorta (AAO), severely hypoplastic left ventricle, and mitral atresia. In this image, the 1.5-mm-diameter ascending aorta is shown longitudinally. The large pulmonary trunk (PT) is also shown. Right pulmonary artery (RPA) is visible in cross-section posterior to small ascending aorta. Left atrium (LA) is present in this image, but ventricular mass is not shown. B, Subcostal image showing four-chamber view of neonate with aortic atresia and mitral atresia, with severely hypoplastic left ventricle (LV). Right atrium (RA) and right ventricle (RV) are visualized and are markedly enlarged. LA is small, and LV cavity is miniscule. There is no direct communication between LA and hypoplastic LV. Ascending aorta and pulmonary trunk are not visualized in this image.
collapse; and death. If the ductus continues to remain patent, a progressive increase in pulmonary circulation and a subsequent decrease in systemic circulation lead to pulmonary edema, coronary hypoperfusion, generalized systemic hypoperfusion, and ultimately death. Rarely, long-term survival will occur if the ductus remains patent and pulmonary vascular resistance (Rp) fails to fall in the perinatal and neonatal period.

**TECHNIQUE OF OPERATION**

There are two basic surgical options—reconstruction and cardiac transplantation—for treating hypoplastic left heart physiology. Reconstructive surgery includes the Norwood procedure and its variants, and the hybrid procedure. In a recent survey of practices related to this condition, 86% of 52 institutions recommend as primary treatment the Norwood procedure or one of its variants, and 14% did not make a recommendation, but left the decision solely up to the parents. No institution recommended primary transplantation, the hybrid procedure, or comfort care.\(^2\)

**Reconstructive Surgery**

The overall goal of reconstructive surgery is similar to that for any patient with single-ventricle physiology (see Chapter 41)—that is, establishing in the neonatal period an effective mixed circulation in which pulmonary (Qp) and systemic (Qs) blood flow are well balanced, followed by one or more operations performed later in infancy or early childhood after Rp has dropped to normal postnatal levels. The purpose of subsequent operations performed outside the neonatal period is to move away from the inefficiency of the completely mixed circulatory state. It should be emphasized that all definitive repairs in hypoplastic left heart physiology are palliative.

The exact form of definitive repair may vary from patient to patient based on the individual’s physiologic status. Given the inherently limited reserve of the single right ventricle, it is generally agreed that a completely mixed circulatory state, even one that provides ideal balance between Qp and Qs, is not an acceptable definitive state for hypoplastic left heart physiology. Acceptable definitive repairs include the completed Fontan procedure, the Fontan procedure with fenestration, superior cavopulmonary anastomosis, and superior cavopulmonary anastomosis with additional limited systemic to pulmonary blood flow.

Regardless of the definitive repair, principles of initial surgical management are generally agreed upon. Some variation of the Norwood procedure is considered optimal initial therapy. Its purpose is to provide (1) a completely unobstructed systemic arterial pathway from the right ventricle to all organs, (2) a restrictive connection between the systemic and pulmonary circulations such that Qp and Qs are adequately balanced, and (3) unobstructed flow of pulmonary venous return across the atrial septum to the right atrium.

**Preoperative Management**

Perinatal preoperative management is critical to successful outcome. This may include prenatal transport of the mother and fetus to a cardiac center following fetal diagnosis.\(^25,33\) Circulatory collapse is usually the result of closure of the ductus arteriosus in the setting of undiagnosed hypoplastic left heart physiology. This may occur when the infant is still in hospital following birth, or after discharge home. If prenatal diagnosis is made and mother and fetus are transferred to an appropriate facility where the infant will undergo surgery, circulatory collapse is all but eliminated.
Low- to moderate-dose dopamine and dobutamine should increase systemic vascular resistance, which profoundly increase systemic vascular resistance and may unpredictably alter systemic circulation. PGE\(_1\) achieves moderate elevation of Pa\(_o\_2\) and Qp/Qs includes a Pa\(_o\_2\) of about 40 mmHg (Torr) and a systemic diastolic blood pressure greater than 30 mmHg. Even these ideal values do not guarantee that the expected blood flow values in fact do exist. For example, Pa\(_o\_2\) can be influenced by other factors: hemoglobin level, metabolic state, temperature, and presence of sepsis to name a few. Furthermore, the inevitable reduction in Rp that occurs over time commonly thwarts all efforts to maintain systemic output and balanced Qp and Qs. If this occurs, operation should be scheduled immediately.

For the typical neonate diagnosed early after birth and in whom circulatory collapse has not occurred, the ideal time for surgical intervention is about 2 to 5 days. In this window of time, the infant completes the profound physiologic changes from fetal life to independent life, yet consequences of a continuously increasing Qp have not yet taken their toll. If circulatory collapse does occur and end-organ damage results, a longer time before operation is often necessary to allow end-organ recovery. Although not always advisable, ideally, normal function of renal, hepatic, neurologic, gastrointestinal, and cardiopulmonary systems should be documented following resuscitation prior to proceeding with operation. It is not uncommon for organ systems to recover fairly rapidly but then plateau short of complete recovery. Further delay of operation at that point is usually detrimental.

Although mild obstruction of flow across the atrial septum is typical at the time of Doppler color flow interroga- tion during diagnostic echocardiography, severe obstruction at the atrial septum may occur, resulting in a clinical presentation similar to that found with obstructive total anomalous pulmonary venous connection (see Chapter 31), with deep cyanosis, pulmonary edema, and eventual hemodynamic instability. This presentation evolves rapidly immediately after birth and must be addressed within hours. Such patients are best managed with percutaneous interventional techniques to create an adequate atrial septal opening, followed by several days of stabilization before proceeding with operation. Management as described earlier continues during transport to the operating room and during surgery until CPB is instituted. The operation can be performed using continuous CPB by way of antegrade cerebral perfusion or using hypothermic circulatory arrest, according to choice of the operating surgeon. Both techniques are described in text that follows.

Neurologic development following operations for hypoplastic left heart physiology is below normal. Although impaired neurologic development is multifactorial, there is little question that circulatory arrest is contributory. Antegrade cerebral perfusion provides the advantage of continuous blood flow and oxygenation to the brain; however, it is possible that this technique also introduces new risks. It is unlikely that techniques of reconstruction that avoid circulatory arrest will result in dramatic changes in short-term

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**Figure 49-7** Survival of neonates with optimal medical treatment. Format of figure is as in Fig. 49-6. Although estimates represent survival before transplantation, similar survival is achieved with optimal medical treatment prior to reconstruction. (Modified from Jacobs and colleagues.)

After diagnosis, the infant is resuscitated, and prostaglandin E\(_1\) (PGE\(_1\)) therapy is initiated. Depending on details of the physiologic status of the infant and stability of the infant at initial diagnosis, subsequent preoperative management may vary from essentially no further intervention on the one hand, to maximal intervention on the other. The typical patient, however, shows signs of pulmonary overcirculation, and preoperative management is aimed at reversing or at least controlling this to preserve end-organ and myocardial function.

Supportive therapy in the perinatal and neonatal periods can substantially alter natural history. Judicious use of inotropic support, PGE\(_1\) therapy, nutritional supplementation, and ventilation with 17% or 19% oxygen along with supplemental CO\(_2\) administration may delay the typical physiologic decompensation for a number of weeks (Fig. 49-7). When indicated, mechanical ventilation can add an extra measure of support. In many cases, the respiratory depression side effect of PGE\(_1\) therapy may warrant mechanical ventilation.

These maneuvers are aimed at achieving a balance of Qp and Qs and maintaining unobstructed and adequate systemic perfusion. Because flow into the pulmonary circuit is unobstructed, Rp at the microvascular level will determine Qp. Any maneuver that causes dilatation of the pulmonary microvasculature will result in excessive Qp. Specifically, avoiding supplemental inspired oxygen is critical to the overall strategy; 21% oxygen or even lower Fi\(_o\_2\) helps maintain tone in the pulmonary microvasculature. If this maneuver is not adequate, controlled ventilation through an endotracheal tube achieves moderate elevation of PaCO\(_2\), causing acidosis, which further constricts pulmonary microvasculature. PGE\(_1\) maintains ductal patency, ensuring unobstructed blood flow to the systemic circulation.

Inotropic agents can be used to enhance cardiac output in the setting of moderate pulmonary overcirculation, but this strategy must be undertaken cautiously because these agents also affect systemic and pulmonary vascular resistances and may unpredictably alter Qp/Qs. Epinephrine and high-dose dopamine, which profoundly increase systemic vascular resistance, should be avoided (see Section IV of Chapter 4). Low- to moderate-dose dopamine and dobutamine should be considered the first-line inotropic agents when supplemen- tal cardiac output is considered necessary.

All these maneuvers are used to create optimal preoperative cardiopulmonary status. Assessing cardiopulmonary status is somewhat indirect. Currently, Qp and Qs cannot be easily directly measured in the cardiac intensive care unit (ICU). Indirect measures of adequate systemic output include normal peripheral perfusion, adequate urine output, and absence of metabolic acidosis. Evidence of a reasonable balance of Qp and Qs includes a Pa\(_o\_2\) of about 40 mmHg (Torr) and a systemic diastolic blood pressure greater than 30 mmHg. Even these ideal values do not guarantee that the expected blood flow values in fact do exist. For example, Pa\(_o\_2\) can be influenced by other factors: hemoglobin level, metabolic state, temperature, and presence of sepsis to name a few. Furthermore, the inevitable reduction in Rp that occurs over time commonly thwarts all efforts to maintain systemic output and balanced Qp and Qs. If this occurs, operation should be scheduled immediately.

For the typical neonate diagnosed early after birth and in whom circulatory collapse has not occurred, the ideal time for surgical intervention is about 2 to 5 days. In this window of time, the infant completes the profound physiologic changes from fetal life to independent life, yet consequences of a continuously increasing Qp have not yet taken their toll. If circulatory collapse does occur and end-organ damage results, a longer time before operation is often necessary to allow end-organ recovery. Although not always advisable, ideally, normal function of renal, hepatic, neurologic, gastrointestinal, and cardiopulmonary systems should be documented following resuscitation prior to proceeding with operation. It is not uncommon for organ systems to recover fairly rapidly but then plateau short of complete recovery. Further delay of operation at that point is usually detrimental.

Although mild obstruction of flow across the atrial septum is typical at the time of Doppler color flow interroga- tion during diagnostic echocardiography, severe obstruction at the atrial septum may occur, resulting in a clinical presentation similar to that found with obstructive total anomalous pulmonary venous connection (see Chapter 31), with deep cyanosis, pulmonary edema, and eventual hemodynamic instability. This presentation evolves rapidly immediately after birth and must be addressed within hours. Such patients are best managed with percutaneous interventional techniques to create an adequate atrial septal opening, followed by several days of stabilization before proceeding with operation. Management as described earlier continues during transport to the operating room and during surgery until CPB is instituted. The operation can be performed using continuous CPB by way of antegrade cerebral perfusion or using hypothermic circulatory arrest, according to choice of the operating surgeon. Both techniques are described in text that follows.

Neurologic development following operations for hypoplastic left heart physiology is below normal. Although impaired neurologic development is multifactorial, there is little question that circulatory arrest is contributory. Antegrade cerebral perfusion provides the advantage of continuous blood flow and oxygenation to the brain; however, it is possible that this technique also introduces new risks. It is unlikely that techniques of reconstruction that avoid circulatory arrest will result in dramatic changes in short-term
survival, because factors related to hypothermia, CPB itself, and myocardial ischemia are not avoided. Long-term benefits related to neurologic development may exist but are yet to be proven.

Norwood Procedure Using Continuous Perfusion
Although several techniques for accomplishing the Norwood procedure using continuous perfusion have been described, the one presented has been used routinely since 1997 by one of the authors (FLH), with some modifications.

After median sternotomy, the thymus is subtotaly removed and the anterior pericardium opened widely. Aortic arch vessels are dissected well above the brachiocephalic vein. The small aorta is separated from the pulmonary trunk and right pulmonary artery, and the ductus arteriosus, aortic arch, and proximal descending thoracic aorta are dissected.

Marking 7-0 monofilament sutures are placed on adjacent portions of the pulmonary trunk and ascending aorta to indicate the point of eventual pulmonary trunk–to-aorta anastomosis. Positions of these marking sutures are chosen with great care because they will determine the correct orientation of, and incisions in, the aorta and pulmonary trunk necessary to create a functional anastomosis; alignment of this anastomosis is critical for unobstructed coronary blood flow in aortic atresia. The first marking suture is placed in the adventitia of the pulmonary trunk 1 to 2 mm above the sinotubular junction and circumferentially exactly where the small ascending aorta lies against it. The second suture on the aortic adventitia is placed so that its position coincides exactly with the pulmonary trunk suture.

A purse-string suture is placed on the brachiocephalic artery about 5 mm distal to the takeoff of the artery from the arch. It is often necessary to place it above the brachiocephalic vein. Purse-string sutures are placed on the superior and inferior venae cavae. A 5-0 monofilament suture is placed around the pulmonary artery end of the ductus arteriosus.

An 8F (or in patients weighing <3 kg, 6F) arterial cannula is inserted into the brachiocephalic artery, and angled 12F venous cannulae are placed into the venae cavae. Alternatively, a single venous cannula can be used, placed in the right atrial appendage (Fig. 49-8, A). Brachiocephalic artery cannulation must be performed accurately; however, experience shows that it can be routinely performed successfully even in patients weighing 3.0 kg or less. Cannulation is best performed by puncturing the artery without using a clamp, and inserting the tip of the cannula to a depth less than the width of the artery, typically 2 to 3 mm.

After venous cannulation and institution of CPB, the ductus arteriosus is immediately ligated (see Fig. 49-8, A). Core temperature is reduced to 20°C. During cooling, the pulmonary trunk is transected just above the pulmonary valve in standard fashion (Fig. 49-8, B). The distal opening in the pulmonary trunk is then closed directly or patched with an oval piece of pulmonary allograft or other material (see Fig. 49-8, B). A clamp is placed across the ascending aorta just proximal to the brachiocephalic artery once the target core temperature has been achieved. Cardioplegia is introduced into the ascending aorta. The ascending aorta is then opened to the level of the transected pulmonary trunk, and the side-to-side anastomosis between proximal pulmonary trunk and ascending aorta is accomplished with interrupted 6-0 or 7-0 monofilament sutures (Fig. 49-8, C).

In preparation for arch reconstruction, direct CPB flow is isolated to the brachiocephalic artery only. This is accomplished by clamping the base of the brachiocephalic, left carotid, and left subclavian arteries individually with delicate neurovascular clips, and placing a C-shaped clamp across the descending thoracic aorta approximately 1.5 to 2 cm below the ductal insertion (Fig. 49-8, D). Perfusion, now through the distal brachiocephalic artery only, is reduced to 30 to 40 mL · kg⁻¹ · min⁻¹, allowing normal brain perfusion.

The original clamp placed across the ascending aorta is removed. The ductus is divided distal to the previously placed suture. The previous incision in the ascending aorta is then continued around the arch, then beyond the ductus, approximately 1.5 cm onto the descending aorta. Ductal tissue is trimmed, and allograft patch reconstruction of the aortic arch, ascending aorta, and pulmonary trunk is performed. The caval cannulae are snared. A right atriotomy is made, and the septum primum is completely removed to create a nonrestrictive interatrial communication. The right atriotomy is closed, and the neurovascular clips on the base of the brachiocephalic artery and the C-clamp on the descending aorta are removed. Total body perfusion is reestablished and increased to normal levels; rewarming is begun.

The last step in the operation is creating a source of pulmonary blood flow. At the choice of the operating surgeon, this can be achieved using either a restrictive systemic arterial–to-pulmonary arterial shunt or a restrictive right ventricular–to-pulmonary arterial conduit. If a shunt is chosen, typically a polytetrafluoroethylene (PTFE) interposition graft is sewn into place from the junction of the brachiocephalic and right subclavian arteries to the proximal portion of the right pulmonary artery (Fig. 49-8, E). Both anastomoses are performed using end graft–to-side artery connections with running 7-0 monofilament or PTFE suture. Variation in positioning the PTFE shunt must be considered based on individual patient characteristics to achieve an appropriate balance of Qp and Qs.

In patients weighing less than 3 kg and in those demonstrating very low Rp preoperatively, it may be necessary to perform the systemic connection of the shunt anastomosis at a more distal site on the right subclavian artery. In most cases, a 3.5-mm-diameter PTFE tube graft is used for the shunt procedure; rarely is a larger diameter necessary. Often in patients weighing less than 3 kg, and most frequently in patients weighing less than 2.5 kg, a 3.0-mm-diameter graft should be considered, although risk of shunt thrombosis may increase with a small-diameter shunt. If the right ventricular–to-pulmonary arterial conduit is performed, a PTFE graft of appropriate diameter is chosen. Alternatively, a composite graft consisting of a proximally positioned PTFE tube and a distally positioned small (6- to 7-mm-diameter) allograft pulmonary or aortic valve can be used (Fig. 49-8, F and G). Regardless of whether a simple conduit or composite conduit is chosen, the diameter of the PTFE tube determines the resistance to flow into the pulmonary arteries. Typically, a 4-mm-diameter graft is used for patients weighing less than 3 kg, a 5-mm-diameter graft for those between 3 and 4 kg, and a 6-mm-diameter graft for those greater than 4 kg.

An incision is made in the infundibular portion of the right ventricle, just below the pulmonary valve. A 5- to 6-mm-diameter circular full-thickness resection of infundibular muscle is then made. It is extremely important that...
the caliber of the resulting hole in the infundibulum is maintained transmurally to prevent premature stenosis at this level postoperatively. Using a running 7-0 monofilament suture, the graft is first sewn end to side to the pulmonary trunk, either to the pulmonary artery directly adjacent to the suture line that previously closed the distal pulmonary trunk, or to the center of the patch that was used to close the distal pulmonary trunk. The graft is then positioned to the left of the reconstructed aorta and tailored in length to reach the infundibulotomy. The proximal end of the graft is carefully beveled to the appropriate angle to ensure a smooth course around the large reconstructed aorta. The anastomosis is performed using a running 6-0 monofilament suture.

Once normothermia is achieved, the patient is separated from CPB and decannulated. Management following separation from CPB is described under “Post–Cardiopulmonary Bypass Management” later in this chapter.

**Norwood Procedure Using Hypothermic Circulatory Arrest**

The heart is exposed by median sternotomy, removal of most of the thymus gland, and opening of the pericardium. If the patient is unstable at this point because of increased $Q_p$, the right pulmonary artery can be exposed immediately and clamped to reduce overall $Q_p$ and maintain systemic circulation until CPB is established.
The patient is prepared for CPB by placing a purse-string suture on the pulmonary trunk just distal to the pulmonary valve. A second purse-string suture is placed around the tip of the right atrial appendage. At that point, if the patient is physiologically stable, the pulmonary trunk is separated from the ascending aorta using either scissors or electrocautery. The ductus arteriosus, aortic arch, and arch vessels are then mobilized using scissors or electrocautery all the way to the first set of intercostal vessels on the descending aorta. Temporary snares are placed around all brachiocephalic arteries.

If the patient becomes physiologically unstable, CPB can be initiated at any time and the great vessel dissection performed with its support. CPB is established using an arterial cannula in the pulmonary trunk and a single venous cannula in the right atrial appendage (Fig. 49-9, A). At initiation of CPB, the branch pulmonary arteries are temporarily occluded with clamps or snares to eliminate pulmonary blood flow.

After initiating CPB, while the pulmonary trunk and aorta are still distended with blood, 7-0 monofilament sutures are placed on adjacent portions of the pulmonary trunk and ascending aorta to mark the point of eventual pulmonary trunk-to-aorta anastomosis. Positions of these marking sutures are chosen with great care because they will determine
completed aortic arch reconstruction. To complete the procedure using a right ventricle to pulmonary artery conduit, an appropriately sized tube of PTFE, or, as shown, composite of PTFE and valved allograft, is used. Prior to placing the conduit, the composite graft is constructed during the initial cooling phase of cardiopulmonary bypass. An aortic or pulmonary allograft valved conduit, either 6- or 7-mm diameter (or a 9- or 10-mm diameter allograft reduced to a bicuspid conduit) is connected end to end to a 3-cm length of PTFE graft. Valved conduit is placed distally within the composite, as shown. A 5- to 6-mm diameter core of infundibular free-wall myocardium is removed from right ventricle just below pulmonary valve. It is critical to remove a uniform full-thickness core of tissue rather than just incise the hypertrophied right ventricle; this prevents stenosis at the inlet to the conduit. Great care should be taken not to injure pulmonary valve or chordae of tricuspid valve (infundibular incision and tissue core removal can, if preferred, be performed before reperfusion of myocardium is initiated; this may provide more controlled conditions). Distal aspect of allograft conduit is connected end to side into transverse pulmonary artery centrally, either near the suture line that closed the distal pulmonary artery stoma created by previous pulmonary trunk transection, or into the patch used to close distal pulmonary artery stoma. This is accomplished with a running suture technique using 7-0 nonabsorbable monofilament suture. Pulmonary arteries are allowed to assume their natural position, and the PTFE proximal portion of the composite is tailored to appropriate length and beveled in preparation for proximal anastomosis of PTFE component to infundibulotomy site. 

**Figure 49-8, cont’d**  
**F.** Completed aortic arch reconstruction. To complete the procedure using a right ventricle to pulmonary artery conduit, an appropriately sized tube of PTFE, or, as shown, composite of PTFE and valved allograft, is used. Prior to placing the conduit, the composite graft is constructed during the initial cooling phase of cardiopulmonary bypass. An aortic or pulmonary allograft valved conduit, either 6- or 7-mm diameter (or a 9- or 10-mm diameter allograft reduced to a bicuspid conduit) is connected end to end to a 3-cm length of PTFE graft. Valved conduit is placed distally within the composite, as shown. A 5- to 6-mm diameter core of infundibular free-wall myocardium is removed from right ventricle just below pulmonary valve. It is critical to remove a uniform full-thickness core of tissue rather than just incise the hypertrophied right ventricle; this prevents stenosis at the inlet to the conduit. Great care should be taken not to injure pulmonary valve or chordae of tricuspid valve (infundibular incision and tissue core removal can, if preferred, be performed before reperfusion of myocardium is initiated; this may provide more controlled conditions). Distal aspect of allograft conduit is connected end to side into transverse pulmonary artery centrally, either near the suture line that closed the distal pulmonary artery stoma created by previous pulmonary trunk transection, or into the patch used to close distal pulmonary artery stoma. This is accomplished with a running suture technique using 7-0 nonabsorbable monofilament suture. Pulmonary arteries are allowed to assume their natural position, and the PTFE proximal portion of the composite is tailored to appropriate length and beveled in preparation for proximal anastomosis of PTFE component to infundibulotomy site. 

**G.** Proximal anastomosis of conduit to infundibulotomy is performed with a running stitch using 6-0 nonabsorbable monofilament suture.

the correct orientation of, and incisions in, the aorta and pulmonary trunk necessary for creating a functional anastomosis; alignment of this anastomosis is critical for unobstructed coronary blood flow in aortic atresia. The first marking suture is placed in the adventitia of the pulmonary trunk 1 to 2 mm above the sinutubular junction and circumferentially exactly where the small ascending aorta lies against it. The second suture on the aortic adventitia is placed so that its position coincides exactly with the pulmonary trunk suture (see Fig. 49-9, A).

When the nasopharyngeal or tympanic membrane temperature reaches 16°C to 18°C after cooling with CPB for an appropriate period (see Section IV of Chapter 2), the snares around the brachiocephalic vessels are tightened and circulatory arrest established. Snares around the left and right pulmonary arteries are removed, and cannulae are removed from the pulmonary trunk and right atrial appendage after draining as much blood volume from the patient into the pump-oxygenator as possible.

Management of myocardial protection is variable. Some experienced centers use no specific cardioplegia and rely on profound hypothermia as the only form of myocardial management. Other experienced institutions use cardioplegia, which can be supplied in several ways. Cannulation of the ascending aorta can be achieved with an appropriately small needle and cardioplegia delivered directly into the aortic
Figure 49-9  Norwood procedure using hypothermic circulatory arrest. **A,** Arterial cannula is placed into pulmonary trunk through a purse-string suture, and the single venous cannula is placed into right atrial appendage. Dashed line on proximal pulmonary trunk shows intended transection site, and dashed line on ascending aorta and aortic arch shows site and extent of intended aortic incision. Marking sutures are placed on pulmonary trunk and ascending aorta precisely where the two dashed lines in this figure converge. After these two marking sutures are placed, aorta and pulmonary trunk should be allowed to assume their natural positions. Under these conditions, examining the two marking sutures with the vessels in their distended state should reveal that these two sutures are touching each other, without even the slightest amount of circumferential or longitudinal offset. As soon as cardiopulmonary bypass (CPB) is instituted, left and right pulmonary arteries must be controlled with either snares or small vascular clamps (not shown in this figure). **B,** After target core temperature is reached, circulatory arrest is instituted and myocardial protection addressed; ductus arteriosus is ligated and transected as shown. It is common practice to temporarily occlude brachiocephalic, left carotid, and left subclavian arteries with snares or small vascular clamps before opening the aorta. Either at this point or following arch reconstruction, atrial septum must be resected. A limited right atriotomy is made and the septum primum identified and resected with scissors. Septum primum should be resected completely, but care taken not to overextend the resection into thickened portion of limbus or conduction area. Right atriotomy is then closed with a running monofilament suture. Dashed lines signify point of pulmonary trunk transection and extent of ascending arch and descending aortic incision. Note that the descending aortic incision extends approximately 5 to 10 mm beyond the ductal insertion site. **C,** Pulmonary trunk has been transected. There is often very little distance between top of pulmonary valve commissures and origin of right pulmonary artery. During pulmonary trunk transection, care should be taken not to injure the commissure of the pulmonary valve or extend incision into orifice of right pulmonary artery. Once transection is completed, the stoma in the distal pulmonary trunk is closed transversely as shown with a running 7-0 absorbable monofilament suture. Incision in aorta is also shown. Proximal extent of this incision is terminated precisely at previously placed marking suture. **D,** Before beginning arch augmentation, allograft patch is tailored to the size of the infant. Patch is roughly triangular in shape; base of triangle will ultimately be sutured to circumference of proximal pulmonary trunk, so width of base should roughly equal circumference of pulmonary trunk. Other two free edges of patch will be anastomosed to posterior and anterior free edges of incised aorta. The edge of the patch that will be sutured to posterior aspect of incised aorta should be shorter than edge that will be sutured to anterior free edge of aorta. If this is not the case, or if entire patch is too long, kinking of reconstruction can result. Also, apical half of the triangularly shaped patch should not be too broad. Patch is sewn into place beginning at most distal aspect of aortic incision, well beyond ductal insertion site. A running 7-0 monofilament nonabsorbable suture is used and posterior suture line is developed first, extending roughly to area opposite brachiocephalic artery origin. Following this, anterior suture line is developed in like fashion.
Continued

Figure 49-9, cont’d  E, Distal aspect of patch suture line is completed. Attention is then turned to proximal aspect of aortic incision and to proximal pulmonary trunk. Interrupted 7-0 monofilament nonabsorbable sutures are placed to connect proximal ascending aorta to proximal pulmonary trunk. First suture in this series of five to seven interrupted sutures should be placed precisely at the points of the two previously placed marking sutures. Once this is completed, proximal end of patch is connected to circumference of proximal pulmonary trunk. Prior to final sutures being placed, a probe that can comfortably pass into proximal aorta to the level of coronary arteries is used to confirm patency and appropriate alignment of proximal aorta. F, Completed aortic arch reconstruction. To complete procedure using a systemic-to-pulmonary shunt, an appropriately sized tube of expanded polytetrafluoroethylene (PTFE) is chosen and connected from systemic circulation into pulmonary circulation. If shunt is placed during circulatory arrest, vascular clamps generally are not necessary. However, if shunt is placed after reestablishing CPB, brachiocephalic artery and its branches and right pulmonary artery must be controlled with side-biting vascular clamps.

The ductus is transected just beyond the previously placed ligature. Redundant ductal tissue is cut away from the distal aorta, leaving a small cuff of ductal tissue at the level of the aortic isthmus. A 5- to 10-mm incision is made from the ductal orifice into the descending aorta to the level of the first set of intercostal vessels (see Fig. 49-9, C). A proximal incision is made beginning at the ductal orifice and moving retrograde toward the aortic valve. This incision proceeds along the undersurface of the aortic arch and extends down the hypoplastic ascending aorta to within several millimeters of the atretic or hypoplastic aortic valve, terminating at the same level as the transected pulmonary trunk at the point of the previously placed marking suture (see Fig. 49-9, C).

The aorta is then augmented throughout its length from the level of the aortic valve around the arch, to the first set of intercostal vessels, using a patch of pulmonary or aortic allograft tissue (Fig. 49-9, D). The patch is tailored to provide adequate but not excessive widening of the aorta. Suturing is begun at the distal end of the incision beyond the isthmus on the upper descending aorta and progresses retrograde until the proximity of the brachiocephalic artery is reached.

root. Alternatively, the cardioplegia system can be connected to the arterial cannula in the pulmonary trunk, and cardioplegia delivered into this cannula after circulatory arrest has been established while the brachiocephalic vessel snare is still in place. The only additional maneuver before proceeding with cardioplegia delivery using this method is to clamp the descending aorta distal to the ductal insertion site. The cardioplegic solution is delivered through the arterial cannula into the pulmonary trunk through the ductus and retrograde around the arch to the coronary arteries. All other peripheral runoff through this circuit must be reliably eliminated (see “Methods of Myocardial Management during Cardiac Surgery” in Chapter 3).

After myocardial protection has been addressed and circulatory arrest established, the ductus arteriosus is ligated distal to the origin of the left pulmonary artery. A small atriotomy is made, and through it the entire septum primum is removed to create an unrestrictive intraatrial communication. To avoid conduction problems, care is taken not to extend the resection beyond the septum primum. The atriotomy is closed (Fig. 49-9, B).

The pulmonary trunk is divided transversely as proximal as possible without risking damage to the pulmonary valve, leaving the previously placed marking suture proximal to the transection. As the transection is made, particular care is taken to avoid the orifice of the right pulmonary artery. The distal end of the divided pulmonary trunk is then closed with a patch (typically autologous pericardium or pulmonary artery allograft) using continuous 7-0 polypropylene. Alternatively, the distal pulmonary trunk may be closed primarily in transverse fashion (Fig. 49-9, C). Direct closure has the advantages of time efficiency and less bulk, and in experienced hands has shown no greater tendency to result in pulmonary trunk stenosis than the patch technique.
Figure 49-9, cont’d  

G, Completed aortic arch reconstruction. To complete procedure using a right ventricular–to–pulmonary artery conduit, an appropriately sized PTFE tube or, as shown, composite of PTFE and valved allograft is used. Before placing conduit, composite graft is constructed during initial cooling phase of CPB. An aortic or pulmonary allograft valved conduit, either 6- or 7-mm diameter (or a 9- or 10-mm-diameter allograft reduced to a bicuspid conduit) is connected end to end to a 3-cm length of PTFE graft. Valved conduit is placed distally within the composite, as shown. Next part of procedure can be performed either under circulatory arrest or after perfusion has been reestablished. A 5- to 6-mm-diameter core of infundibular free-wall myocardium is removed from right ventricle just below pulmonary valve. To prevent stenosis at the inlet to the conduit, it is critical to actually remove a uniform full-thickness core of tissue rather than just incise the hypertrophied right ventricle. Great care should be taken not to injure pulmonary valve or tricuspid valve chordae. Distal aspect of allograft conduit is connected end to side into transverse pulmonary artery centrally, either near suture line that closed the distal pulmonary artery stoma created by previous pulmonary trunk transaction, or into the patch used to close distal pulmonary artery stoma. This is accomplished with a running suture technique using 7-0 nonabsorbable monofilament suture. Pulmonary arteries are allowed to assume their natural position, and PTFE proximal portion of composite is tailored to appropriate length and beveled in preparation for proximal anastomosis of PTFE component to right ventriculotomy site. 

H, Proximal anastomosis of conduit to infundibulotomy is performed with a running stitch using 6-0 nonabsorbable monofilament suture.

The posterior suture line is developed first, using a running technique and 6-0 or 7-0 nonabsorbable monofilament suture, followed by the anterior suture line.

At this point, the allograft augmentation of the arch is temporarily set aside, and the proximal end of the divided pulmonary trunk is anastomosed side to side to the incised hypoplastic aorta (Fig. 49-9, E). This portion of the anastomosis is typically performed with five to seven interrupted 6-0 or 7-0 monofilament nonabsorbable sutures. The first of these connects the end of the aortic incision to the cut edge of the pulmonary trunk exactly where the previously placed marking suture was positioned. On each side of this interrupted suture, two to three other interrupted sutures are placed, attaching first the posterior and then the anterior edge of the longitudinally incised aorta to the circumference of the proximal pulmonary trunk. Care should be taken with small aortas (<3 mm diameter) not to connect them to too broad a segment of pulmonary trunk circumference, because this can stretch the aortic tissue and flatten and obstruct the orifice leading to the coronaries.
Finally, the allograft patch suture line progresses from the level of the brachiocephalic artery down to the aortic-to-pulmonary anastomosis and around the remaining free edge of the proximal portion of the right pulmonary artery (see Fig. 49-9, F). This completes the right ventricular-to-systemic arterial outflow reconstruction.

The last step in the operation is creating a source of pulmonary blood flow. At the choice of the operating surgeon, this can be achieved using either a restrictive systemic arterial–to–pulmonary arterial shunt or a restrictive right ventricle–to–pulmonary arterial conduit. If a shunt is chosen, typically a PTFE interposition graft is sewn into place from the junction of the brachiocephalic and right subclavian arteries on the systemic side to the proximal portion of the right pulmonary artery (see Fig. 49-9, F). Both anastomoses are performed using end graft–to–side artery connections with running 7-0 monofilament or PTFE suture. Variation in positioning of the PTFE shunt must be considered, based on individual patient characteristics, to achieve an appropriate balance of $Q_p$ and $Q_s$.

In patients weighing less than 3 kg and in those demonstrating very low Rp preoperatively, it may be necessary to perform the systemic pulmonary arterial shunt anastomosis at a more distal site on the right subclavian artery. In most cases, a 3.5-mm-diameter PTFE tube graft is used for the shunt procedure; a larger diameter is rarely necessary. Often in patients weighing less than 2.5 kg, a 3.0-mm-diameter graft should be considered, although risk of shunt thrombosis may increase with a smaller-diameter shunt. If circulatory arrest is prolonged, or by surgeon preference, the shunt may be placed after reestablishing flow on CPB.

If a right ventricular–to–pulmonary arterial conduit is chosen, a PTFE graft of appropriate diameter is selected. Alternatively, a composite graft consisting of a proximally positioned PTFE tube and a distally positioned small (6- to 7-mm diameter) allograft pulmonary or aortic valve can be used (Fig. 49-9, G and H). Regardless of whether a simple conduit or composite conduit is chosen, the diameter of the PTFE tube determines the resistance to flow into the pulmonary arteries. Typically, a 4-mm-diameter graft is used for patients weighing less than 3 kg, a 5-mm-diameter graft for those between 3 and 4 kg, and a 6-mm-diameter graft for those greater than 4 kg.

An incision is made in the infundibular portion of the right ventricle, just below the pulmonary valve. A 5- to 6-mm-diameter circular full-thickness resection of infundibular muscle is then made. It is extremely important that the caliber of the resulting hole in the infundibulum is maintained transmurally to prevent premature stenosis at this level postoperatively. Using a running 7-0 monofilament suture, the graft is first sewn end to side to the pulmonary trunk, either to the pulmonary artery directly, adjacent to the suture line that previously closed the distal pulmonary trunk, or to the center of the patch that was used to close the distal pulmonary trunk. The graft is then positioned to the left of the reconstructed aorta and tailored in length to reach the infundibulotomy. The proximal end of the graft is carefully beveled to the appropriate angle to ensure a smooth course around the large reconstructed aorta.

The anastomosis is performed using a running 6-0 monofilament suture. The right atrial and systemic arterial cannulae are reinserted, CPB is reestablished, and rewarming begun. If a systemic-to-pulmonary shunt has been placed, it is occluded with a vascular clamp during the rewarming phase of CPB. When the patient’s tympanic membrane or nasopharyngeal temperature reaches 25°C to 30°C, perfusate ionized calcium concentration is measured and calcium chloride added to bring the ionized calcium concentration to a normal level (see Section III of Chapter 2). Separation from CPB is accomplished and decannulation achieved. Details of post-CPB management follow.

**Post–Cardiopulmonary Bypass Management**

Whether the operation is performed using continuous perfusion or circulatory arrest, post-CPB management is generally the same. Before the patient is separated from CPB, inotropic support is initiated, and particular attention is given to complete reexpansion of both lungs. Endotracheal suctioning by the anesthesiologist is routine. If a systemic-to-pulmonary shunt was used, after complete rewarming has been achieved, approximately 5 minutes before discontinuing CPB, the clamp on the shunt is removed.

Careful attention is given to the mean arterial pressure on CPB at this point; typically a decrease of 10 to 15 mmHg should be expected, indicating adequate runoff into the pulmonary vascular bed. If this decrease is not observed, the cause must be identified. The systemic-to–pulmonary trunk shunt should be immediately assessed for obstruction due to a technical problem. If a right ventricle–to–pulmonary arterial conduit was used, diastolic blood pressure is not affected.

After rewarming has been completed, CPB is discontinued and the aortic and venous cannulae removed. Postoperative care begins immediately (see Special Features of Postoperative Care later in this chapter). Two separate polyvinyl catheters (or a single double-lumen catheter) are placed directly into the right atrial appendage and brought out through the chest wall to continuously monitor atrial pressure and provide reliable access for delivering blood products and pharmacologic support. Arrial and ventricular temporary epicardial pacing wires are placed. Chest drainage tubes are placed appropriately for neonates undergoing CPB (see “Completing Operation” in Section III of Chapter 2).

It may be beneficial to leave the sternum and soft tissue temporarily unapproximated during the early recovery period. This allows for maximal cardiopulmonary function during the first 24 to 48 hours postoperatively and easy accessibility to the mediastinum if aggressive resuscitative measures are necessary. When this “open chest” option is exercised, the skin is sealed with an oval silicone rubber sheet or some other appropriate material. After the patient’s cardiopulmonary status has stabilized (48 to 96 hours postoperatively), the sheet is removed under sterile conditions, and the sternum and soft tissues closed in standard fashion. This can be accomplished routinely and effectively in the ICU without returning the patient to the operating room. At some institutions, the “open sternum” option is standard following first-stage reconstruction for hypoplastic left heart physiology.

**Technical Modifications of the Norwood Procedure**

A number of modifications of the standard ascending aorta and arch reconstruction described in the preceding text have been developed. However, the physiologic principles of providing unobstructed ventricular-to-systemic arterial output and appropriately balanced $Q_p$ and $Q_s$ remain the same. Several groups have introduced techniques of reconstructing
the ventricular-to-systemic arterial outflow without use of patch material.\textsuperscript{10,12} Much experience has been obtained, and perioperative outcome and some midterm outcome data are available using these alternative techniques. Theoretical advantages include avoiding foreign patch material and the possibility of a modest reduction in circulatory arrest time. Disadvantages include potential problems with suture line tension, left pulmonary artery and left bronchus compression, and increased resistance to flow to the coronary system.

Currently, there is no clear evidence that these alternative techniques are better or worse than the more standard arch reconstruction technique. Other modifications in the surgical treatment of neonates with hypoplastic left heart physiology have been reported.\textsuperscript{58,74} The right ventricle-to-pulmonary artery conduit, if used, can be placed to the right side of the reconstructed ascending aorta rather than to the left side as described. This is believed by some to have advantages.\textsuperscript{89}

Hybrid Procedure

Some surgeons prefer the hybrid procedure to the Norwood procedure or one of its variants as a primary procedure in high-risk patients (i.e., those with prematurity, low birth weight, associated genetic or other noncardiac comorbid conditions, extreme shock, or various real or perceived cardiac risk factors, such as severe tricuspid regurgitation, depressed right ventricular function, intact or highly restrictive atrial septum, aortic atresia with mitral stenosis, and very small-diameter ascending aorta). The procedure is ideally performed in a hybrid operating suite, essentially a cardiac catheterization laboratory that also has the dimensions and capability to support major surgery and use of CPB.

Preoperative management is the same as for a patient undergoing a Norwood procedure. The patient is anesthetized, prepped, and draped in the supine position, just as in a formal operating room. CPB support is available. Pulmonary artery branch bands are prepared from segments of PTFE tube grafts. For patients weighing 3 kg or more, 3-mm-diameter grafts are selected. For patients weighing less than 3 kg, 2.5-mm grafts are chosen. The bands are cut to a width of approximately 2 mm.

A median sternotomy incision is made, the pericardium opened, and the branch pulmonary arteries exposed. If the patient is unstable because of pulmonary overcirculation, the right branch pulmonary artery can be temporarily occluded with a delicate neurovascular clip. Care must be taken not to distort the small ascending aorta, particularly if aortic atresia is present. The right and left branch pulmonary arteries are sequentially exposed and banded (Fig. 49-10, A). The bands are performed before the ducal stent is placed to prevent migration of the stent during manipulation of the pulmonary artery branches. Position of the bands is confirmed by angiography (Fig. 49-10, B). A purse-string suture is placed on the pulmonary trunk immediately proximal to the take-off of the right pulmonary artery, and a 5F or 6F sheath system is inserted through the purse string and advanced over a guidewire through the ductus and into the descending aorta.\textsuperscript{33}

Accurate delineation of the ductal anatomy by angiography is important before deploying the ductal stent. After determining ductal dimensions with angiography, the stent is inserted and deployed (Fig. 49-10, C). Another angiogram is performed to assess stent position. If the stent does not cover the entire length of the ductus, ductal narrowing and systemic outflow obstruction may result. If the stent is too long, it could obstruct the origin of the pulmonary arteries or retrograde flow into the proximal arch and ascending aorta, which could be catastrophic in patients with aortic atresia (Fig. 49-10, D).

Once position of the stent is confirmed, PGE\textsubscript{1} infusion is discontinued. Based on hemodynamic and echocardiographic data, adequacy of the atrial septal communication is assessed. If deemed restrictive, and depending on the nature of the restriction, a balloon atrial septotomy or deployment of an atrial septal stent is performed. The completed procedure is shown in Fig. 49-10, E. Routine echocardiographic assessment is performed on arrival in the ICU and weekly until the patient is discharged. The chest is closed over a single drainage tube. Postoperative care is similar to that after the Norwood procedure.

Alternative techniques have been described for the hybrid procedure. These include a left thoracotomy approach,\textsuperscript{91} different methodology and materials for the pulmonary artery bands,\textsuperscript{94} and use of long-term PGE\textsubscript{1} (avoiding stents) to maintain ductal patency.\textsuperscript{57}

Bidirectional Superior Cavopulmonary Anastomosis (Hemi-Fontan Procedure)

These procedures are performed as a second stage following the Norwood procedure. Bidirectional superior cavopulmonary anastomosis and the hemi-Fontan procedure are described under Technique of Operation in Chapter 41. Because it is generally accepted that there remains substantial risk of mortality in the period between hospital discharge following a successful first-stage reconstruction for hypoplastic left heart physiology and creation of the bidirectional superior cavopulmonary anastomosis,\textsuperscript{1,8} the second-stage procedure should be performed relatively soon, typically between age 3 and 6 months. Following creation of the bidirectional superior cavopulmonary anastomosis, hemodynamic efficiency is markedly improved and mortality risk substantially reduced.\textsuperscript{1,8} Data suggest that somatic growth does not occur in patients with first-stage palliation after age 4 months.\textsuperscript{45}

Early construction of the bidirectional superior cavopulmonary shunt has two other advantages:

1. It allows use of a relatively small-diameter systemic-to-pulmonary shunt or right ventricular-to-pulmonary conduit at the time of first-stage reconstruction. This creates an ideal Qp/Qs ratio during the first months following birth and does not require the initial shunt or conduit to have a life expectancy of more than 6 months. As a result, the initial shunt or conduit does not have to be “oversized” in anticipation of the growing infant requiring increased Qp in later infancy. This promotes early hemodynamic stability.

2. It reduces duration of inefficient mixed circulation that is present with a shunt or conduit. This allows maximal preservation of right ventricular function by reducing right ventricular volume work, mortality risk, and chance of distortion of the pulmonary arteries caused by tethering from the PTFE graft.

Comprehensive Second-Stage Procedure Following Hybrid Procedure

This is a complex operation requiring CPB, aortic clamping, and (by preference) either antegrade cerebral perfusion or hypothermic circulatory arrest. Exposure is by median
A, Inset shows preparation of bands from appropriately sized polytetrafluoroethylene (PTFE) tube grafts. (See text for criteria used to choose correct tube graft diameter). Main figure shows the PTFE band placed on right pulmonary artery. Care must be taken not to place the band too proximal, thereby potentially obstructing the small ascending aorta, and not too distal, thereby potentially distorting upper-lobe branch of right pulmonary artery. Left pulmonary artery band is being positioned, preferably midway between the origin and the lobar arterial branching point. Bands are secured to adventitia of branch pulmonary arteries to avoid migration. B, Angiogram confirming positioning of right pulmonary artery band. C, Pulmonary artery bands are in place. Purse-string suture of 5-0 polypropylene is placed anteriorly in pulmonary trunk. Using the Seldinger technique, a 5F or 6F sheath system is inserted through purse string and advanced over a guidewire into descending aorta. A hand injection of contrast using a lateral projection is used to demonstrate ductal anatomy. After determining ductal dimensions, a (premounted) Palmaz Genesis stent (Cordis Co., Miami, Fla.) is advanced through the sheath system into position and expanded with the balloon angioplasty catheter.

Reconstruction involves removing the ductus arteriosus and stent, Norwood neoaorta and arch reconstruction, removing the pulmonary artery bands with possible branch pulmonary artery reconstruction, atrial septectomy or removal of atrial septal stent, and creating a bidirectional superior cavopulmonary anastomosis. In essence, it embodies most of
the technical components of the Norwood operation, with
the addition of a reoperative setting. Technical details of
the procedure are shown in Fig. 49-11.

Fontan Operation
The Fontan operation is described under Technique of
Operation in Chapter 41. Once the bidirectional superior
cavopulmonary shunt has been constructed, considera-
tions for completing the Fontan procedure, although somewhat
complex, remain no different from those for any other
single-ventricle anomaly.

Cardiac Transplantation
Principles of preoperative management are generally similar
to those described for reconstructive surgery, but donor
hearts are not usually available within the 3- to 5-day period
thought to be ideal for performing the Norwood procedure.
The waiting period for a donor heart may extend to several
weeks or longer. Infants who maintain relatively high Rp can
be discharged from the acute care facility, but they must be
maintained on a constant infusion of PGE₁ by a portable
intravenous pump (see Fig. 49-7). Infants in whom pulmo-
nary overcirculation with systemic undercirculation develops
require constant intensive care with varying degrees of
support to maintain cardiopulmonary stability.

General techniques of cardiac transplantation are described
under Technique of Operation in Chapter 21. The special
methods necessary for patients with forms of hypoplastic left
heart physiology have been described as well. Donor
hearts are harvested with the ascending, transverse arch, and
upper descending thoracic aorta intact.

After recipients are placed on CPB as described for
the Norwood procedure, cooling to 16°C to 18°C is begun.

The ductus arteriosus is excised from the aorta as in the
Norwood procedure. An aortic incision is made into the
descending aorta approximately 1 cm beyond the ductal
insertion site and retrograde around the aortic arch to the
base of the brachiocephalic artery. Native cardiectomy is per-
formed by transecting the ascending aorta proximal to the
brachiocephalic artery and the pulmonary trunk near its bifur-
cation. The atrial-level incisions are performed in standard
fashion.

The donor heart is then implanted. The broadly beveled
aorta is anastomosed to the recipient aortic arch beginning
at a level opposite the origin of the brachiocephalic artery
and extending to the proximal descending aorta beyond
the ductal insertion. Donor pulmonary trunk is anastomosed
to recipient distal pulmonary trunk. Atrial anastomoses
are performed in standard fashion. The transplantation
procedure is modified appropriately when the patient has
already undergone first-stage reconstruction (Norwood
procedure).

SPECIAL FEATURES OF POSTOPERATIVE CARE
Care after first-stage reconstruction is particularly complex
and important (see “Management of Hypoplastic Left Heart
Physiology” in Section I of Chapter 4 and Section IV of
Chapter 5). Many of the same physiologic issues present
preoperatively remain. Qp/Qs must still be balanced; however,
an appropriately sized shunt or conduit makes this
more manageable postoperatively. Maintaining adequate sys-
temic cardiac output despite well-balanced systemic and
pulmonary blood flow distribution is more of a challenge
postoperatively because of depressed cardiac function result-
ning from operation. Aggressive use of inotropic support is
usually more warranted postoperatively than preoperatively.
Chapter 49  Aortic Atresia and Other Forms of Hypoplastic Left Heart Physiology

Figure 49-11  Comprehensive second-stage procedure following hybrid reconstruction. A, Pre–second-stage illustration showing bilateral pulmonary artery banding and ductal stenting in place. B, Excision of ductus and ductal stent en bloc in preparation for aortic arch and neoaortic reconstruction, performed as a standard Norwood arch reconstruction using pulmonary artery allograft patch. Patch closure of distal pulmonary trunk as well as proximal end of ductus is performed using pulmonary artery allograft patch. Pulmonary artery bands have been removed. Note mild distortion at band sites. If stenosis is present at band sites, patch augmentation using pulmonary artery allograft patch is performed (not shown). C, Endarterectomy-like removal of ductal stent through transected distal pulmonary trunk. As shown, depending on the time elapsed since initial palliation, partial removal of intima and part of the media is common, without complete disruption of vascular wall, therefore reducing magnitude of reconstruction. D, Completed second-stage reconstruction with superior bidirectional cavopulmonary anastomosis. (From Pizarro and colleagues.6)

Following transport from the operating room to the cardiac ICU, these infants are managed with aggressive sedation and pharmacologic paralysis for at least 24 hours. Sedation is typically administered using intravenous fentanyl and midazolam, and paralysis is achieved with a continuous infusion of pancuronium. Thus, the infant’s metabolic demands are minimized, and complete ventilatory control is possible. Depending on status of $Q_p/Q_s$—assessed by clinical evaluation and arterial blood gases—rate of ventilation, tidal volume, and $F_{O_2}$ can all be manipulated to maximize $Q_p/Q_s$ balance. An appropriate combination of tidal volume and ventilatory rate is used to achieve optimal $PaCO_2$. If assessment of the infant is that $Q_p$ is inadequate, either due to a restrictive shunt or conduit or pulmonary hypertension, ventilation is increased to reduce $PaCO_2$ to approximately 30 to 35 mmHg (Torr). If the assessment is that $Q_p$ is excessive, ventilation is adjusted to allow $PaCO_2$ to increase to approximately 45 to 50 mmHg. If $Q_p$ is assessed to be adequate, $PaCO_2$ is adjusted to 40 mmHg. Similarly, $F_{O_2}$ can be adjusted over a range from 17% to 100%, depending on $Q_p$ and $R_p$. Higher levels of $F_{O_2}$ are used when $Q_p$ is judged to be inadequate, and lower levels if it is judged to be excessive. In a patient whose
Qp is considered adequate, FiO₂ is usually reduced to approximately 25% to 30% within several hours after operation.

Some institutions suggest using additional inspired CO₂ both to limit excessive Qp and independently improve Qs. This practice is somewhat controversial.

Use of nitric oxide in the setting of reduced Qp should be limited to patients in whom there is clear evidence of an adequately sized shunt or conduit and elevated pulmonary Rp. Use of nitric oxide for a patient with inadequate Qp caused by an excessively restrictive shunt or conduit is ineffective and inappropriate. Such a patient should immediately be returned to the operating room for shunt or conduit revision.

A typical level of inotropic support in the early postoperative period includes moderate dopamine (3 to 10 mg · kg⁻¹ · min⁻¹, continuous infusion) and milrinone (0.5 mg · kg⁻¹ · min⁻¹), with or without addition of low-dose epinephrine (0.03 to 0.05 mg · kg⁻¹ · min⁻¹) (see Section IV of Chapter 5). Substantially larger doses of inotropic drugs are as likely to harm as help. Specifically, for the patient who shows evidence of excessive Qp and reduced systemic perfusion, increasing inotropic support is likely to exacerbate the physiologic imbalance.

Other maneuvers that maximize oxygen delivery to the systemic tissues include optimizing cardiac output by taking advantage of the Frank-Starling curve (see “Cardiovascular Subsystem” in Section I of Chapter 5). Typically, adjusting atrial filling pressures with volume supplementation to achieve pressures between 6 and 12 mmHg addresses this point. Optimizing oxygen-carrying capacity by adjusting the hematocrit to a minimum of 45% is advised. Despite maximizing cardiac output and balancing Qp and Qs, it is not uncommon for patients to show evidence of marginally inadequate systemic perfusion during the first 24 hours after operation.

Metabolic acidosis with base deficits ranging from 0 to −5 are not uncommon and should be treated aggressively with either intermittent bicarbonate or continuous bicarbonate infusion.

Urine output is also commonly reduced during the first 24 hours (<1 mL · kg⁻¹ · h⁻¹), and periods of anuria may occur. If anuria or oliguria persists beyond the first 6 hours postoperatively, serious consideration should be given to placing a peritoneal dialysis catheter (see “Renal Subsystem” in Section I of Chapter 5).

If the infant is returned to the ICU from the operating room with the sternum left open, it should not be closed until hemodynamic status is stabilized. This typically takes 36 to 48 hours. If instability persists, sternal closure can be delayed for as long as 4 to 5 days. If the infant arrives in the ICU from the operating room with the sternal wound completely closed, consideration should be given to opening it in the ICU if hemodynamics are inadequate during the first 24 hours. Substantial cardiac and pulmonary stability can be achieved with this simple maneuver.

After approximately 36 to 48 hours, or after sternal closure, sedation and paralysis can be gradually removed, allowing the patient to take over respiratory function. The weaning process from the ventilator follows the standard principles that apply to all infants following cardiac surgery (see “Pulmonary Subsystem” in Section I of Chapter 5). Prolonged ventilatory support is not unusual following the Norwood procedure and may extend to 5 to 10 days, even in patients who have no definable cardiovascular or pulmonary problem. Under these circumstances, nutrition becomes critical.

Typically, total parenteral nutrition is begun within 48 hours of operation and may be continued or converted to direct enteral feeding using a nasogastric tube. Enteral feeding should be used as soon as cardiovascular stability has been achieved and return of intestinal function is documented.

Some form of antiplatelet therapy is generally recommended to inhibit thrombosis of the shunt or conduit. A typical regimen is to institute aspirin therapy (1 mg · kg⁻¹ · d⁻¹) as soon as perioperative hemorrhage is controlled. Care after the bidirectional superior cavopulmonary shunt and Fontan operation is described under Special Features of Postoperative Care in Chapter 41. Postoperative care following transplantation is similar to that for other cardiac transplant patients (see Features of Postoperative Care in Chapter 21).

RESULTS
First-Stage Reconstruction (Norwood Procedure)

Early (Hospital) Death
Early mortality remains variable among institutions. At institutions with a large experience in neonatal cardiac surgery, mortality following first-stage reconstruction steadily improved in the decades between 1985 and 2005, and then subsequently plateaued, with current hospital mortality of approximately 20%, 41,3,13,3,5,5,6,8,7,1,7,1 In a report from a single institution with a large experience (Mott Children’s Hospital, Ann Arbor, Mich.), hospital mortality after first-stage reconstruction was 58% (CL 51%-65%) between 1986 and 1989, and 15% (CL 11%-20%) between 1990 and 1993, reflecting the trend in improved results experienced at most institutions committed to neonatal cardiac surgery. 41

Other single-institution studies reporting cases from 2002 to 2005 indicated hospital mortality of 6.2% (2/32; CL 2.2%-14%), 44 9.1% (6/66; CL 5.4%-14%), 41 and 11% (10/88; CL 7.8%-16%). 45 The Congenital Heart Surgeons Society (CHSS) report of 622 cases performed between 2001 and 2004 indicated early mortality of 17% (CL 16%-19%). 51 In contrast, at less experienced institutions, hospital mortality still approached 50%. The University Hospital Consortium reported 53% mortality (118/222) among 40 institutions, each performing an average of 7.2 procedures during the 5-year period of the study; however, all cases were performed before 1995. 41,16

Survival following first-stage reconstruction performed in multiple institutions between 1994 and 1997 for patients specifically with aortic atresia is shown in Fig. 49-12. Survival was about 10% higher at all intervals at the two institutions with the best outcomes in this multicenter study.

Time-Related Survival
Overall, 12-month survival after first-stage reconstruction has been approximately 60%, with nearly all deaths occurring before the second-stage procedure (bidirectional superior cavopulmonary shunt). In one large series, survival was 66% at 1 month, 48% at 12 months, and 44% at 18 months, emphasizing ongoing risk of death even after successful first-stage reconstruction. 41,14 In another series, 6 of 41 early survivors (15%) died within 3 to 5 months after operation. 43 In the recently completed 15-center study conducted by the
**Figure 49-12** Non-risk-adjusted survival and hazard function for 253 patients with hypoplastic left heart physiology initially entered into a protocol of staged reconstructive surgery (Norwood procedure) at multiple institutions. **A,** Survival after entry. **B,** Hazard function for death. Lines, bars, and numbers have representation similar to Fig. 49-6. (From Jacobs and colleagues.\(^2\))

**Figure 49-13** Death or transplantation among infants undergoing Norwood procedure, randomized to either modified Blalock-Taussig shunt (MBT shunt) or right ventricle–to–pulmonary artery conduit (RVPA shunt). \(P = .02\) for difference in treatment effect for period before and period after 12 months. **A,** Transplantation-free survival. **B,** Hazard function. (From Ohye and colleagues.\(^5\))

Pediatric Heart Network, 1-year survival was 74% for patients with a right ventricle–to–pulmonary trunk conduit procedure, and 64% for those with a systemic artery–to–pulmonary artery shunt procedure\(^6\) (Fig. 49-13). Recognition of this pattern of ongoing mortality after hospital discharge has spawned the term *interstage death.* Interstage death of 10%\(^4\) and 16%\(^8\) are typical.\(^4\)

Establishment of home monitoring programs, designed to engage parents and primary cardiologists in recognizing early signs and symptoms of patient destabilization, has substantially decreased mortality between a successful first operation and the anticipated second-stage operation, with some reports showing no interstage deaths.\(^4,11\)

**Incremental Risk Factors for Death after Operation** Morphologic factors have been associated with risk of death in some series but not in others. In an early study from 1986 by Norwood’s group, atrial septal anatomy, preoperative right ventricular hypertrophy, ascending aorta diameter, and coarctation were not correlated with early survival.\(^5\) Although not supported by the two largest institutional experiences, some institutions suggest that aortic atresia and very small size of the ascending aorta (diameter < 2 mm) may be associated with increased risk for death, both early\(^7\) and late\(^3\) after first-stage reconstruction. Intact or highly restrictive atrial septum has been widely associated with increased risk of both early and interstage death.\(^9,14,15\)
The combination of mitral stenosis and aortic atresia has recently been identified as a risk, particularly when left ventricular-to-coronary artery fistulae are present. In one study, fetal diagnosis has been shown to decrease the risk of death following first-stage reconstruction, suggesting that factors such as prenatal transport and early postnatal stabilization may improve survival. In another, however, prenatal diagnosis was strongly correlated with superior preoperative clinical status but did not influence surgical outcome. Moderate or severe tricuspid valve regurgitation preoperatively and depressed right ventricular function preoperatively have correlated with increased risk of death after first-stage reconstruction.

An initially low arterial pH has not correlated with increased risk of deaths in some studies; whereas in others it has. Small size at operation has been identified as a risk. Associated noncardiac anomalies (e.g., tracheoesophageal fistula, renal dysplasia, biliary atresia, intracranial abnormalities, pulmonary dysplasia) have been shown to increase risk. In one large single-institution study, age older than 7 days at time of first-stage reconstruction was a risk factor for interstage death. In another study, postoperative bradycardia and reduced ventricular function were noted to be risks. A less-than-optimal technical operation has also been identified as a risk factor for death.

These various studies that identify different risk factors underscore the wide variability among institutions.

**Hemodynamic and Morphologic Results**

Atrial septectomy performed at first-stage reconstruction usually results in a nonrestrictive opening between the two atria. A gradient in excess of 4 mmHg across the atrial septum develops in about 4% of patients. About 10% of patients have significant (grade 3 or 4) tricuspid valve regurgitation late after first-stage reconstruction. In interpreting this, the fact that this physiologic variable is a risk factor for death after first-stage operation must be considered.

Systolic pressure gradients are rarely present between right ventricle and reconstructed ascending aorta, indicating that the native pulmonary valve functions well in the setting of systemic outflow. In approximately 10% to 15% of patients, the distal portion of the aortic arch is narrowed such that a systolic pressure gradient greater than 25 mmHg is present. This gradient typically occurs at the distal limit of the allograft patch. It is most likely due to lack of growth potential at this site resulting from a combination of patch material and circumferential ductal tissue in the native aorta. All patients who have undergone reconstruction for hypoplastic left heart physiology should be evaluated for potential gradients at this site. Aggressive treatment is necessary; often this can be accomplished effectively with percutaneous balloon dilatation.

Most patients have a $Q_p/Q_s$ of 0.8 to 2.0 at the time of cardiac catheterization performed in preparation for the second-stage superior cavopulmonary shunt. Approximately 15% to 20% of patients have elevated Rp greater than 4 Wood units. Pulmonary artery distortion is present in a minority of patients, typically at the central pulmonary trunk site under the aortic arch, or at the shunt or conduit insertion site. Right ventricular end-diastolic pressure is typically somewhat elevated but is greater than 12 mmHg in approximately 10% of patients. A hypoplastic left pulmonary artery has been associated with larger diameter of the reconstructed aorta.

**First-Stage Reconstruction (Hybrid Procedure)**

**Early (Hospital) Death**

Early mortality has been as low as 2.5% (1/40; CL 0.41-8.2%) and as high as 29% (6/21; CL 18%-42%), with other series reporting 5.6% (1/18; CL 0.90%-18%), 12% (4/33; CL 6.3%-21%), 18% (2/11; CL 6.8%-38%), and 20% (2/10; CL 7.0%-41%).

**Time-Related Survival**

Time-related survival after the hybrid procedure, which includes interstage survival and survival following comprehensive second-stage surgery, is about 60%. It is influenced by development of obstruction to retrograde flow in the aortic arch caused by the ductal stent in patients with aortic atresia.

Fig. 49-16 shows time-related survival following the hybrid procedure. Other reports confirm a relatively high interstage mortality (21%) and comprehensive second-stage mortality (14%).

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**Figure 49-14** Survival after first-stage reconstruction for hypoplastic left heart physiology in anatomic subtype aortic atresia with mitral stenosis. Survival is stratified by presence or absence of echocardiographic or angiographic presence of left ventricle (LV)-to-coronary artery fistulae. Risk appears to reside in this subgroup having fistulae because mortality for aortic atresia with mitral stenosis without fistulae is more favorable, similar to other anatomic subtypes. (From Pigula and colleagues.)

**Figure 49-15** Early survival after the first-stage Norwood operation (October 1984–March 1987), according to degree of preoperative tricuspid regurgitation. (From Barber and colleagues.)
Based on results from several institutions with a large experience managing hypoplastic left heart physiology, early mortality following bidirectional superior cavopulmonary anastomosis currently is about 5\%^{12,25} (Fig. 49-17).

**Time-Related Survival**
Because of the marked improvement in physiologic status following bidirectional superior cavopulmonary anastomosis, mortality following the perioperative period and before the Fontan procedure is generally extremely low\(^{12}\) (see Fig. 49-17).

**Third-Stage Reconstruction (Fontan Operation)**
In theory, there should be no difference in outcome following the Fontan operation for patients with hypoplastic left heart physiology than for patients having other forms of univentricular heart. The logic behind this statement is the same as that given in the previous discussion of outcome following bidirectional superior cavopulmonary anastomosis. This has been confirmed by at least one large single-institution study.\(^{12}\) The outcomes discussed here for the Fontan operation in patients with hypoplastic heart physiology should be supplemented by the general discussion of outcomes following the Fontan procedure for all forms of univentricular heart (see Results in Chapter 41).

**Early (Hospital) Death**
In the early era, mortality after the Fontan operation for hypoplastic left heart physiology was high—8 patients in 50 (16%; CL 11%-23\%) reported by Chang and colleagues from Norwood’s group.\(^{6}\) More recent estimates of hospital mortality in larger patient cohorts from several institutions is about 5\%^{12,25} (see Fig. 49-17).

**Incremental Risk Factors for Death after Operation**
Aortic atresia with obligatory retrograde flow in the aortic arch appears to be a risk factor for death after the hybrid procedure (see Fig. 49-16).

**Hemodynamic and Morphologic Results**
About 50\% of patients undergoing the hybrid procedure require an interstage catheter-based intervention or surgical intervention before comprehensive second-stage reconstruction.\(^{14}\)

**Second-Stage Reconstruction (Bidirectional Superior Cavopulmonary Anastomosis)**
Outcome following bidirectional superior cavopulmonary anastomosis or hemi-Fontan procedure in hypoplastic left heart physiology is similar to that for patients with other forms of univentricular heart. This naturally follows from the fact that all patients with univentricular heart, including those with hypoplastic left heart physiology, are selected for bidirectional superior cavopulmonary anastomosis based on similar physiologic criteria.

Because a number of institutions with extensive experience with surgery for hypoplastic left heart physiology have reported outcomes, there are ample data on survival following each stage of operation in these patients. These data are supplemented by the more general discussion of outcome following bidirectional superior cavopulmonary anastomosis in all forms of univentricular heart (see Results in Chapter 41).

Although there is probably no difference in survival between hypoplastic left heart physiology patients and other univentricular heart patients following bidirectional superior cavopulmonary anastomosis, it is not clear whether hypoplastic left heart physiology patients are as likely as other univentricular heart patients to meet the physiologic criteria necessary to undergo bidirectional superior cavopulmonary anastomosis. Based on a number of factors, including marginal hemodynamics after first-stage reconstruction and ongoing mortality, it is likely that a smaller percentage of these patients will eventually undergo bidirectional superior cavopulmonary anastomosis.
Incremental Risk Factors for Death
Incremental risk factors for death following the Fontan operation are similar in all forms of univentricular heart (see Chapter 41).

Other Commonly Performed Operations
The two most commonly performed additional procedures performed in patients undergoing the standard three-stage protocol are repair of recurrent arch obstruction and tricuspid valve repair for regurgitation. These can be performed either at the time of the second- or third-stage procedure, or separately.

Recurrent arch obstruction can be effectively addressed in most cases with catheter-based balloon dilatation. Typically, recurrent arch obstruction is noted in infancy, and commonly in the first 6 months after the initial Norwood procedure.\(^\text{5,10,15}\) It occurs in about 20% of survivors.\(^\text{5,10,15}\) Overall risk is low, and gradient relief is excellent. Two single-institution studies revealed no mortality related to the procedure, and gradient relief in all patients, which persisted at midterm follow-up.\(^\text{5,10,15}\) One multicenter analysis showed initial success of 89%, with three deaths occurring within 48 hours of the dilatation in patients with poor ventricular function, and freedom from repeat arch intervention of 74% at 18 months.

Tricuspid valve repair can be accomplished with low mortality and midterm (mean 26 months) success (defined as less than moderate residual regurgitation) of 62%.\(^\text{13}\) Patients with poor right ventricular function after valve repair, even if the repair was initially successful, tended to do poorly, with progressive deterioration of the valve over time. Patients with an unsuccessful initial valve repair but preserved ventricular function often benefited from a second valve repair.

Cardiac Transplantation
Experience with cardiac transplantation in neonates with hypoplastic left heart physiology is small relative to the experience with reconstructive surgery and is limited to a few institutions. General information on the results of cardiac transplantation (see Results in Chapter 21) is applicable to this subpopulation. The early concept that neonates receiving cardiac transplants were “privileged hosts” does not appear to have held up. Rejection frequency and severity in neonates appears to be similar to that in the broader cardiac transplantation experience.\(^\text{16}\)

In the Loma Linda experience, 84 neonates have received cardiac transplants, with 13% (CL 7%-23%) early (30-day) mortality and 5-year survival of 82% (CL 71%-88%).\(^\text{16}\) Including patients who died while awaiting transplant, 5-year survival was 61% (CL 52%-70%).\(^\text{16}\)

A recent multicenter study shows similar midterm survival in institutions accomplished with these procedures\(^\text{12}\) (Fig. 49-18). Early in the experience, suppressive immunotherapy included cyclosporine and azathioprine without use of long-term steroid therapy. Steroids and antithymus globulin were used only for early rejection episodes. Currently, suppressive immunotherapy varies somewhat among institutions; however, in general, long-term therapy varies little relative to that given other cardiac transplant recipients (see Chapter 21).
High early survival has been the rule following neonatal cardiac transplantation for patients with hypoplastic left heart physiology, based on individual reports of several experienced institutions. Intermediate-term results have been acceptable and comparable with intermediate-term results for cardiac transplantation in general. On the other hand, surgical mortality (excluding preoperative death) for transplantation was 42% (17/40; CL 34%-52%) among a consortium of institutions infrequently performing this procedure. In contrast, the more recent report from the Pediatric Heart Transplant Study Group reports 5-year survival (also excluding preoperative death) of 72%, with most of the deaths occurring in the first 3 months after operation. When preoperative death is included, survival at 5 years falls to 54%. An important factor that is difficult to quantify is the death rate of neonates born with hypoplastic left heart physiology while awaiting an appropriate donor organ.

Because of limitations of donors heart availability, the typical neonate must wait several weeks to months before receiving a heart. The intrinsic instability of hypoplastic left heart physiology in its natural state can result in mortality during this time. Attempts have been made to quantify recipient mortality while awaiting a donor organ, but reliable information is scarce. In a multicenter study from 1998, 36 of 49 patients (73%) entered into a transplant protocol received a donor heart; the estimate of time-related interim mortality while awaiting transplant is shown in Fig. 49-7. A more recent multicenter study from the Pediatric Heart Transplant Study group analyzed 262 patients; 25% of listed patients died while awaiting transplantation (Fig. 49-19). The mean waiting period for those receiving an organ was 1.3 months.

**INDICATIONS FOR OPERATION**

Hypoplastic left heart physiology is a fatal condition; death usually occurs within 1 month of birth and certainly within 1 year (see Fig. 49-7). Surgical intervention is therefore advisable unless economic conditions or lack of institutional capability deny this possibility, or the patient’s legal guardians choose to withhold surgical therapy. Curiously, this latter practice remains relatively widespread, even though current treatment outcomes for hypoplastic left heart physiology are now comparable with outcomes for other cardiac defects for which the option to withhold support is not offered by managing physicians and other healthcare providers.

If intervention is to be accomplished, management should begin as soon as possible, preferably with prenatal arrangements for delivery at an institution capable of neonatal resuscitation and subsequent surgical management. Treatment begins at birth or as soon as diagnosis has been made, and consists initially of intensive preoperative therapy. Neonates with hypoplastic left heart physiology usually can be resuscitated and maintained in stable condition with such intervention, and the surgical procedure can be performed as an elective procedure, ideally between 2 and 5 days of life.

Whether staged reconstruction or cardiac transplantation is the treatment of choice remains controversial. Although reconstructive surgery remains the predominant method of managing patients with hypoplastic left heart physiology, there currently are no clear data to recommend reconstruction or transplantation as the procedure of choice. Equivalent outcomes, as judged by early and midterm survival, can be achieved with either treatment.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Aortic Atresia with Large Ventricular Septal Defect**

Although this lesion includes aortic atresia, it is not representative of hypoplastic left heart physiology. A two-ventricle repair is recommended because such patients commonly have a normal mitral valve and left ventricle. One approach is to perform a typical first-stage reconstruction in the neonatal period, followed by a definitive repair in which the left ventricle is baffled to the pulmonary trunk using a Rastelli-type repair (see “Rastelli Operation” under Intraventricular Repair in Chapter 52). In this repair, left ventricular outflow is baffled to the pulmonary trunk by an intracardiac patch, a
right ventricular to distal pulmonary artery conduit is placed, and takedown of the previously placed systemic–pulmonary trunk shunt is performed.

Alternatively, a one-stage complete repair in the neonate can be accomplished. Anecdotal reports of success with this procedure were reported in the 1980s and 1990s. In this procedure, the pulmonary trunk and hypoplastic aorta are reconstructed in typical fashion for first-stage reconstruction for hypoplastic left heart physiology. After completing the extracardiac portion of the procedure, the left ventricle is baffled to the pulmonary trunk with a Rastelli-type intracardiac patch. The operation is completed by placing a valved conduit from right ventricle to distal pulmonary arteries. More recently, single-institution series, reporting experience ranging from 11 to 21 cases, indicate that the operation can be performed with very low early and midterm mortality.15,22,30,31,34

Borderline Hypoplastic Left Heart Physiology

Because of the continuum of morphologic and physiologic compromise among patients with left heart anomalies, clinical decision making can be extremely difficult. Individual patients are positioned along this continuum, yet the surgeon is forced to make a dichotomous management decision. Whether to proceed with a two-ventricle repair or disregard the left-sided structures and perform a single-ventricle repair can be a difficult decision. Although a number of studies have addressed this issue, attempting to quantify the various physiologic and morphologic components of the left heart, the decision remains subjective.22,35,39,46

Pulmonary autograft aortic valve replacement (Ross procedure) in infants and neonates in recent years introduces another factor into this decision-making process (see “Autograft Pulmonary Valve” under Technique of Operation in Chapter 12, and “Repair of Tunnel Stenosis by Aortoventriculoplasty [Konno Operation]” and “Modified Konno Operation” in Section II of Chapter 47). Ability to perform the Ross procedure along with Konno enlargement of the left ventricular outflow tract, in combination with arch reconstruction and resection of left ventricular endocardial fibroelastosis, provides the opportunity to create two-ventricle repairs in patients considered to be poor candidates using older criteria.35,46

Using aggressive left heart reconstructive techniques, it is possible to physiologically normalize the entire left ventricular outflow tract and improve left ventricular cavity size and diastolic function by resecting the constricting endocardial fibroelastosis. In a small experience of one of the authors (FLH) with such borderline hypoplastic left heart patients, it has been found that the true limiting factor for successful two-ventricle repair is size and function of the mitral valve. Except for the mitral valve, it appears that all morphologic components of the left heart can be adequately addressed surgically using these techniques. Although long-term success has been achieved in a small number of patients, it remains controversial regarding when these aggressive techniques should be applied rather than opting for the single-ventricle approach.

Fetal balloon valvuloplasty provides an additional therapeutic option for patients with a borderline left heart. The sole purpose of the procedure is to convert patients to biventricular physiology who otherwise are destined for single-ventricle physiology. This procedure was first performed in 1989, but only 12 cases were performed between 1989 and 1997. Recently, McElhinney and colleagues reported their experience in 47 cases.30 After a learning curve, they currently quote 75% technical success and 10% fetal demise. Thirty percent of those undergoing a technically successful fetal procedure ultimately achieved a two-ventricle circulation. In all of these, additional postnatal, surgical, or interventional procedures were necessary. This experience convincingly demonstrates that fetal balloon valvuloplasty can be technically performed with reasonable safety in the majority of selected patients. However, it is not clear that the procedure plays a causal role in converting patients from a univentricular to a biventricular circulation. The physiologic and morphologic selection criteria for entry into the fetal treatment program were not dissimilar to those of the patients treated by one of the authors, cited earlier, who achieved biventricular repair after a postnatal Ross Konno, arch repair, and endocardial fibroelastosis resection—without fetal intervention.

Use or Avoidance of Circulatory Arrest

When performing the Norwood procedure, the decision to use either hypothermic circulatory arrest or continuous perfusion, most commonly in the form of antegrade cerebral perfusion, is made based on surgeon preference. Surgeon preference is most heavily influenced by personal experience and expert opinion, and less so by objective data.30 Hypothermic circulatory arrest techniques have been available for more than 40 years and continue to evolve. Antegrade cerebral perfusion techniques have been available for a little over a decade and are rapidly evolving as well.

Techniques are also now available for reliably performing complex neonatal cardiac surgery, including the Norwood procedure and its variants, without using total body circulatory arrest.31,44,48,53,54 Only limited evidence unequivocally demonstrates that avoiding circulatory arrest is beneficial, but a number of compelling arguments can be made supporting the position that continuous circulation, especially to the brain, should be maintained.

Although numerous maneuvers have been used to minimize unwanted sequelae of controlled cerebral ischemia that attends circulatory arrest, both clinical and animal studies indicate that profound metabolic changes take place within minutes of cessation of blood flow, regardless of temperature of the brain tissue (see Section I of Chapter 2 for details and references). Based on these studies, it is difficult to pinpoint with confidence the threshold for a safe period of circulatory arrest, although several clinical studies have attempted to define that point. The safe period concept is only valid as a tool to be applied prospectively in clinical decision making for individual patients if one assumes that all patients are equally susceptible to cerebral ischemia. There is increasing evidence that this is not the case; it is becoming recognized that genetic polymorphism can influence vulnerability of the brain to ischemic insult from individual to individual.33

Based on data showing that metabolic derangements begin immediately with circulatory arrest, and on carefully conducted animal and clinical studies demonstrating that neurologic sequelae correlate with increasing length of circulatory arrest (see “Safe Duration of Circulatory Arrest” in Section I of Chapter 2), it can be argued that clinical studies
failing to show sequelae following circulatory arrest are simply using end-point criteria that are insensitive to subtle cognitive injury that may occur with shorter arrest periods or are underpowered to demonstrate a difference. The strongest justification for using circulatory arrest has been that instrumentation, cannulae, and techniques are not available to allow repair of complex aortic arch problems in neonates using continuous perfusion. This justification, however, no longer exists.\(^{11,13,15,21}\) Although it is clear that continuous perfusion can eliminate the metabolic derangements that occur with cessation of cerebral blood flow, potential complications relating to techniques required to maintain ongoing perfusion can also occur, and these must be defined and studied.

Safeguards that are necessary to avoid perfusion-related complications, however, should be no different from those of standard CPB. There are limited data directly comparing continuous perfusion and hypothermic circulatory arrest in patients undergoing the Norwood procedure and its variants. There is a single randomized prospective study comparing it with antegrade cerebral perfusion.\(^{31}\) That study did not examine early mortality or morbidity, but focused on neurodevelopmental outcome at midterm follow-up in a single institution; no difference in outcome between the two techniques was demonstrated. This conclusion is of limited value, however, because the methodology used for the antegrade cerebral perfusion group involved periods of hypothermic circulatory arrest, multiple cannulation maneuvers, and baseline perfusion rates (20 mL · kg\(^{-1}\) · min\(^{-1}\)) that many would consider in the low flow range. The critique of this manuscript, which accompanies the publication, emphasizes these limitations and further points out that the compelling theoretical advantages of continuous perfusion must be supplemented by both developing a rigorous physiologic understanding of techniques such as antegrade cerebral perfusion, and standardizing operative techniques that minimize morbidity. The current state-of-the-art of antegrade cerebral perfusion lacks these important components.\(^{33,34}\) Several single-institution studies have established that the Norwood procedure can be performed using continuous perfusion, with early morbidity and mortality comparable with outcomes achieved using hypothermic circulatory arrest.\(^{34,35,28,29}\) Some studies indicate an early survival advantage using antegrade cerebral perfusion.\(^{31}\)

Comparison of Right Ventricle–to–Pulmonary Trunk Conduit and Systemic-to–Pulmonary Artery Shunt as Source of Pulmonary Blood Flow in First-Stage Reconstruction

For decades, a systemic–pulmonary arterial shunt has been the mainstay for providing regulated Qp to the lungs in first-stage reconstruction. The most commonly used procedure for accomplishing this is the modified Blalock-Taussig shunt using a PTFE graft. Its potential disadvantages include excessive volume load, acute thrombosis, and low diastolic blood pressure leading to coronary insufficiency. Although Norwood originally experimented with right ventricle–to–pulmonary artery conduits as the source of pulmonary blood flow in first-stage reconstruction,\(^{37}\) this was quickly abandoned.

Over the past decade, the concept of the right ventricle–to–pulmonary trunk conduit as the source of pulmonary blood flow has been reexamined.\(^{12,34}\) These techniques use either a valved or nonvalved conduit between right ventricle and central distal pulmonary trunk. They have several potential advantages, the most important of which is lack of diastolic runoff from the systemic circulation. This provides importantly elevated diastolic blood pressure in the aorta and coronary arteries compared with the systemic-pulmonary shunt, with the potential advantage of promoting more stable cardiac performance by reducing myocardial oxygen supply/demand mismatch that undoubtedly occurs in the standard Norwood operation, in which the single right ventricle has marked pressure and volume load, yet decreased coronary perfusion. Additional potential advantages include (1) improved development of the left pulmonary artery system because the source of pulmonary blood flow enters the pulmonary arteries more centrally, and (2) ability to easily perform second-stage bidirectional superior cavopulmonary anastomosis without need for CPB. The potential disadvantages of this technique are (1) a right ventriculotomy is required to place the conduit, which may lead to ventricular dysfunction and dysrhythmias; (2) damage to the pulmonary valve may occur at the time of the ventriculotomy; (3) excessive thrombosis is theoretically possible because of relative stasis during diastole; and (4) central pulmonary arterial distortion may occur.

One of the authors (FLH) has exclusively used a composite right ventricle–to–pulmonary trunk valved conduit for first-stage reconstruction since January 2002.\(^{35}\) With this technique, it is immediately apparent that postoperative diastolic blood pressure is markedly improved (Fig. 49-20) compared with both preoperative diastolic blood pressure and traditional expectations for postoperative diastolic blood pressure using a standard systemic-pulmonary shunt. Early postoperative management is simplified, and hospital mortality as low as 8% can be achieved. Others have also noted these hemodynamic advantages.\(^{12}\) Over the past decade, use of the right ventricle–to–pulmonary trunk conduit has increased

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**Figure 49-20** Difference in preoperative and early postoperative diastolic blood pressure (Δ diastolic pressure) in five patients undergoing first-stage reconstruction utilizing a valved right ventricle–to–pulmonary artery composite graft. Note marked improvement in diastolic blood pressure in all cases.
steadily, and currently it is chosen about as frequently as the systemic-to-pulmonary artery shunt.

Superiority of one technique over the other has not been unequivocally demonstrated, but a number of studies address this question. Many of these are retrospective single-institution studies and are not randomized; important reports are cited and discussed here. Mair and colleagues retrospectively evaluated 32 patients, 18 with a shunt and 14 with a right ventricle-to-pulmonary artery conduit.\textsuperscript{345} They demonstrated better diastolic blood pressure, lower hospital and interstage mortality, and better ventricular function by catheterization at 3 months in the conduit group. There were no thrombotic events. One concern with this study is that the first 18 patients received shunts, and the last 14 conduits.

In another nonrandomized single-institution study of 66 patients, Cua and colleagues showed no difference in morbidity or mortality in 37 shunt patients and 29 conduit patients.\textsuperscript{G11} The conduit group had higher diastolic blood pressure, faster recovery, and shorter hospital stay. Ruffer and colleagues retrospectively analyzed 54 patients, 31 receiving a shunt and 23 a conduit.\textsuperscript{R8} Diastolic blood pressure was higher in the conduit group, and mortality was lower (8.7% vs. 19%, \(P = .12\)). Hospital length of stay and interstage mortality were similar. Pruett and colleagues retrospectively report 159 cases, 103 receiving a shunt and 56 a conduit.\textsuperscript{P9} Mortality was 42% prior to second-stage surgery in the shunt group, compared with 23% in the conduit group. The left pulmonary artery grew more in the conduit group, but the pulmonary trunk was more likely to be hypoplastic. The conduit group was more likely to need reintervention prior to standard second-stage intervention. Caspi and colleagues showed that the Nakata index for conduit patients was greater (240 ± 18 mm\(^2\) · m\(^{-2}\) vs. 190 ± 10 mm\(^2\) · m\(^{-2}\), \(P = .03\)), and branch pulmonary arteries were more equal in size than those in shunt patients.\textsuperscript{C3}

Graham and colleagues reported similar findings as well as higher diastolic blood pressure and lower right ventricular end-diastolic pressure in conduit patients at catheterization in preparation for second-stage intervention.\textsuperscript{G12} Pizzaro and colleagues demonstrated lower operative mortality in the conduit group compared with the shunt group (8% vs. 30%, \(P = .05\)) as well as less need for ventilator manipulation, extracorporeal membrane oxygenation, and delayed sternal closure.\textsuperscript{P5} Tanoue and colleagues demonstrated that overall ventricular performance was comparable at midterm follow-up in both shunt and conduit groups.\textsuperscript{T2} Griselli and colleagues retrospectively evaluated 367 patients and showed lower hospital (15% vs. 31%, \(P < .05\)) and midterm (22% vs. 41%, \(P < .05\)) mortality in the conduit group.\textsuperscript{G13}

Atallah and colleagues showed lower hospital and 2-year mortality in conduit patients compared with shunt patients, as well as improved psychomotor development; however, shunt patients underwent initial surgery between 1996 and 2002, whereas conduit patients underwent surgery between 2002 and 2005.\textsuperscript{A4} In contrast, Tabbutt and colleagues showed similar hospital and midterm survival and hospital length of stay in 149 patients (95 shunts, 54 conduits) but also an increased need for early reintervention in the conduit group.\textsuperscript{T1} Lai and colleagues reviewed 80 patients and showed similar early mortality in the conduit and shunt groups, but noted that six of 41 shunt survivors died before second-stage intervention, whereas none of the 29 conduit patients died.

Morbidity and mortality associated with second-stage intervention were similar.\textsuperscript{L11}

Several studies note the requirement for reintervention for inadequate Qp prior to standard second-stage intervention in patients who receive the right ventricle-to-pulmonary trunk conduit.\textsuperscript{D3,P7,R5,T1} Whether this is an intrinsic problem with the conduit procedure or part of the learning curve related to a relatively new technique is unclear at this time. When this problem occurs, it can be managed either by surgical or interventional revision of the conduit\textsuperscript{D3,P7,T1} or by placing a systemic-to-pulmonary artery shunt, preferably with take-down of the conduit.\textsuperscript{H6} The question is whether or not right ventricular function is impaired as a result of the right ventriculotomy or other factors related to the conduit procedure.

Although there are currently no definitive answers, several studies\textsuperscript{G12,R3,T2} and the literature review by Raja and colleagues\textsuperscript{R1} indicate that there is no evidence that right ventricular function is impaired either early or at midterm follow-up. A single randomized prospective multicenter study comparing the right ventricle-to-pulmonary trunk conduit with the systemic artery-to-pulmonary artery shunt has been performed.\textsuperscript{T35} Fifteen institutions enrolled 549 patients. Transplantation-free 1-year survival was higher in the conduit group (74% vs. 64%, \(P = .01\)). The hazard function for death is higher for shunt patients from month 1 to month 12 after operation, becomes equal to that for conduit patients from months 13 to 36, then again rises above the hazard for conduit patients from months 36 to 48 (see Fig. 49-13). Unintended reinterventions were higher in the conduit group. Ventricular function was similar in both groups.

To summarize, current evidence suggests that the right ventricle-to-pulmonary trunk conduit is associated with improved early and midterm survival and more favorable early hemodynamics, including diastolic blood pressure and shorter hospital length of stay, and does not negatively affect right ventricular performance at midterm follow-up. Branch pulmonary artery development may be improved. An increased number of unintended procedures have been documented using this technique, but it is likely these will decrease as experience with the technique grows.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{./figure49-21.png}
\caption{Survival according to hybrid and Norwood management strategies in high-risk patients with hypoplastic left heart physiology. (From Pizarro and colleagues.\textsuperscript{G4})}
\end{figure}
Hybrid versus Norwood Procedure

It is difficult to compare these two procedures, mainly because hybrid procedures are usually performed in higher-risk patients. Despite this, a direct comparison of early mortality after neonatal surgery suggests that hybrid outcomes are at least as good as Norwood outcomes. Interstage and second-stage mortality, however, appear to be higher. The only study that examines outcomes following the Norwood procedure and the hybrid procedure in matched high-risk patient cohorts suggests that survival is similar p4 (Fig. 49.21).

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18. Butnor WJ, Kilby MD, Davies B, Wright JG, Jones TJ, Brawn WJ. The hybrid procedure in matched high-risk patient groups: at least as good as Norwood outcomes. Interstage and second-stage mortality, however, appear to be higher. The only study that examines outcomes following the Norwood procedure and the hybrid procedure in matched high-risk patient cohorts suggests that survival is similar (p4 (Fig. 49.21).

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Congenital mitral valve disease is a developmental malformation of one or more of the components of the mitral valve apparatus, including that portion of left atrial wall immediately adjacent to the mitral anulus that produces stenosis or regurgitation or, occasionally, a combined lesion. It often coexists with other cardiac anomalies, particularly those involving the left-sided cardiac chambers and aorta.

Left atrioventricular valve (AV) anomalies associated with AV septal defects (see Chapter 34), aortic atresia and other forms of hypoplastic left heart physiology (see Chapter 49), various forms of AV discordant connection (see Chapter 55), or transposition of the great arteries (see Chapter 52) are special situations discussed in the chapters describing these conditions. Mitral valve anomalies associated with straddling or univentricular AV connections are described in Chapters 35 and 56, respectively. Regurgitation from mitral valve prolapse as part of the syndrome of myxomatous degeneration is described in Chapter 11.

**HISTORICAL NOTE**

Heterogeneity of congenital mitral valve disease and frequency of its association with other cardiac anomalies make it difficult to trace the historical evolution of knowledge about this entity. However, as early as 1902, Fisher described two cases of congenital disease of the left side of the heart, one of which was a stenotic supravalvar ring. In 1961, parachute mitral valve, another entity in this spectrum, was not described until 1963. In 1962, Creech and colleagues reported repairing congenital mitral regurgitation resulting from a cleft in the posterior leaflet in a 2-year-old girl. Although the child’s condition was
improved by suturing the cleft, moderate mitral regurgitation persisted.\textsuperscript{c10}

**MORPHOLOGY**

The congenital anomaly may involve any component of the mitral apparatus and may result in stenosis with or without regurgitation or in pure regurgitation. Although only one component may be involved, more often the entire valve is affected.\textsuperscript{c2} Congenital mitral stenosis without or with regurgitation may result from supravalvar, anular, or valvar narrowing and may be accentuated by subvalvar obstruction produced by hypertrophied and misplaced papillary muscles or sheets of fused chordae.\textsuperscript{c3} Frequently, stenosis is a result of abnormalities at multiple levels. Although embryologic origins of these complex anomalies are poorly understood, recent studies suggest that abnormal development of a transient left ventricular (LV) structure, a horseshoe-shaped ventricular myocardial ridge, results in various obstructive mitral valve lesions, including parachute mitral valve and formation of asymmetric mitral valves.\textsuperscript{c51} Congenital mitral regurgitation may result from anular dilatation secondary to anterior or posterior leaflet prolapse or to posterior leaflet hypoplasia with chordal shortening. Chordal elongation and valve prolapse may be so severe that chordal rupture can develop even in young children, producing severe regurgitation. Congenital mitral regurgitation may also be produced by clefts, gaps, or perforations in the anterior mitral leaflet, by accessory commissures, or by leaflet hypoplasia at medial or lateral commissures.

**Supravalvar Ring**

A tough fibrous ring may be situated just on the left atrial side of the mitral anulus.\textsuperscript{A4} The pulmonary veins and left atrial appendage enter the left atrium above (proximal to) the ring, in contrast to the situation in cor triatriatum (see Chapter 32). The supravalvar ring may be nonobstructive and an incidental finding, or it may protrude into the orifice, producing a variable degree of obstruction.\textsuperscript{A4,D2} A ring may also occur on the left atrial aspect of the mitral valve leaflets that, when circumferential, prevents their adequate opening, causing obstruction. This lesion may be particularly difficult to identify echocardiographically.

A supravalvar ring is an isolated lesion in about half the cases in which it contributes importantly to death in the first year of life\textsuperscript{D2,S14} (Fig. 50–1). In the other half, it coexists with other cardiac anomalies, particularly with other mitral valve anomalies and with LV outflow tract obstruction.\textsuperscript{S6}

**Mitral Anulus**

The mitral anulus uncommonly is small and obstructive in the absence of severe LV hypoplasia or other valvar abnormalities.\textsuperscript{C3} It may be small but not obviously obstructive, particularly in hearts with coarctation of the aorta.\textsuperscript{R2} The anulus may be enlarged, usually secondary to mitral regurgitation resulting from some other deformity of the valve. However, the basic valvar anomaly leading to regurgitation may be subtle and difficult to identify. Carpentier and colleagues found essentially isolated anular dilatation in 8 (17%) of 47 cases with congenital mitral valve disease, although some deficiency of commissural tissue is implied by their description.\textsuperscript{C3}

**Leaflet Anomalies**

The orifice through the mitral valve is frequently narrowed by congenital absence of one or both commissures, which are replaced by a continuous sheet of leaflet tissue. Small perforations may be present at what is usually a commissure (Fig. 50–2). The leaflets often then take the form of an inverted
Chapter 50  Congenital Mitral Valve Disease

...none. Chordae tendineae may pass from the edges of an accessory commissure to ventricular septum or rudimentary papillary muscles (as was the case in two of five cases reported by Carpentier and colleagues\textsuperscript{C3}), or the cleft may simply represent leaflet deficiency in that area (Fig. 50-4) without chordal support.\textsuperscript{B4,F3}

Rarely, there may be a hole in the anter...
Papillary Muscle Anomalies

There may be a single large papillary muscle with all chordae attaching to it, the so-called parachute valve described first by Schiebler and colleagues and emphasized by Shone and colleagues\(^2,6\) (Figs. 50-6 and 50-7). Usually the chordae are short and thick and limit leaflet movement. This restricts the primary orifice through the opened valve as well as secondary orifices between chordae, resulting in mitral stenosis. In other cases, there is a single large papillary muscle, and near it is a hypoplastic one with only a few chordae attached; the valve orifice is narrowed by the same mechanisms. A parachute valve usually produces only severe stenosis, but it may also produce mitral regurgitation.\(^3\)

Two hypertrophied and abnormally placed contiguous papillary muscles, usually situated posteriorly, are also a cause of subvalvar obstruction.\(^3,4,12\) Obstruction is often further aggravated by coexistence of short, thick chordae and anomalous thick muscular bands.\(^5\) In other cases, there are three or more closely placed and hypoplastic or bulky papillary muscles, a situation in which short, thick chordae are often also present and contribute to stenosis. In all these cases, absence of the normal wide interpapillary distance contributes to obstruction in the mitral pathway.

An anomalous papillary muscle arcade (mitral arcade) formed by a bridge of fibrous tissue running through the free aspect of the anterior mitral leaflet, between the anterolateral and posteromedial papillary muscles, may produce mitral regurgitation\(^3,2,1\) (Fig. 50-8).

Coexisting Cardiac Anomalies

Patients with congenital mitral regurgitation often have coexisting cardiac anomalies, but they tend to be less severe than in congenital mitral stenosis (Table 50-1).

Congenital mitral stenosis is rarely an isolated malformation. In about 30% of cases, it coexists with ventricular septal defect (VSD). In more than 50%, it coexists with one or
of patients demonstrate congenital mitral valve disease.\textsuperscript{3} All of this supports considering congenital mitral valve disease as an important component in the entity known as hypoplastic left heart physiology (see Chapter 49).

RARE COEXISTENCE OF A STENOSONG SUPRAVALVAR RING WITH TETRALOGY OF FALLOT IS NOTEWORTHY BECAUSE, IF UNDETECTED, IT MAY CAUSE DEATH AFTER TETRALOGY REPAIR.\textsuperscript{5,6} Congenital mitral valve disease and subaortic stenosis may rarely coexist with subpulmonary stenosis and intact ventricular septum, subpulmonary stenosis and VSD, or valvar pulmonary stenosis.\textsuperscript{15,23}

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

#### Symptoms and Signs

**Isolated Mitral Valve Disease**

Symptoms and clinical signs are identical to those of acquired mitral valve disease, the congenital etiology being apparent only when presentation is in infancy or early childhood and there is no rheumatic history (see Clinical Features and Diagnostic Criteria in Section I of Chapter 11). Symptoms of pulmonary venous hypertension include dyspnea, orthopnea or paroxysmal nocturnal dyspnea, and recurrent pulmonary infection.\textsuperscript{15} Pulmonary hypertension is usually present in severe lesions, terminating in heart failure, often with peripheral and central cyanosis.\textsuperscript{18}

Mitral stenosis is associated with a prominent apical mid-diastolic murmur, sometimes with presystolic accentuation, and there may be an opening snap, although the morphologic features commonly resulting in limitation of leaflet movement make this less common than in acquired mitral stenosis.\textsuperscript{14,21} Mitral regurgitation is evidenced by an apical pansystolic murmur radiating to the axilla, frequently with a third heart sound or a short mid-diastolic murmur and LV overactivity. When there is pulmonary hypertension, the second heart sound is accentuated and there is a right ventricular lift.

**Mitral Valve Disease and Left Ventricular Outflow Tract Obstruction**

Unless a VSD or patent ductus arteriosus is also present, the mitral signs are usually clinically diagnostic, particularly when the only additional important site of obstruction is a

### Table 50-2  Associated Cardiac Anomalies in Infants with Congenital Mitral Valve Stenosis\textsuperscript{a}

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>No.</th>
<th>% of 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Subaortic, subvalvar stenosis</td>
<td>47</td>
<td>55</td>
</tr>
<tr>
<td>Coarctation</td>
<td>33</td>
<td>39</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>28</td>
<td>33</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>21</td>
<td>25</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>21</td>
<td>25</td>
</tr>
<tr>
<td>DORV</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Small left ventricle</td>
<td>15</td>
<td>18</td>
</tr>
<tr>
<td>Tetralogy of Fallot</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

Data from Moore and colleagues.\textsuperscript{5,6}

\textsuperscript{a}Age 7.1 ± 6.4 months; weight 5.6 ± 2.3 kg.

Key: DORV, Double outlet right ventricle.

---

Figure 50-8  Specimen of a heart with mitral arcade producing mitral regurgitation. There is a thick fibrous band stretching between tips of the two papillary muscles along edge of anterior leaflet. Key: A, Anterior mitral leaflet; ALP, anterolateral papillary muscle; FW, left ventricular free wall; LAA, left atrial appendage; P, posterior mitral leaflet; PFO, patent foramen ovale; PMP, portion of posteromedial papillary muscle; S, muscular septum.
coarctation. When there is severe congenital aortic stenosis, the mitral lesion, unless also severe, may not be clinically obvious, although it worsens the clinical presentation.

Electrocardiography

Electrocardiographic (ECG) evidence of left atrial hypertrophy of greater degree than is usually found in the coexisting cardiac anomaly suggests associated congenital mitral valve disease. Right ventricular hypertrophy is evident on the ECG when there is the usual raised pulmonary vascular resistance and right atrial enlargement, whereas LV hypertrophy is evident on the ECG when there is severe mitral regurgitation or associated LV outflow tract obstruction. Atrial fibrillation is rare.

Chest Radiography

Left atrial enlargement out of proportion to that usually present in any coexisting cardiac anomaly is the most important clue in the chest radiograph of the possible presence of congenital mitral valve disease. There is cardiac enlargement regardless of whether the disease is isolated or complex. Signs of pulmonary venous hypertension and occasionally overt pulmonary edema may be present in severe cases, but pulmonary plethora from a coexisting left-to-right shunt may obscure these signs.

Two-Dimensional Echocardiography

Two-dimensional echocardiography combined with Doppler interrogation can provide a complete analysis of the morphology and function of congenitally abnormal mitral valves \(^{35,64,89,74,72}\) (Fig. 50-9, A-F). However, diagnosis by echocardiography of some forms of congenital mitral valve disease, especially supravalvar ring and double orifice mitral valve, requires considerable care and can easily be missed. \(^{35,54}\) Three-dimensional echocardiography can provide important morphologic details that may not be visible with standard imaging (see Fig. 50-2).

Cardiac Catheterization and Cineangiographic Studies

Cardiac catheterization and cineangiographic studies are often performed to evaluate possible associated lesions and define the degree of pulmonary vascular disease. \(^{2}\) Morphology of the congenitally abnormal valve can be further evaluated by its cineangiographic appearance. \(^{34}\)

Computed Tomography and Magnetic Resonance Imaging

Computed tomography (CT) plays a limited role in evaluating the congenitally abnormal mitral valve, but magnetic resonance imaging (MRI) can provide important morphologic information that may supplement that provided by echocardiography (see Figs. 50-5 and 50-7). In addition, MRI can provide functional information such as quantification of mitral regurgitant fraction and valve area in diastole (Fig. 50-10).

NATURAL HISTORY

Congenital mitral valve disease is a rare congenital cardiac anomaly, occurring in 0.6% of autopsied patients with congenital heart disease and 0.21% to 0.42% of clinical cases of congenital heart disease. \(^{2}\)

Natural history is highly variable and depends most importantly on severity of resultant stenosis or regurgitation and on type and severity of coexisting lesions, rather than on the particular morphologic mitral valve lesion itself. For example,
in one study, parachute mitral valve was associated with 95% freedom from mitral valve surgery at 6 months and 80% freedom at 10 years. However, associated cardiac defects were present in essentially all cases, particularly LV outflow tract abnormalities, atrial septal defect, VSD, coarctation, and hypoplastic LV; these strongly influence natural history. In another study, only 4% of patients with parachute mitral valve required a procedure on the valve, with intervention dominated by associated cardiac anomalies. Parachute mitral valve presenting in the adult is rare but does occur and is more likely to be an isolated anomaly than when diagnosed in infants and children. Nine patients have been identified in the literature over the past 50 years; three were asymptomatic without important hemodynamic abnormalities, three presented with stenosis, and three with regurgitation.

Isolated congenital mitral stenosis usually is severe and often produces symptoms and death if untreated during the first 4 to 5 years of life. When congenital mitral stenosis coexists with other important cardiac anomalies, symptoms occur even earlier. When it is associated with other components of hypoplastic left heart physiology, severe symptoms often develop during the first year of life.

Isolated congenital mitral regurgitation is often only moderate in severity in early life, and about half the patients with it do not show development of important symptoms. Symptoms and need for intervention usually come earlier when it coexists with other important cardiac anomalies.

**TECHNIQUE OF OPERATION**

The overall approach to the neonate, infant, and young child is different from that for older patients. Preservation of the native valve is of paramount importance, even if it means accepting residual valve disease that might otherwise not be
considered acceptable in a fully grown patient. The valve must be carefully studied preoperatively and at operation, seeking ways in which it can be repaired rather than replaced. Specific techniques such as rectangular resection, which if unsuccessful will result in obligatory valve replacement as a fallback option, should generally be avoided. Some techniques used for congenital mitral valve disease are the same as those used for older patients with acquired disease, and these are described for both mitral stenosis and regurgitation under Technique of Operation in Section I of Chapter 11. However, many techniques are specific for congenital abnormalities such as supramitral ring (Fig. 50-11), mitral arcade (Fig. 50-12), and single papillary muscle (Fig. 50-13). In general, repair is possible in 50% to 80% of patients. Additional comments specific to congenital mitral valve disease follow.

Repair of Congenital Mitral Stenosis

When the valve leaflets are fused into one and are stenotic, leaflet incisions may be made in the areas in which commissures would be expected to have developed. Consideration is given to inserting polyester or polytetrafluoroethylene (PTFE) chordae (see “Repair of Chordae” later in this chapter). At times, fused papillary muscles or chordae may be split or partly excised in an attempt to enlarge the orifice (see Fig. 11-7 in Chapter 11).

Because these maneuvers may result in regurgitation, immediately after discontinuing cardiopulmonary bypass (CPB), a regurgitant mitral jet may first be detected by palpating the posterior left atrial wall and then the superior left atrial wall beneath the aorta. Intraoperative transesophageal echocardiography (TEE) is invaluable at this stage in determining that mitral valve function is sufficiently good to avoid valve replacement. If TEE documents important regurgitation accompanied by high left atrial pressure and a suboptimal hemodynamic state, CPB is reestablished and the valve repaired further or replaced; otherwise, early and late results are unsatisfactory. If hemodynamics are acceptable but regurgitation is moderate to severe, the decision to replace the valve is complex. Importantly, the smaller the patient and mitral anulus, the more likely will be the tendency to

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**Figure 50-10** Short-axis view at level of mitral valve orifice during diastole: high-velocity mitral inflow is seen as white. During systole, regurgitant jet can be visualized and analyzed, and a regurgitant fraction can be calculated as a percentage of inflow. Mitral orifice area in diastole can be calculated by planimetry and is expressed in square centimeters. Two papillary muscles are demonstrated. (From Hamilton-Craig and colleagues.)

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**Figure 50-11** Repair of supramitral ring. A, Long-axis depiction of left heart showing left atrium, left ventricle, and mitral and aortic valves. A supramitral ring (SMR) is present on mitral valve. B, Close-up cutaway view of mitral valve and anulus showing SMR. Ring can be cut away circumferentially using sharp dissection as shown here, but in some cases, it can be peeled away bluntly once the plane between underlying endocardium and ring tissue is established. Ring may be discrete (as shown here) but may also extend to a variable degree onto mitral leaflets, sometimes extending across length of leaflet onto chordal structures, causing thickening, contraction, and immobility. In this case, using both sharp and blunt dissection, as much of the abnormal tissue as possible is removed from leaflet without damaging underlying leaflet tissue. (From Chauvaud.)
accept the result, recognizing that this will be a temporary solution.

Repair of Congenital Mitral Regurgitation

The mitral valve is carefully examined with the possible pathologic bases for congenital mitral regurgitation clearly in mind, because these determine the most appropriate type of operation. Repair based on pathology is performed whenever possible. Specific maneuvers include anuloplasty, repair of cleft leaflet, various forms of chordal repair including shortening, lengthening, and resuspension of ruptured chords, partial leaflet resection, chordal replacement, and partial commissural closure (see Technique of Operation in Section I of Chapter 11).

Anuloplasty

Occasionally, anular dilatation is the dominant pathology even in young children, but it is usually associated with some abnormal thickening and prolapse of a billowing anterior leaflet. If a reasonable anterior leaflet without ruptured chordae is present, anuloplasty is indicated. Anuloplasty is also appropriate when there is marked hypoplasia or near absence of the posterior leaflet, which probably initially was responsible for the regurgitation and subsequent anular

Figure 50-12  Repair of mitral arcade. A, En face view of mitral valve with arcade formation of subvalvar mechanism. Note fused, or hammock-like, nature of papillary muscles, and crowded thickened chordal arrangement. B-E, Repair involves splitting the lateral attachments between chords, and the papillary muscle between chordal groups. (From Chauvaud.)

Figure 50-13  Repair of parachute mitral valve. A, Note single papillary muscle with all chordal structures attaching to it. B, Repair involves splitting the papillary muscle between the two large chordal groups supporting each commissure. Commissural fusion and lateral attachments of chords may also be present, requiring commissurotomy and splitting of lateral chordal attachments. (From Chauvaud.)
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competence. If there is insufficient leaflet tissue, the cleft closure can be augmented with a patch (Fig. 50-15). A posteromedial (Wooler type) anuloplasty using interrupted simple sutures of monofilament nonabsorbable material, or a Reed anuloplasty, may be helpful.

Mitral Valve Replacement

When repair is not possible, mitral valve replacement is performed (see “Mitral Valve Replacement” under Technique of Operation in Section I of Chapter 11). Stent-mounted glutaraldehyde-preserved porcine xenografts are not appropriate in infants and children because of their rapid degeneration and bulk (see “Reoperation,” later). The favorable orifice-to-anulus ratio of the St. Jude Medical valve (see “Choice of Device for Valve Replacement” under Indications for Operation, Selection of Technique, and Choice of Device
dilatation. Following anuloplasty, the mitral valve is essentially converted to a monoleaflet valve.

Although use of an anuloplasty ring is optimal in adults, it is not used in infants and children because it precludes growth of the anulus. Thus, a technique such as the Reed asymmetric measured anuloplasty is chosen (see Fig. 11-15 in Chapter 11).

Repair of Chordae

When regurgitation is caused by ruptured chordae to less than half the posterior leaflet, a rectangular excision and leaflet repair, usually combined with anuloplasty, may be indicated (see Figs. 11-9 and 11-10 in Chapter 11). A result similar to that obtained with rectangular excision can be achieved by simply folding the unsupported component of the leaflet on itself and securing the folds with sutures, rather than excising the leaflet tissue. If the repair attempt is unsuccessful, the folded leaflet tissue can be taken down or unfolded, allowing further valve-sparing reparative maneuvers to be attempted.

A sliding plasty has been used by Carpentier and colleagues to correct congenital elongation of chordae to part of a papillary muscle. The papillary muscle is incised longitudinally and reconstructed by suturing the halves together asymmetrically, with the part attached to the elongated chordae fixed at a lower level. Elongation of all chordae to a papillary muscle may be treated by chordal shortening (Fig. 50-14). The extremity of the papillary muscle is incised longitudinally, redundant chordae buried in the trench thus created, and the papillary muscle closed firmly around them by sutures. In these situations, placement of polyester or PTFE chordae can also be useful (see “Repair of Mitral Regurgitation” under Technique of Operation in Section I of Chapter 11).

Chordal repair often involves splitting or separating papillary muscles as well as leaflet commissures. An approach through the LV apex has been described but is not recommended. Use of artificial chordae for mitral valve reconstruction in children has been described; expanded PTFE sutures are employed in the technique, and early and midterm results have been encouraging.

Repair of Cleft Mitral Leaflet

When sufficient anterior or posterior mitral leaflet tissue is present on both sides of a cleft leaflet, the cleft is sutured closed with interrupted simple sutures to achieve competence. If there is insufficient leaflet tissue, the cleft closure can be augmented with a patch (Fig. 50-15). A posteromedial (Wooler type) anuloplasty using interrupted simple sutures of monofilament nonabsorbable material, or a Reed anuloplasty, may be helpful.

Mitral Valve Replacement

When repair is not possible, mitral valve replacement is performed (see “Mitral Valve Replacement” under Technique of Operation in Section I of Chapter 11). Stent-mounted glutaraldehyde-preserved porcine xenografts are not appropriate in infants and children because of their rapid degeneration and bulk (see “Reoperation,” later). The favorable orifice-to-anulus ratio of the St. Jude Medical valve (see “Choice of Device for Valve Replacement” under Indications for Operation, Selection of Technique, and Choice of Device

Figure 50-14  Repair of elongated chordae by chordal shortening. A, Papillary muscle is split along its length between elongated chord and normal chords. B-C, Tip of papillary muscle attached to elongated chord is buried into base of papillary muscle, using a pledgeted suture such that chord is now of proper length. D, Papillary muscle is sutured closed. (From Chauvaud.)

Figure 50-15  Repair of mitral valve cleft. A, Cleft is identified over its full extent, with its central limit defined by the first chordal attachments on the leaflet normal edge. A simple suture is placed precisely at this point to appropriately align cleft. B, Simple sutures are placed to close remainder of cleft. C, If leaflet deficiency is present (as shown here), a patch is used. D, Patch has been secured in place using multiple interrupted sutures, again paying close attention to alignment of edges. (From Chauvaud.)
SPECIAL FEATURES OF POSTOPERATIVE CARE

The usual practices and protocols are used (see Chapter 5). Patients, even infants, who receive mitral valve replacement with prosthetic valves are maintained on anticoagulation with warfarin using the same general protocols as in adults (see “Special Features of Postoperative Care” in Section I of Chapter 11). Small valves in infants may be prone to dysfunction, either because of thrombosis or leaflet immobility caused by adjacent tissue at or near the small anulus. Placing a left atrial pressure catheter at the time of operation is mandatory, and using intraoperative and postoperative echocardiography to document normal movement of both valve leaflets is important in managing these patients.

RESULTS

Survival

Early (Hospital) Death

In the past, early mortality after operation for mitral valve disease in the pediatric age range was highly variable, ranging between 1% and 50%. In most reports after 1990, mitral valve surgery in infants and children has a consistently low mortality (0%-10%) for both repair and replacement (Table 50-3).

Despite these encouraging reports, the role of patient selection in determining early outcome remains unclear in these complex anomalies. In a series of 31 severely symptomatic patients with mitral stenosis requiring intervention within the first 2 years of life, 18 underwent balloon dilatation and 13 surgical intervention. Early mortality for the surgical patients was 31% (CL 16%-49%). In a series of seven patients presenting within the first year of life with mitral regurgitation, four required surgical intervention, and three were managed medically. Two of the four surgical patients died in hospital; both required urgent operation. The two survivors underwent elective operation. Yet, in another study of 17 patients presenting with mitral regurgitation, mitral valve repair was performed in all, and there was no early or late mortality. Mean age was 11 months, with 10 patients younger than age 1 year and 15 in heart failure (5 of whom required preoperative mechanical ventilation).[316]

Time-Related Survival

In the early surgical era, only about 50% of patients receiving valve repair or replacement for congenital mitral valve disease were alive 10 years later. Many deaths were related to coexisting cardiac anomalies and reoperation. Current results are better. In reports after 1990, 5- and 10-year survival appears to be between 80% and 100% (Table 50-4). Notably, there has been little or no further improvement in late survival during the last 2 decades.

Table 50-3 Hospital Mortality after Operation for Congenital Mitral Valve Disease

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL (%)</th>
<th>Age</th>
<th>Anomaly</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aharon et al.[61]</td>
<td>1994</td>
<td>79</td>
<td>3</td>
<td>3.8</td>
<td>1.7-7.5</td>
<td>2 m-17 y</td>
<td>5 MS, MR</td>
</tr>
<tr>
<td>Chauvaud et al.[66]</td>
<td>1998</td>
<td>145</td>
<td>7</td>
<td>4.8</td>
<td>3.0-7.4</td>
<td>0.17-12 y; 19 &lt; 2 y</td>
<td>MR</td>
</tr>
<tr>
<td>Barbero-Marcial et al.[63]</td>
<td>1993</td>
<td>12</td>
<td>0</td>
<td>0</td>
<td>0-15</td>
<td>2-74 m</td>
<td>MS</td>
</tr>
<tr>
<td>Harada et al.[61]</td>
<td>1990</td>
<td>28</td>
<td>0</td>
<td>0</td>
<td>0-6.7</td>
<td>4 m-15 y</td>
<td></td>
</tr>
<tr>
<td>Honjo[65]</td>
<td>2006</td>
<td>17</td>
<td>0</td>
<td>0</td>
<td>0-11</td>
<td>3 m-13 y</td>
<td>MR</td>
</tr>
<tr>
<td>Matsumoto et al.[46]</td>
<td>1999</td>
<td>16</td>
<td>0</td>
<td>0</td>
<td>0-11</td>
<td>5 m-13 y</td>
<td></td>
</tr>
<tr>
<td>McElhinney et al.[66]</td>
<td>2005</td>
<td>108</td>
<td>7</td>
<td>6.5</td>
<td>4.1-9.9</td>
<td>1 m-18 y</td>
<td>78 MS, 46 MR, 28 PMV, 11 DOMV</td>
</tr>
<tr>
<td>Balloon valvuloplasty</td>
<td></td>
<td>64</td>
<td>3</td>
<td>4.7</td>
<td>2.1-9.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical valvuloplasty</td>
<td></td>
<td>33</td>
<td>1</td>
<td>3.0</td>
<td>0.5-9.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Valve replacement</td>
<td></td>
<td>11</td>
<td>3</td>
<td>27</td>
<td>13-47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Murakami et al.[69]</td>
<td>1998</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0-47</td>
<td>1.4 y, 4.6 y, 5.1 y</td>
<td></td>
</tr>
<tr>
<td>Oppido et al.[62]</td>
<td>2008</td>
<td>71</td>
<td>3</td>
<td>4.2</td>
<td>1.9-8.3</td>
<td>3 d-21 y</td>
<td>11 MS, 60 MR</td>
</tr>
<tr>
<td>Stellin et al.[61]</td>
<td>2010</td>
<td>93</td>
<td>7</td>
<td>7.5</td>
<td>4.7-11</td>
<td>5.8 ± 4.9, 13 &lt; 12 m</td>
<td>45 MS, 48 MR</td>
</tr>
<tr>
<td>Sugita et al.[63]</td>
<td>2001</td>
<td>41</td>
<td>0</td>
<td>0</td>
<td>0-4.5</td>
<td>4 &lt; 12 m</td>
<td>MR</td>
</tr>
<tr>
<td>Uva et al.[61]</td>
<td>1995</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0-9.2</td>
<td>&lt;1 y</td>
<td>10 MR, 10 MS</td>
</tr>
<tr>
<td>Yoshimura et al.[72]</td>
<td>1999</td>
<td>56</td>
<td>2</td>
<td>3.6</td>
<td>1.2-8.3</td>
<td>3 m-15 y</td>
<td>Both MS and MR</td>
</tr>
<tr>
<td>TOTAL</td>
<td></td>
<td>689</td>
<td>29</td>
<td>4.2</td>
<td>3.4-5.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Mitral valve replacement only.
* Artificial chordae repair only.
* Not mutually exclusive.
* Nineteen repairs, 1 replacement.
* Thirty-six repairs, 30 replacements.

Key: DOMV, Double orifice mitral valve; m, months; MR, mitral regurgitation; MS, mitral stenosis; PMV, parachute mitral valve; y, years.
Table 50-4  Time-Related Survival after Operation for Congenital Mitral Valve Disease

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>Operation</th>
<th>n</th>
<th>Follow-up Interval</th>
<th>Survival (%) or Mean ± SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aharon et al.</td>
<td>1994</td>
<td>Repair</td>
<td>79</td>
<td>1, 2, 5 y</td>
<td>94, 84, 82</td>
</tr>
<tr>
<td>Chauvaud et al.</td>
<td>1998</td>
<td>Repair</td>
<td>138</td>
<td>10 y</td>
<td>86 ± 8</td>
</tr>
<tr>
<td>Chauvaud et al.</td>
<td>1998</td>
<td>Replacement</td>
<td>7</td>
<td>10 y</td>
<td>91 ± 30</td>
</tr>
<tr>
<td>Harada et al.</td>
<td>1990</td>
<td>Replacement</td>
<td>28</td>
<td>10 y</td>
<td>90</td>
</tr>
<tr>
<td>Honjo et al.</td>
<td>2006</td>
<td>Repair</td>
<td>17</td>
<td>Median 95 m</td>
<td>100</td>
</tr>
<tr>
<td>Matsumoto et al.</td>
<td>1999</td>
<td>Repair</td>
<td>16</td>
<td>26 m</td>
<td>100</td>
</tr>
<tr>
<td>McElhinney et al.</td>
<td>2005</td>
<td>Balloon valvuloplasty</td>
<td>33</td>
<td>1, 5, 10 y</td>
<td>85, 80, 77</td>
</tr>
<tr>
<td>McElhinney et al.</td>
<td>2005</td>
<td>Surgical valvuloplasty</td>
<td>33</td>
<td>1, 5, 10 y</td>
<td>95, 85, 85</td>
</tr>
<tr>
<td>Oppido et al.</td>
<td>2008</td>
<td>Repair</td>
<td>71</td>
<td>5 y</td>
<td>94 ± 2.8</td>
</tr>
<tr>
<td>Stellin et al.</td>
<td>2010</td>
<td>Repair</td>
<td>93</td>
<td>5, 10, 20, 30</td>
<td>85, 85, 75</td>
</tr>
<tr>
<td>Sugita et al.</td>
<td>2001</td>
<td>Partial plication</td>
<td>41</td>
<td>Median 15 y</td>
<td>100</td>
</tr>
<tr>
<td>Uva et al.</td>
<td>1995</td>
<td>Artificial chords, 19 repairs, 1 replacement</td>
<td>20</td>
<td>7 y</td>
<td>94 (CL 88-100)</td>
</tr>
<tr>
<td>Yoshimura et al.</td>
<td>1999</td>
<td>Repair</td>
<td>36</td>
<td>10 y</td>
<td>87 (95% CL 75-99)</td>
</tr>
<tr>
<td>Yoshimura et al.</td>
<td>1999</td>
<td>Replacement</td>
<td>30</td>
<td>10 y</td>
<td>90 (95% CL 77-100)</td>
</tr>
</tbody>
</table>

Key: CL, Confidence limits; m, months; SE, standard error; y, years.

Incremental Risk Factors for Premature Death

Incremental risk factors have been identified in many individual series, but there is little consistency among studies, other than younger age, era of surgery, and coexisting cardiac anomalies—all of which appear in multiple analyses. In the analysis of 79 children undergoing mitral valve repair by Aharon and colleagues, no incremental risk factors for early or late death could be identified. Incremental risk factors for early death have also been identified in one study involving predominantly surgical valve replacement. Schaverien and colleagues and Marino and colleagues both report that associated cardiac anomalies are a risk factor for death in patients with parachute mitral valve, even when no surgical procedure on the valve itself is performed. Calderone and colleagues, reporting a multicenter study of 139 patients undergoing valve replacement, identified AV septal defect and Shone’s complex as risk factors. Calderone and colleagues, reporting a multicenter study of 139 patients undergoing valve replacement, identified AV septal defect and Shone’s complex as risk factors. Calderone and colleagues, reporting a multicenter study of 139 patients undergoing valve replacement, identified AV septal defect and Shone’s complex as risk factors. Calderone and colleagues, reporting a multicenter study of 139 patients undergoing valve replacement, identified AV septal defect and Shone’s complex as risk factors.

Preoperative Functional Class

Patients in higher New York Heart Association (NYHA) functional classes are at a considerably greater risk of dying after operation, particularly early postoperatively (Table 50-5). Preoperative cardiothoracic ratio > 0.6 has also been identified as a risk for midterm death after valve repair. This is likely a surrogate for lower functional class.

Age

A number of studies identify younger age as a risk factor for death after either valve repair or replacement. Most studies categorize age groups into younger than 2 years or younger than 1 year. Age younger than 2 years was identified as a risk in one study involving predominantly surgical repair and balloon valvotomy. Age younger than 2 has also been identified as a risk factor following mitral valve replacement. Prifti and colleagues and Selamet Tierney and colleagues identified age younger than 1 year as a risk for midterm death after valve repair. This is likely a surrogate for lower functional class.

Coexisting Cardiac Anomalies

Hypoplastic left heart syndrome has a large influence on survival. However, Bolling and colleagues report no deaths (0%; CL 0%-6%) among 30 patients undergoing their first operation for Shone syndrome, although among 17 undergoing a second operation, 4 (24%; CL 12%-39%) died. Prifti and colleagues report that associated cardiac anomalies are a risk for both reoperation and midterm death after valve repair.

Mitrval Regurgitation versus Stenosis; Repair versus Replacement

Neither of these factors can be definitively related to the probability of death early or late postoperatively.
There is conflicting evidence regarding whether survival is worse after mitral valve replacement than after repair; furthermore, the evidence that can be cited to address this question is indirect. This is understandable for several reasons. First, there are no reports randomizing the two techniques, and second, it is generally acknowledged that repair is preferable to replacement in small patients because of growth reasons, thereby introducing a strong selection bias. One report shows 10-year survival of only 51% (Fig. 50-16) for patients undergoing mitral valve replacement when the primary diagnosis was mitral regurgitation; however, only 7 of the 145 patients underwent initial mitral valve replacement. The study by McElhinney and colleagues was similar, with only 11 of 108 patients undergoing initial valve replacement; replacement carried a higher mortality. Another report shows that for a primary diagnosis of mitral stenosis, initial mitral valve replacement was an independent predictor of worse survival over time. However, another study examining patients with primary diagnoses of either stenosis or regurgitation showed no difference between repair and replacement (Fig. 50-17). Other studies with larger numbers of patients undergoing mitral valve replacement have shown that replacement, relative to repair, is not an incremental risk factor for death. There are several large series reporting outcomes exclusively for mitral valve repair or replacement. Repair series tend to show better outcome than replacement series. This is not surprising, for the same reasons stated in the previous paragraph. In one report of 71 repairs, outstanding early and midterm outcome (4.2% early mortality [CL 1.9%-8.3%] and 94% 5-year survival) was demonstrated. In another report of 94 patients, early mortality was 8.5% (CL 5.5%-13%) and 5-year survival 89%. Two separate series of mitral repair exclusively for mitral regurgitation showed no early or late mortality. Both series have fewer associated cardiac anomalies and simpler anomalies than most series with a mixture of stenosis and regurgitation patients.

A number of studies exclusively examine valve replacement. Early mortality ranges from 11% to 36% according to a review by Alsoufi and colleagues, which examined 13 recent institutional series. Furthermore, from the same review, early mortality is even higher in patients younger than age 2: up to 52%. In a multicenter study of 139 patients undergoing replacement, 5-year survival was 75% overall, but survival was strongly affected by the ratio of valve size to patient weight, with higher size/weight ratio associated with decreased survival (Fig. 50-18). In a single-institution study of valve replacement in 25 patients between 1996 and 2006, 5-year survival was 83%.

### Table 50-5 Hospital Deaths after Operation for Congenital Mitral Valve Disease, According to Preoperative New York Heart Association Functional Class

<table>
<thead>
<tr>
<th>NYHA Functional Class</th>
<th>UAB Hospital Deaths</th>
<th>GLH Hospital Deaths</th>
<th>Total Hospital Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>I</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>12</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>III</td>
<td>7</td>
<td>1</td>
<td>14</td>
</tr>
<tr>
<td>IV</td>
<td>10</td>
<td>4</td>
<td>40</td>
</tr>
<tr>
<td>V</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>37</td>
<td>7</td>
<td>19</td>
</tr>
</tbody>
</table>

P (logistic) = 0.01

*Patients are from the surgical experience at GLH and UAB, 1967 to 1984.

NYHA class V indicates emergency operation for shock or metabolic acidosis. Key: CL, 70% confidence limits; NYHA, New York Heart Association.

![Figure 50-16](https://example.com/figure5016.png)

**Figure 50-16** Survival after operation for mitral valve regurgitation in children, stratified by type of operation. Patient cohort in replacement group is small. Numbers along horizontal axis are patients at risk. (From Chauvaud and colleagues)

There is conflicting evidence regarding whether survival is worse after mitral valve replacement than after repair; furthermore, the evidence that can be cited to address this question is indirect. This is understandable for several reasons. First, there are no reports randomizing the two techniques, and second, it is generally acknowledged that repair is preferable to replacement in small patients because of growth reasons, thereby introducing a strong selection bias.
Reoperation Following Mitral Valve Repair

Early and midterm freedom from reoperation following mitral valve repair in the current era is high but decreases substantially over time. In one study, freedom from reoperation was 97% at 2 years and 83% at 8 years\(^1\) (Fig. 50-19). In another, it was 95% (95% CL 90%-98%) at 1 year, 80% (95% CL 71%-87%) at 10 years, and 67% (95% CL 52%-80%) at 15 years.\(^6\) In still another, it was 76% (CL 70%-82%) after 5 years.\(^2\)

Masuda and colleagues, however, reported no early mortality (0%; CL 0%-5.0%) and 5 late deaths in 37 patients undergoing valve replacement.\(^3\)

Similarly, for patients undergoing valve replacement after 1990, Alexiou and colleagues reported an early mortality of 3.6% (1 of 28; CL 0.6%-12%) and 10-year survival of 86%.\(^2\)

Reoperation

In the past, many reoperations were required because of degeneration of bioprostheses. This is part of the incremental risk of young age on bioprosthesis degeneration, particularly in older children who have little remaining growth potential—first, because mechanical prostheses rather than bioprostheses are used when replacement is necessary; and second, because less-than-perfect repairs are now considered unacceptable.

Reoperation may take one of several forms: repeat repair of a previously repaired valve, replacement of a previously repaired valve, replacement of a previously placed prosthesis, or revision and salvage of a previously placed prosthesis.
Other series examining patients undergoing first valve-replacement surgery at younger than 6 years of age show freedom from re-replacement at 5 years in the range of 70% to 80%, and at 10 years in the range of 25% to 60%.82,1,94

Reoperation generally suffices because a prosthesis two to three times larger can usually be inserted.2 In older children receiving larger initial valves (≥23 mm), 10- and 15-year freedom from re-replacement is 83% and 83%, respectively.2

**Influence of Young Age at Operation**

Reoperation was more frequent in a series of 20 patients with mitral valve disease undergoing operation before age 1 year.107

Six early reoperations were performed in five patients, with mitral valve replacement in four, a second valve repair in one, and a mechanical prosthesis thrombectomy in one. Late reoperations on the mitral valve were performed five times, with mitral valve repair in two and replacement in three. Overall freedom from reoperation was 58% (CL 47%-69%) at 7 years, and was similar for patients with an original diagnosis of mitral regurgitation and stenosis (Fig. 50-21). As noted under “Reoperation Following Mitral Valve Replacement,” in a multicenter study of mechanical prostheses in a cohort of patients younger than age 5, younger age at first valve placement predicted shorter prosthesis longevity.101

![Figure 50-21](image-url) **Figure 50-21** Freedom from reoperation among 20 patients (10 with mitral regurgitation and 10 with mitral stenosis) undergoing surgical correction within first year of life. (From Uva and colleagues.101)

**Reoperation and Use of Artificial Chordae Tendineae**

In 16 patients undergoing mitral valve repair using artificial chordae tendineae, no reoperations were required during follow-up of up to 26 months.44

**Functional Result**

Most patients who have had a reoperative operation for congenital mitral stenosis have a lessened diastolic gradient after repair but continue to have a residual gradient up to about 10 mmHg.68 An exception is isolated supravalvar ring, in which complete relief of the diastolic gradient may be obtained.69,81,101

Most patients with either congenital mitral stenosis or regurgitation have at least some regurgitation after repair. Carpentier and colleagues reported that in 22 of 34 such patients, there was an apical systolic murmur late postoperatively, and only 7 of the 34 showed important decrease in heart size.68 Of 12 patients recatheterized, 7 had moderate or severe regurgitation. Flege and colleagues reported a virtually complete repair in only 4 of 13 patients with congenital mitral regurgitation.107

At follow-up to 15 years, 85% to 100% of patients are in NYHA functional class I81,9,68,103,101,1 (Table 50-6). Among patients undergoing repair for mitral valve regurgitation, follow-up echocardiography commonly reveals some regurgitation of mild to moderate degree68,101 (see Table 50-6). However, more recent reports suggest improving functional results (see Table 50-6). Among those undergoing mitral valve repair for stenosis, important residual stenosis is uncommon.81,11

In the series of 33 late-surviving patients following mitral valve repair in whom no reoperation was performed, Yoshimura and colleagues found that eight patients had grade 1+/6+ or 2+/6+ systolic murmurs with echocardiographic findings of trivial or mild mitral regurgitation.107

The hemodynamic state after replacement of a congenitally abnormal mitral valve depends on type and size of the replacement device used (see Table 11-9 in Chapter 11). In general, hemodynamic state and valve function are satisfactory unless a device complication develops. In echocardiographic studies by Uva and colleagues, among patients receiving prosthetic mitral valves, transprosthesis gradient was 6.2 ± 3.7 mmHg.56

Prosthetic valves in children have resulted in no higher incidence of thromboembolism and complications from anticoagulation with warfarin than in adults.66,102 The possible exception to this may be with use of very small mechanical

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**Table 50-6** Functional and Hemodynamic Status after Operations for Congenital Mitral Valve Disease

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
<th>Average Follow-up Time Mean (±SD)</th>
<th>NYHA Class I (%)</th>
<th>Residual or Recurrent Mitral Regurgitation after Repair by Echocardiography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aharon et al.51</td>
<td>79</td>
<td>4 ± 2.5 y</td>
<td>98</td>
<td>9% moderate, 9% severe</td>
</tr>
<tr>
<td>Chauvaud et al.66</td>
<td>145</td>
<td>9 ± 7 y</td>
<td>85</td>
<td>12%</td>
</tr>
<tr>
<td>Barbero-Marcial et al.81</td>
<td>12</td>
<td>24 ± 15 m</td>
<td>91</td>
<td>17% moderate MR, 0% MS</td>
</tr>
<tr>
<td>Harada et al.103</td>
<td>28</td>
<td>4.2 ± 2.8 y</td>
<td>100</td>
<td>Valve replacement</td>
</tr>
<tr>
<td>Uva et al.101</td>
<td>20</td>
<td>68 ± 43 m</td>
<td>95</td>
<td>10% moderate MR</td>
</tr>
<tr>
<td>Yoshimura et al.107</td>
<td>33</td>
<td>92 m</td>
<td>100</td>
<td>6% moderate MR</td>
</tr>
</tbody>
</table>

Key: m, Months; MR, mitral regurgitation; MS, mitral stenosis; NYHA, New York Heart Association; SD, standard deviation; y, years.
prostheses (15 - to 17-mm diameter) placed in the supraanular position in infants. Information regarding this observation is, however, anecdotal.

**INDICATIONS FOR OPERATION**

In view of its natural history, severe symptoms and signs of important pulmonary venous hypertension are an indication for prompt operation in infants with congenital mitral valve disease. A reparative operation is indicated if feasible. These same indications prevail in children and young adults. When symptoms are mild or even moderate, operation is delayed in the hope that when it becomes necessary, and if valve replacement is required, an adult-sized device can be used. Operation is indicated even in the absence of marked symptoms when pulmonary hypertension is severe; in this situation, there may be right-to-left shunting across a patent ductus arteriosus or foramen ovale.

Surgery may be indicated in asymptomatic patients with moderate or worse mitral regurgitation in whom a simple and reliable reparative procedure is anticipated, such as closure of a regurgitant cleft. Delay in repair may lead to progressive damage to the valve, increasing the chance that repair will not be effective.

When repair is performed, long-term follow-up is indicated because of need in some patients for reoperation. When valve replacement is performed in infants, children, and young adults, a bioprosthesis is contraindicated because of its rapid degeneration in these age groups. A mechanical prosthesis is currently the device of choice, with long-term warfarin anticoagulation.

It is important to identify coexisting congenital mitral valve disease in patients being considered for repair of LV outflow tract obstruction, VSD, tetralogy of Fallot, or double outlet right ventricle. When mitral disease is present and is moderate or severe, the mitral disease must also be treated operatively.

**SPECIAL SITUATIONS AND CONTROVERSIES**

Valved Conduit Bypass of the Mitral Valve

When the mitral anulus is very small, a valved conduit (similar to that used for right ventricular–pulmonary trunk reconstruction) may be placed between the left atrium and LV. Laks and colleagues reported such a procedure (which was unsuccessful) in 1980, and Lansing and colleagues reported a successful case in a 10-year-old girl in 1983. Others have used this technique with good early results. Late results are not available.

Pulmonary Autograft Mitral Valve Replacement

Replacing the mitral valve with a pulmonary autograft, sometimes known as the Ross II operation, was initially described in 1967. It is only in the last decade that this procedure has been widely used, primarily in countries with a high prevalence of rheumatic disease, limited financial resources, and poor programs for follow-up anticoagulation monitoring. A 2004 review of worldwide use of the procedure identified 103 cases from 14 reports, with one report accounting for 80 patients. In that series, 78 of 80 patients had rheumatic disease, and 2 had congenital mitral valve disease; ages of the latter two patients were 4 years (primary mitral stenosis) and 6 years (primary mitral regurgitation). Overall early mortality was 5.0% (4 of 80; CI 2.6%-8.9%), and late mortality 6.25%, but no follow-up specific to the two congenital patients was reported, other than that the 6-year-old developed stenosis of the right ventricle–pulmonary artery trunk conduit at 1 year.

Brown and colleagues reported eight patients, four of whom had congenital mitral valve disease; two of the four had previously placed prosthetic valves that required re-replacement, and two had previously repaired atrioventricular septal defects. Ages of the four ranged from 12 to 22 years at autograft mitral valve replacement. There was no early or late mortality at a mean follow-up of 6.2 months, although one patient required autograft replacement owing to stenosis.

Four other case reports, totaling five patients, describe use of a pulmonary autograft for congenital mitral valve disease in infants ranging from age 2 to 11 months; among these, one died (20%; CI 3.2%-53%), one required immediate reoperation, and three survived with no more than short-term follow-up. One other case report describes emergency pulmonary autograft mitral valve replacement in a 36-month-old with a thrombosed mechanical valve originally placed for endocarditis. Again there was no mid- or long-term follow-up. A pulmonary autograft currently cannot be recommended for congenital mitral valve disease, especially in infants. The experience is limited, and important problems have been demonstrated upon early assessment, with no long-term follow-up available.

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**Section I  Vascular Ring**

**DEFINITION**

Vascular ring is a congenital anomaly in which the aortic arch and its branches completely or incompletely encircle and compress the trachea or esophagus or both.

**HISTORICAL NOTE**

Double aortic arch was apparently first described by Hommel in 1737 (cited by Turner) and a century later by Von Siebold. Wolman is credited with describing the syndrome of tracheal and esophageal compression produced by a double arch in 1939. A description of a patient with dysphagia thought to be due to a retroesophageal right subclavian artery was published in 1794 by Bayford, although the vessel was illustrated to pass between the esophagus and trachea rather than in its actual position posterior to the esophagus.

Modern interest in these anomalies was prompted by the first surgical correction of a double aortic arch by Gross in 1945. Subsequently, he pioneered surgical treatment of most other forms of vascular ring. The basis for radiologic diagnosis was initially described by Neuhauser.

The complex development and regression of the aortic arches during fetal development was elucidated by Congdon in 1922, but until Gross's pioneering surgical work, this information was little used by clinicians. In 1948, Edwards introduced the hypothetical double aortic arch scheme to conceptualize the numerous anomalies of the arch complex. This was further elaborated by Kirklin and Clagett in 1950 and by Stewart, Kincaid, and Edwards in 1964. In 1951, Barry provided a clear anatomic summary and review of Congdon’s basic work. In 1999, Momma and colleagues, followed by McElhinney and colleagues, identified chromosome 22q11 deletions associated with isolated anomalies of laterality or branching of the aortic arch.

**MORPHOLOGY**

Variations in arrangement of the ascending, transverse, and descending aorta and its branches are numerous in patients with vascular rings. Several of these may produce compression of the trachea or esophagus, or both, and are of surgical importance. They may be grouped as (1) complete or (2) incomplete vascular rings, including compression by the brachiocephalic artery or left common carotid artery (Box 51-1).

Of 301 patients with vascular ring or sling reported by Backer and Mavroudis, 84% fit into the categories of double aortic arch (30%), right arch with retroesophageal component (27%), and brachiocephalic artery compression syndrome (27%).

**Complete Vascular Ring**

**Double Aortic Arch**

In patients with double aortic arch, the ascending aorta arises normally, but as it leaves the pericardium it divides into two branches, a left and right aortic arch, that join posteriorly to form the descending aorta. The left arch passes anteriorly and to the left of the trachea in the usual position and is joined by the ductus arteriosus (or more often a ligamentum arteriosum), where it becomes the descending aorta. The right aortic arch passes to the right and then posterior to the esophagus to join the left-sided descending aorta, thus completing the vascular ring (Fig. 51-1). Occasionally the descending aorta is right sided, in which case the left arch (or its remnant) passes behind the esophagus. This was the case in 13 of 19 cases reported by Lincoln and colleagues. Alternatively, the descending aorta may be essentially a midline structure.

The right arch gives origin to two vessels, the right common carotid and right subclavian arteries, and the left arch gives origin to the left common carotid and left subclavian arteries in that order. The right aortic arch is most often...
PART VII Congenital Heart Disease

This fibrous chord, at its origin from the base of the left subclavian artery, lies close to the ligamentum arteriosum. The latter structure passes from this point to the adjacent proximal part of the left pulmonary artery (Fig. 51-3; double arch, left dominant). Less commonly (20% of cases) the left aortic arch is larger (left dominant) than the right, which although smaller in its distal part after the origin of the right subclavian artery, is rarely atretic (Fig. 51-4; see also Fig. 51-3). Size of the right and left aortic arches is nearly equal (balanced) in about 5% of cases.

Associated cardiovascular anomalies are uncommon but include tetralogy of Fallot and transposition of the great arteries.

**Right Aortic Arch with Retroesophageal Component**

In the situation of right aortic arch with a retroesophageal vascular or ligamentous component, a vascular ring is usually present, but the anatomic details vary depending on site of regression (interruption) of the embryonic left arch.

In the common situation of right aortic arch without retroesophageal segment, no vascular ring is present. The arch branches arise in mirror image of the normal (Fig. 51-5). This arrangement is the result of interruption of the embryonic left arch distal to the ductus arteriosus, in which the anterior ligamentum courses from the brachiocephalic artery to the proximal left pulmonary artery (Fig. 51-6, A, type 1 right aortic arch). This type is particularly common in tetralogy of Fallot (see Chapter 38) and truncus arteriosus (see Chapter 43).

**Mirror-Image Branching and Retroesophageal Ligamentum Arteriosum**

 Interruption of the left arch is proximal (upstream) to the ductus arteriosus (Fig. 51-6, B, type 2 right aortic arch). The left-sided ligamentum arteriosum extends from a diverticulum (Kommerell) on the upper descending thoracic aorta, behind the esophagus, forward to the left pulmonary artery. The vascular ring is formed by the ascending portion of the right arch and brachiocephalic artery anteriorly, by the aortic diverticulum posteriorly, and by the ligamentum arteriosum laterally. In the surgical series reported by Backer and colleagues, this anomaly represented about one third of right arch vascular rings.
carotid artery, and the descending aorta gives origin to the retroesophageal left subclavian artery as the fourth branch. The ductus or ligament arises with the left subclavian artery from an aortic diverticulum or from the left subclavian artery itself near its origin, where the subclavian artery may be narrowed. The descending aorta can be left or right sided. This is the most common type of vascular ring associated with right arch (see Fig. 51-6, C), accounting for about two thirds of right arch vascular rings. It is usually loose, so compression of either the esophagus or trachea is uncommon. Associated cardiac anomalies are rare.

Retroesophageal Left Brachiocephalic Artery

Here interruption occurs between the left common carotid and the right arch (Fig. 51-6, D, type 4 right aortic arch). A vascular ring is present, but the anomaly is rare. Bein and colleagues reported a case of long-segment coarctation with this anomaly.

Left Aortic Arch and Right Descending Aorta

Vascular rings are likely in the uncommon combination of left aortic arch and right descending aorta. The left arch crosses behind the esophagus. In combination with right patent ductus arteriosus or ligamentum arteriosum, a vascular ring is formed.

Cervical Aortic Arch Complex

Cervical aortic arch is a developmental entity consisting of persistence of the right or left third branchial arch and regression of the fourth branchial arch. The cervical aortic arch complex consists of a cervical position of the apex of the aortic arch with separate origin of the contralateral carotid artery, a retroesophageal descending aorta coursing contralaterally to the arch, and anomalous origin of the subclavian artery from the descending aorta. The cervical arch usually
Figure 51-6  Vascular ring associated with right aortic arch. Center drawing depicts a double aortic arch with descending thoracic aorta as a midline or left-sided structure. Ligamentum arteriosum (dashed line) is shown originating from junction of right or left arch and descending aorta. Right-sided ligamentum arteriosum to right pulmonary artery usually forms in association with a right-sided descending aorta. Left-sided ligamentum arteriosum is the common configuration connecting midline or left descending thoracic aorta to left pulmonary artery near bifurcation. The four possible sites (dotted lines) of regression (interruption) of left arch during fetal development are shown. Various types of right aortic arch are depicted depending on site of interruption. Vascular ring results from a retroesophageal component of left arch giving rise to the ligamentum. A, Type 1 right aortic arch. Aortic arch branches arise in mirror image of normal. Anterior ligamentum arteriosum courses from brachiocephalic artery to proximal left pulmonary artery (see Fig. 51-5). There is no vascular ring. B, Type 2 right aortic arch. Left arch regresses just distal to left subclavian artery, leaving a retroesophageal aortic diverticulum. Ligamentum (ductus) arteriosum arises posteriorly from descending aorta and courses to left pulmonary artery, completing a vascular ring. C, Type 3 right aortic arch. Left arch regresses between left common carotid and left subclavian arteries, leaving a retroesophageal subclavian artery, with ligamentum (ductus) arteriosum forming a complete vascular ring. D, Type 4 right aortic arch. Left arch regresses between right arch and left common carotid artery. Complete vascular ring is present in this rare anomaly.
is right sided. The aorta is usually redundant and crosses to the opposite side posterior to the esophagus. The retro-esophageal segment of the aorta may be tortuous and severely narrowed.\(^{14}\) A vascular ring is formed when there is an aberrant subclavian artery on the side contralateral to the aortic arch and a ligamentum arteriosum. There is considerable variability in anatomic configuration of the aortic arch and its branches.\(^{37}\) Abnormalities of brachiocephalic arterial branching and arch laterality are common in patients with cervical aortic arch.\(^{84}\) Vascular ring is frequently present, usually formed by the right aortic arch and aberrant left subclavian artery, but occasionally by double aortic arch. Rarely, a left cervical aortic arch, right ligamentum arteriosum, and right descending aorta form the vascular ring (see also discussion under “Left Aortic Arch and Right Descending Aorta”).\(^{93}\)

### Incomplete Vascular Ring

#### Left Aortic Arch and Retroesophageal Right Subclavian Artery

The relatively common (0.5% of the general population\(^{31}\)) retroesophageal right subclavian artery arising as the fourth branch of an otherwise normal aortic arch and passing upward and to the right behind the esophagus was once thought to be a cause of dysphagia (dysphagia lusoria, or “difficulty swallowing due to a trick of nature”).\(^{84,1,3,10}\) This condition does not form a complete ring and is generally not considered the true cause of vague symptoms related to swallowing. Rarely, a right ligamentum arteriosum passing from the retroesophageal right subclavian artery to the right pulmonary artery forms a vascular ring that is symptomatic.

#### Tracheal Compression by Brachiocephalic or Left Common Carotid Artery

The brachiocephalic or left common carotid artery may be drawn taut across the anterior wall of the trachea, a potential but uncommon cause of respiratory obstruction.\(^{2,2,3,3,1,3,4}\) It is not known why they occasionally compress the trachea. Presumably, the brachiocephalic artery originates more posteriorly from the aortic arch than usual, so it crosses the trachea more posteriorly.\(^{44}\)

#### Ductus Arteriosus Sling

Binet and colleagues described an infant with respiratory obstruction in which an anomalous vessel (presumed to be the ductus arteriosus) originated from the right pulmonary artery, crossed to the left between the esophagus and trachea, and joined the descending aorta adjacent to the origin of a retroesophageal right subclavian artery.\(^{81}\)

#### Severe Malrotation of Heart with Patent Ductus Arteriosus

Compression of the lower trachea can occur with a normal left arch when there is severe malrotation of the heart into the right chest in association with aegesis or hypoplasia of the right lung.\(^{81,92}\) Scherer and Westcott described a patient with dextrocardia and normal lungs in whom the pulmonary trunk lay anterior to the trachea and somewhat to the right. The patent ductus arteriosus connecting with a normally positioned descending aorta pulled the pulmonary trunk backward, compressing the front of the trachea. Compression was relieved by dividing the patent ductus arteriosus.\(^{93}\)

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

#### Symptoms and Signs

Symptoms of vascular ring relate to the consequences of tracheal and esophageal compression.\(^{34,41,30}\) Presentation is usually within the first 6 months of life and often within the first month. Inspiratory stridor may be present at birth, often in association with an expiratory wheeze and tachypnea. Stridor may be worse in various positions—for example, when the baby is lying on his or her back rather than side. Often, stridor is relieved by extending the neck. The baby’s cry may be hoarse and, in the absence of frank stridor, the breathing noisy. Persistent barking cough is frequently present. There may be episodes of apnea, severe cyanosis, and unconsciousness. When obstruction is severe, subcostal retraction is obvious. Recurrent respiratory infections are common and aggravate the respiratory obstruction; when obstruction is less severe, obstructive symptoms may be apparent only at such times.

The baby often feeds poorly, and there may be obvious difficulty in swallowing liquids, with episodes of choking and increased respiratory obstruction at these times. Dysphagia for solids is common (most severe cases are operated on before the babies are old enough to be offered solid food), with the baby refusing to swallow them or choking and regurgitating.

Dysphagia lusoria is often attributed to retroesophageal origin of the right subclavian artery from the upper descending thoracic aorta.\(^{84,1,3,10}\) The artery courses to the right, posterior to the esophagus, producing an indentation of the esophagus that has been blamed for vague symptoms in children, but that is usually not the cause. Should it become ectatic or aneurysmal later in life, difficulty swallowing is more likely.

Symptomatic vascular rings manifesting in adults are rare, and reports often emphasize dysphagia as the predominant symptom. Grathwohl and colleagues\(^{81}\) reviewed case reports of 24 adults with vascular rings. Two thirds had symptoms, 63% respiratory. Dysphagia was less prominent, occurring in 33%. Vascular rings occurring in adults may mimic chronic asthma.\(^{81,92}\)

#### Chest Radiography

Plain chest radiograph in the frontal view is either normal (10%) or shows a right aortic arch (85%).\(^{75}\) Anterior tracheal bowing is present on 92% of lateral views, and tracheal narrowing on 77%.

#### Esophagography

The esophagram is a useful diagnostic measure.\(^{34,1,3}\) Video esophagography at the time of cineangiography is optimal because it permits a detailed study showing the pulsatile nature of the obstruction and trachea.

With double aortic arch, the esophagram shows left- and right-sided indentations, with that for the right arch usually higher and deeper (Fig. 51-7, A). In addition, the retro-esophageal component produces a prominent posterior indentation that courses downward and to the left. In contrast, a retroesophageal left subclavian artery arising from the right arch produces a narrower esophageal impression that
courses upward and rightward. Right arch and left ligamentum arteriosum show more marked right-sided than left-sided indentation (Fig. 51-7, B).

Bronchoscopy

Bronchoscopy is rarely done, although it does identify sites of tracheal compression and shows its pulsatile nature.\textsuperscript{10}

Two-Dimensional Echocardiography

Two-dimensional echocardiography is useful in diagnosing vascular ring, at least in neonates and infants, and is critically important for identifying associated cardiac anomalies.\textsuperscript{17} However, it is inferior to computed tomography (CT) in demonstrating details of arch anatomy.

Computed Tomography

CT with contrast usually provides an excellent image of the structures and complements two-dimensional echocardiography. Ultrafast CT with three-dimensional reconstruction provides even greater anatomic detail.\textsuperscript{14} In many institutions, CT has become the standard modality for delineating details of vascular ring anatomy.\textsuperscript{87}
B, Right aortic arch with retroesophageal aortic diverticulum giving origin to a retroesophageal left subclavian artery and ligamentum arteriosum. AP views show typical bilateral indentations, lateral views a posterior indentation. Key: ANT, Anterior aspect of patient; L, left side of patient; POST, posterior aspect of patient; R, right side of patient.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is diagnostic and delineates severity of tracheal narrowing.\(^{54}\)

Aortography

Because of the accuracy of noninvasive imaging, aortography is rarely necessary. Aortography may be performed via a catheter positioned in the ascending aorta and is usually combined with cineangiography to assess associated congenital cardiac anomalies. Using biplane techniques, the first injection depicts both lateral and anteroposterior views, and the second both left and right oblique views. A degree of cranial tilt may separate the arches better in oblique views.\(^{51}\) Aortography can establish that the anomaly is a complete double aortic arch and show sites of narrowing in the left or (rarely) right arch (see Figs. 51-2 and 51-4). It cannot distinguish between a double arch with an atretic segment and a right aortic arch with a retroesophageal component. Sharp angulation of one of the brachiocephalic arteries may indicate the site of an atretic segment in a double arch or a constricting ligamentum arteriosum in a right arch with retroesophageal component (Fig. 51-8).

NATURAL HISTORY

Vascular rings of aortic arch origin account for 1% to 2% of cases of congenital heart disease.\(^{51}\) Only fragmentary information exists concerning the natural history of these anomalies. Untreated severe respiratory obstruction in the first 6 months of life is presumably fatal before age 1 year, particularly when symptoms are present from birth. Symptoms first appearing after age 6 months are less severe and rarely progressive, except at times of respiratory infection or regurgitation and choking.

When symptoms are of borderline severity, they usually disappear as the child grows. Godtfredsen and colleagues followed 11 patients with symptoms not severe enough to justify surgery.\(^{63}\) Of the six who had either double aortic arch or right arch with retroesophageal component, four outgrew their symptoms by age 4 years, and two with persistent symptoms had other anomalies to explain them.
Figure 51-8  Aortogram of right aortic arch with retroesophageal left subclavian artery and ligamentum arteriosum arising from a retroesophageal aortic diverticulum. Frontal views (A-B) and right anterior oblique views (C-D) are at different phases in cardiac cycle. Angulation at origin of left subclavian artery from diverticulum suggests presence of a ligamentum arteriosum under tension passing forward to left pulmonary artery (as was the case at operation). Angulation is downward in frontal view and anterior in right anterior oblique view. Absence of a similar angulation along course of left common carotid artery suggests that this artery is not connected to the diverticulum by an atretic ligament that forms part of a complete left aortic arch.
oversewn with two rows of 4-0 or 5-0 polypropylene sutures. Its mediastinal surface is then dissected further to free it and allow the divided ends to separate. The descending aorta is also mobilized and sometimes sutured to the rib periosteum to keep it away from the esophagus. In this and other operations for relief of vascular rings, “all strands or bands of tissue which form a part of the constricting mechanism” must be dissected away from the trachea or esophagus. Operation is completed by closing the chest wound in layers after inserting a single intercostal tube for drainage.

More often, the distal left arch is narrowed, and approach is made from the left side. The vascular structures and ligamentum arteriosum are dissected out and separated thoroughly from surrounding tissues (Fig. 51-9, A). The ligamentum arteriosum is divided, taking care to avoid injury to the recurrent laryngeal nerve. The junction of the left arch with the descending aorta is divided between vascular clamps and the ends oversewn (Fig. 51-9, B). The end of the left arch is then further dissected from underlying mediastinal tissues to allow it to retract forward. The medial surface of the descending aorta and distal divided end are also dissected.

Figure 51-9 Operative repair of vascular ring caused by right dominant double aortic arch. A, Surgeon’s view of anomaly through left posterolateral thoracotomy. Both arches, their branches, and ligamentum arteriosum are dissected and separated thoroughly from surrounding tissues. Site of division of smaller left arch is shown by dashed line. B, Ligamentum arteriosum is divided between surgical clips. Aortic arch is divided and ends ligated or oversewn. Anteromedial surface of aorta is dissected away from esophagus. Adventitia of lateral wall of aorta is sutured to periosteum of an adjacent rib to pull aorta laterally and posteriorly away from esophagus.

Generally, symptoms are milder and of later onset, and dysphagia is less prominent, in patients having right aortic arch with retroesophageal component than in those with double aortic arch.

TECHNIQUE OF OPERATION

Double Aortic Arch

In all cases of double aortic arch with a left-sided ligamentum, the repair may be approached through a left thoracotomy via the fourth interspace or bed of the nonresected fifth rib, as in the operation for patent ductus arteriosus (see Chapter 37, Fig. 37-3) or coarctation (see Chapter 48, Fig. 48-15). However, a similar approach from the right side may also be used when the left arch is dominant. Median sternotomy may be used when coexisting cardiac anomalies require repair.

When the left arch is dominant, the right arch can be dissected out via a left-sided approach, including the part passing behind the esophagus, and is divided between clamps close to its junction with the descending aorta. Its ends are oversewn with two rows of 4-0 or 5-0 polypropylene sutures. Its mediastinal surface is then dissected further to free it and allow the divided ends to separate. The descending aorta is also mobilized and sometimes sutured to the rib periosteum to keep it away from the esophagus. In this and other operations for relief of vascular rings, “all strands or bands of tissue which form a part of the constricting mechanism” must be dissected away from the trachea or esophagus. Operation is completed by closing the chest wound in layers after inserting a single intercostal tube for drainage.

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aorta is dissected away from the esophagus and sutured to the adjacent rib periosteum to pull it laterally and posteriorly away from the esophagus.

Techniques have been developed to divide vascular rings using video-assisted thoracoscopy. Compared with standard thoracotomy techniques, it is equally safe (no mortality), and length of stay in the intensive care unit or hospital, duration of intubation, and hospital charges are similar.

Right Aortic Arch with Retroesophageal Component

Right arch with retroesophageal component is generally approached from the left side. After dissection is completed, the ligamentum arteriosum is divided. The aortic diverticulum (Kommerell) is resected when it is large enough to independently compress the esophagus or trachea. Backer and colleagues recommend routine reimplantation of the left subclavian artery into the left common carotid artery if it arises from the diverticulum (Fig. 51-10). The descending aorta is dissected away from the esophagus and sutured to the periosteum of the rib if necessary to keep it away from the esophagus.

A robotic approach for dividing a left-sided ligamentum has been reported in a type 4 right aortic arch vascular ring.

Left Aortic Arch

Right-sided thoracotomy is used for left aortic arch and right-sided ligamentum arteriosum with or without a retroesophageal right subclavian artery (Fig. 51-11). The ligamentum is dissected and divided in the same fashion as for right arch with retroesophageal component.

Tracheal Compression by Brachiocephalic or Left Common Carotid Artery

When the lower trachea is compressed by an anomalous brachiocephalic artery (Fig. 51-12) or a malrotated left aortic

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Figure 51-10  Repair of right aortic arch with retroesophageal component. A, Anatomy of patient with right aortic arch, retroesophageal left subclavian artery (LSA), and large Kommerell diverticulum (embryologic remnant of left fourth aortic arch). Diameter of Kommerell diverticulum is usually equal to size of descending aorta. Ligamentum arteriosum is not illustrated. B, Resection of Kommerell diverticulum through left thoracotomy. Vascular clamp partially occludes descending thoracic aorta at origin of Kommerell diverticulum. Clamp on LSA is not illustrated. Kommerell diverticulum has been completely resected. C, Completed repair. Orifice at which Kommerell diverticulum was resected is usually closed primarily or (inset) can be patched with polytetrafluoroethylene if necessary. LSA has been implanted into side of left common carotid artery (LCAA) with fine running polypropylene sutures. Key: RCCA, right common carotid artery; RSA, right subclavian artery. (Redrawn from Backer and colleagues.)
arch associated with severe rightward malrotation of the heart, approach may be through a median sternotomy. A short left anterolateral thoracotomy also works well and leaves the sternum intact; the suspending sutures may be passed through the sternum. The anomalous vessel is fully dissected, then suspended from the posterior aspect of the sternum or adjacent ribs with 3-0 or 4-0 polypropylene pledgeted mattress sutures that pick up the adventitia of the vessel.

Hawkins and colleagues have proposed an alternative midline approach in which the brachiocephalic artery is reimplanted more proximally on the ascending aorta and to the right of the trachea. Hawkins and colleagues have proposed an alternative midline approach in which the brachiocephalic artery is reimplanted more proximally on the ascending aorta and to the right of the trachea. Hawkins and colleagues have proposed an alternative midline approach in which the brachiocephalic artery is reimplanted more proximally on the ascending aorta and to the right of the trachea. Hawkins and colleagues have proposed an alternative midline approach in which the brachiocephalic artery is reimplanted more proximally on the ascending aorta and to the right of the trachea.

RESULTS

Complete Vascular Ring

In the current era, hospital mortality after repair of vascular ring without major associated lesions should approach zero. Good functional results are obtained in 90% of surviving patients. In a 45-year analysis by Backer and colleagues, early mortality was primarily related to major associated cardiac or respiratory anomalies.

Late outcomes after repair of complete vascular ring are generally good, but persistent respiratory symptoms are frequent—54% after repair of double aortic arch in a longitudinal study by Alsenaidi and colleagues, possibly associated with previous compression-related tracheobronchial damage or maldevelopment. Gastrointestinal symptoms are uncommon.

Incomplete Vascular Ring

Results are also good in about 90% of patients with incomplete vascular ring.

Tracheal Compression by Brachiocephalic or Left Common Carotid Artery

Results of arteriopexy for tracheal compression by the brachiocephalic or left common carotid artery were excellent in 93% of a group of 76 patients. Death occurred in 3 of 79 (3%; CI 1.7%-7.5%) patients. Similar results have been achieved by the reimplantation technique.

INDICATIONS FOR OPERATION

Operation is indicated in all patients with important obstructed airway symptoms. Treatment should not be delayed, because hypoxic and apneic spells may occur, as well as further damage to the trachea and bronchi. Operation is not indicated if symptoms are mild or absent.

SPECIAL SITUATIONS AND CONTROVERSIES

Resection of Kommerell Diverticulum

Most surgeons have routinely left alone a Kommerell diverticulum or performed an aortopexy in the vicinity of the diverticulum by tacking it to the adjacent chest wall. However, Backer and colleagues recommend its routine excision because of the occasional need to reoperate for symptom recurrence secondary to tracheoesophageal compression by the diverticulum. Further longitudinal studies are needed to clarify the role of routine diverticular resection.

DEFINITION

Vascular sling is a congenital anomaly in which the left pulmonary artery (LPA) arises from the right pulmonary artery (RPA) extrapericardially (anomalous LPA), courses to the left...
Figure 51-12  Operative repair of tracheal compression by brachiocephalic artery. A, Brachiocephalic artery originates from aortic arch more distally than usual, causing compression of trachea. It is shown in midline exposure. B, Brachiocephalic artery is disconnected from aorta and its origin closed by suture and reimplanted more proximally on ascending aorta. C, Anomaly is approached through a left anterior thoracotomy. Anomalous vessel is completely separated from trachea and attached (D) by suture to periosteum of posterior aspect of sternum.
behind the tracheal bifurcation and in front of the esophagus to reach the left lung hilum, and forms a sling around the trachea.

**HISTORICAL NOTE**

Anomalous LPA was first recognized by Glave and Doehle in 1897 during an autopsy performed on a 7-month-old child who died of asphyxia. The next report was that of Scheid in 1938, again in the German literature and again from autopsy findings, this time in a 7-month-old child who died of respiratory obstruction. Description of the anomalous origin and course of the artery is accurate in both reports, but Scheid also described in detail an associated diffuse tracheal stenosis caused by presence of complete cartilaginous rings. This latter condition was again accurately described by Wolman 3 years later.

Quist-Hanssen from Norway detailed the clinical findings of pulmonary artery sling premortem in 1949, although exact diagnosis was not made until autopsy. Welsh and Munro first suggested, based on their autopsy findings, that in this anomaly the barium swallow should show an anterior esophageal indentation; Wittenborg and colleagues soon after accurately defined these features on an esophagram. In 1980, Stone and colleagues described diagnosis by CT, and in 1988, Malmgren and colleagues by MRI.

In 1958, Contro and colleagues coined the term *vascular sling* to distinguish the condition from vascular ring. Much later, Berdon and colleagues introduced the phrase *ring-sling complex* to emphasize the often coexisting tracheal anomaly.

In 1954, Potts and colleagues were the first to report successful operation in a patient in whom the anatomy of the malformation was not established before operation. Potts divided the LPA at its origin from the RPA, transferred the vessel in front of the trachea, and reanastomosed it to the proximal stump. Soon after, Morse and Gladding reported a case diagnosed at right thoracotomy and confirmed at autopsy, in which the anomalous LPA was dissected away (but not divided) from the trachea in an attempt to relieve compression.

Hiller and Maclean operated successfully on a patient correctly diagnosed by barium swallow and angiography in 1955; after mobilizing and dividing the anomalous LPA, they anastomosed it to the side of the pulmonary trunk (the operation currently practiced). The patient’s stridor was relieved completely, and the chest radiograph was normal. However, angiogram 3 weeks later showed LPA occlusion. In 1962, Mustard and colleagues reported relief of respiratory obstruction following division of the ligamentum arteriosum only. One year later, Lochlor and colleagues reported a case in which the right mainstem bronchus was successfully resected in front of the anomalous LPA. Neither of the latter two procedures is practiced currently.

MORPHOLOGY

**Anomalous Left Pulmonary Artery**

The anomalous LPA arises extrapericardially from the posterosexterior wall of a normally positioned RPA lying in front of the proximal right main bronchus. The RPA is a direct continuation of the pulmonary trunk, the junction between them marked by attachment of the ligamentum arteriosum (or ductus arteriosus). From its point of origin, the LPA curves upward and backward over the proximal right main bronchus, then to the left behind the lower trachea and its bifurcation at or slightly above the carina (Fig. 51-13). It courses slightly inferior to lie behind the proximal left mainstem bronchus, then appears immediately superior to it to enter the left lung, and then divides. The left lung hilum is lower than normal in relation to the pulmonary trunk.

The LPA usually indents the posterior wall of the trachea and left main bronchus as it passes behind them and displaces (bows) the distal trachea and carina toward the left. The right main bronchus is bowed anteriorly. The LPA passes in front of the esophagus, which is usually indented across its entire anterior aspect or, less often, on its leftward anterior surface only.

The anomalous LPA is frequently slightly smaller than normal (see Chapter 1). Rarely, the right upper lobe artery comes off the LPA near its origin. Bamman and colleagues described one case in which the left lung was partly supplied by an LPA in normal position; the anomalous LPA supplied only the left lower lobe and crossed behind the left atrium rather than behind the tracheal bifurcation.

The ligamentum arteriosum (or ductus arteriosus) follows a normal course from the junction of the pulmonary trunk RPA, passing backward directly superior to the left main bronchus and anomalous LPA (not between them as depicted by Williams and colleagues) to join the descending aorta. It may participate with the anomalous LPA in forming a vascular ring.

**Tracheobronchial and Pulmonary Abnormalities**

The trachea near the bifurcation is usually narrowed as a result of posterior compression by the anomalous LPA. This mainly affects the origin of the right main bronchus and trachea just above the carina. Rarely, the left main bronchus may be narrowed by a similar mechanism.

In about 50% of patients, narrowing of the trachea or proximal main bronchi is secondary to presence of complete ring cartilages (ring-sling complex), which often are more numerous than normal. In these areas, the pars membranacea is absent and the lumen is usually severely narrowed. This process may involve the entire length of the trachea or only its proximal or distal portions. The major bronchi may be similarly involved, or their cartilaginous rings may be wide and irregular and the bronchi variable in diameter and length.

The so-called bronchus suis, consisting of separate high origin from the trachea of the right superior lobar bronchus to the right upper lobe, is more frequent than normal. It is not itself a cause of obstruction.

When the right main bronchus is selectively narrowed, there is hyperinflation of the right lung (not affecting the right upper lobe when there is a bronchus suis present); when
the left main bronchus is narrowed, there is hyperinflation of the left lung. More complete obstruction leads to atelectasis. When obstruction of the right main bronchus is important in utero, there may be retention of fetal fluid in the right lung at birth.

Either the left or right lung may be unilobar. Rarely, the right lung may be hypoplastic. The lung hypoplasia may be part of scimitar syndrome.

Other Cardiovascular Anomalies
Other cardiovascular anomalies coexist with half the cases of anomalous LPA. Most common are left superior vena cava, atrial septal defect, patent ductus arteriosus, and ventricular septal defect. There may also be tetralogy of Fallot, single ventricle, transposition of the great arteries, tricuspid atresia, or aortic arch anomalies.

Noncardiovascular Developmental Anomalies
A variety of noncardiovascular developmental anomalies coexist relatively frequently.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA
Symptoms and Signs
Symptoms of vascular sling relate to the consequences of tracheal and esophageal compression. Up to 90% of patients have important and usually severe symptoms that develop soon after birth.

The most common presentation is with wheezing and stridor, often with prolongation of the expiratory phase, suggesting asthma, and with a harsh cough and intercostal indrawing. In addition, there may be choking and rapid breathing or apneic spells and associated episodes of cyanosis. Symptoms are episodic, but acute episodes of dyspnea and cyanosis or severe exacerbations of respiratory obstruction are common and may result in unconsciousness, convulsions, or even death. In severe cases, hypercapnia and right lung emphysema requiring mechanical ventilation may be present from birth.

Symptoms may be precipitated by respiratory infections and are occasionally altered by changes in posture of the infant. They may be made worse by feeding, with or without regurgitation and choking. Dysphagia, however, is uncommon.

Chest Radiography
Plain chest radiograph gives important clues to correct diagnosis. It shows anterior bowing of the right main bronchus and deviation of the lower trachea and carina to the left. In addition, the left lung hilum is lower than normal in relation to position of the pulmonary trunk, and unequal aeration of the lungs frequently is present. Usually the right lung is overinflated, but sometimes the left may be. When obstruction is more complete, there may be areas of atelectasis. There is mediastinal density between the trachea and esophagus on the lateral view and, in older patients in particular, right-sided mediastinal density opposite the carina in the posteroanterior view.

In newborns, the initial chest radiograph may show retention of fetal fluid in the right lung, evidenced by a uniform opacity without loss of volume (this is in fact increased) and without an air bronchogram. Once the fetal fluid has been resorbed or suctioned off, the lung will appear hyperinflated.
Bronchoscopy

Bronchoscopy is required in all patients to evaluate tracheal abnormalities (complete tracheal rings) and identify areas of stenosis that may need surgical repair and affect airway and ventilatory management.

Cardiac Catheterization and Angiography

Cardiac catheterization and angiography display the anomaly well, can confirm diagnosis (Fig. 51-15), and demonstrate

**Figure 51-14** Esophagram (lateral) of anomalous left pulmonary artery. Prominent indentation of anterior wall of esophagus is seen immediately above tracheal bifurcation.

**Figure 51-15** Cineangiogram of vascular sling (anomalous left pulmonary artery). A, Preoperative study showing left pulmonary artery originating from right pulmonary artery. Small patent ductus arteriosus (arrow) is present between distal left pulmonary artery and pulmonary trunk. Concavity apparent in upper surface of left pulmonary artery just lateral to the ductus is impression of descending aorta. B, Late postoperative study showing stenosis at anastomosis of left pulmonary artery to pulmonary trunk. This was successfully treated by percutaneous balloon dilatation.
associated cardiovascular anomalies. The LPA is visualized best in a cranially tilted frontal view.

**NATURAL HISTORY**

Vascular sling is a rare condition. The largest series includes 15 patients accumulated over 45 years in a high-volume children’s hospital. Therefore, information about natural history is incomplete.

**TECHNIQUE OF OPERATION**

Repair is advantageously performed through a median sternotomy using CPB, although it can be done through a left thoracotomy. **Reimplantation of Left Pulmonary Artery**

*With Cardiopulmonary Bypass*

After usual preparations and bronchoscopy (if not previously performed) and median sternotomy, the pericardium is opened and retraction sutures applied. The aorta is dissected completely away from both pulmonary arteries. The ligamentum arteriosum, which is often stretched tightly across the carina and is part of the vascular sling, is dissected and divided between ligatures. The decision is then made either to reimplant the LPA or excise a tracheal stenosis (if this exists), move the dissected but undivided LPA anteriorly, and reconstruct the trachea end to end.

When the tracheal rings are normal and no tracheal stenosis or softening is demonstrated, CPB is established using a single venous cannula and a perfusate temperature of about 32°C (see Chapter 2). The left pleural space is opened widely, either then or later. The LPA is identified coming off the RPA. It is dissected out well distally, completely separating it from surrounding structures, including the trachea anteriorly and the esophagus posteriorly. The plane of dissection must be on the adventitia of the LPA to avoid damage to the membranous portion of the trachea (Fig. 51-16, A). The LPA is cut away from the RPA, and the defect in the latter is closed with two rows of 5-0 or 6-0 polypropylene sutures. The LPA is then pulled out into the left pleural space. A large window is made in the pericardium behind the phrenic nerve and alongside the pulmonary trunk, and the LPA is brought into the pericardial space through it. An incision is made in the left lateral aspect of the pulmonary trunk. Taking care that the LPA lies nicely without kinking or rotation, its proximal end is anastomosed to the side of the pulmonary trunk with continuous 6-0 or 7-0 polypropylene suture (Fig. 51-16, B).

After rewarming the patient, CPB is discontinued and cannulae removed. A polyvinyl pressure-recording catheter may be brought out from the pulmonary trunk via the right ventricle. The remainder of the operation is completed as usual.

*Without Cardiopulmonary Bypass*

A left posterolateral thoracotomy is made, entering the chest via the fourth interspace or fifth rib bed. Alternatively, some have preferred median sternotomy. The anomalous LPA is identified by dissecting the superior part of the left lung hilum (Fig. 51-17, A). The ligamentum arteriosum is divided because this improves exposure and may possibly relieve compression of the left main bronchus. Dissection of the LPA is continued medially (centrally) and behind the proximal left main bronchus and tracheal bifurcation. The artery is freed completely from the posterior wall of these structures and followed as far as possible into the mediastinum to gain adequate length. Care is taken not to obstruct flow into the RPA by undue tension on the LPA. The patient is given heparin (1.5 mg · kg⁻¹) to obtain systemic anticoagulant effect. The LPA is then divided between vascular clamps, its proximal end on the RPA oversewn with continuous 6-0 or 7-0 polypropylene suture, and the clamp removed (Fig. 51-17, B).
The pericardium is opened with a vertical incision anterior to the phrenic nerve to expose the pulmonary trunk, and a second similar incision is made posterior to this structure, through which the distal end of the anomalous LPA is passed. The tip of the left atrial appendage is retracted by a ligature tied to it, and the left wall of the pulmonary trunk is excluded in a curved vascular clamp. The clamp is positioned to allow the LPA to reach the pulmonary trunk without kinking or tension. The excluded portion of the pulmonary trunk is opened and an end-to-side anastomosis performed between it and the LPA (see Fig. 51-17, B), refashioning the LPA end obliquely to increase the diameter of the anastomosis. The posterior layer of the anastomosis is performed from within the vessels, using continuous 6-0 or 7-0 polypropylene suture and the anterior layer from outside. Clamps are then removed. Heparin is not reversed.

The pericardium is left open and the chest closed, leaving one intercostal tube for drainage.

**Tracheal Resection and Relocation of Left Pulmonary Artery**

When there is a localized area of tracheal stenosis, the trachea is minimally mobilized, and the tip of the endotracheal tube is ascertained to lie proximal to the proposed resection. A median sternotomy is performed and CPB established in the manner just described. The anomalous LPA is completely freed from surrounding structures and the stenotic area of
trachea excised (Fig. 51-18, A). The LPA is brought through the tracheal gap and positioned anterior to the trachea. The patient’s neck is flexed if necessary, and an end-to-end tracheal anastomosis is performed (Fig. 51-18, B and C) using continuous 5-0 or 6-0 polydioxanone suture. CPB is discontinued after the patient has been rewarmed, and the remainder of the operation is completed in the usual manner (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). Before muscle relaxants are discontinued in the intensive care unit, the patient is fitted with a back brace to prevent cervical extension.

If tracheal disease is of considerable length and associated with complete tracheal rings, local excision may not be corrective. These longer segments of tracheal stenosis are treated by tracheoplasty. Using CPB, either a slide tracheoplasty or a long tracheoplasty with pericardium is performed. For pericardial reconstruction, a vertical anterior incision is made in the trachea through the complete

Figure 51-18 Repair of anomalous left pulmonary artery (LPA) with tracheal stenosis caused by complete tracheal rings (tracheomalacia). Operation is performed through median sternotomy with cardiopulmonary bypass. A, Anomalous LPA is freed from surrounding structures. Trachea is divided (dotted lines) above and below stenotic area. Excision of stenotic trachea leaves a gap through which anomalous pulmonary artery is pulled and positioned anterior to trachea. B, End-to-end anastomosis of trachea is constructed using absorbable suture. LPA is shown positioned anterior to trachea. C, Completed repair shows LPA still attached anomalously to right pulmonary artery but positioned anterior to trachea to avoid tracheal compression.
rings under bronchoscopic guidance. A pericardial patch is inserted with polydioxanone suture to widen the trachea. The patch appears to be adequate for enlarging the trachea but does not provide support to it and may collapse during inspiration, partially obstructing the trachea and resulting in noisy respiration for months to a year. Options that do provide support are a tracheal insert fashioned from costal cartilage or a prosthesis constructed from prosthetic mesh hardened with cyanoacrylate to which the pericardium is attached with biological glue.

The LPA is transected at its origin, repositioned, and anastomosed to the side of the distal pulmonary trunk to complete the operation. When major associated cardiac anomalies are present, they can be repaired along with LPA reimplantation on CPB. Tracheal reconstruction, if needed, can be deferred for 2 to 4 days and performed as a separate procedure.

Because of the unavoidable mediastinal contamination from an open trachea, Konstantinov and colleagues recommend placing a pericardial flap between the great vessels and anterior tracheal suture lines.

SPECIAL FEATURES OF POSTOPERATIVE CARE

Care is as described in Section I. Special attention is required for tracheal care and secretion management if the trachea has been reconstructed.

RESULTS

Survival

Percent survival is not meaningful when derived from the small number of patients known to have been treated surgically. In the series reported by Backer and colleagues, there were no hospital deaths among 12 patients (0%; CL 0%-15%), but two (17%) patients died during the first postoperative year.

Mode of death is usually respiratory and related to tracheal abnormalities. When these abnormalities are not present, prognosis is excellent.

Left Pulmonary Artery Patency

In many groups of patients operated on in an earlier era, usually through a left thoracotomy, the LPA anastomosis frequently was not patent late postoperatively. With currently used methods, the anastomosis usually remains patent.

Freedom from Postoperative Respiratory Obstruction

When respiratory obstruction is due only to compression of the trachea by an anomalous LPA, relief is virtually always complete after simple reimplantation of the artery. Relief of symptoms has been obtained in a few such patients in whom only the ligamentum arteriosum or a patent ductus arteriosus has been divided. When tracheal stenosis is a component of respiratory obstruction, tracheal resection and relocation of the LPA aided by CPB has provided complete relief of symptoms. When there is diffuse anatomic tracheal stenosis associated with complete cartilaginous rings, relief of respiratory obstruction has been variable, but results after pericardial patch tracheoplasty can be good.

INDICATIONS FOR OPERATION

When anomalous LPA is present and there are symptoms and radiologic signs of important respiratory obstruction, operation is indicated. When respiratory symptoms are due to tracheal compression without fixed stenosis and without complete tracheal rings, either relocation and reimplantation of the LPA (preferably with CPB) or relocation after tracheal transection and reanastomosis is indicated. When a localized tracheal stenosis is present, resection of the stenosis, relocation of the LPA, and end-to-end anastomosis of the trachea are indicated.

When there is severe diffuse tracheal stenosis with complete cartilaginous rings, the surgical problem is more difficult. Correction of the left pulmonary arterial problem and simultaneous tracheal reconstruction of some type are indicated, but the outcome has been unpredictable.

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DEFINITION

Complete transposition of the great arteries (TGA) is a congenital cardiac anomaly in which the aorta arises entirely or largely from the right ventricle (RV) and in which the pulmonary trunk arises entirely or largely from the left ventricle (LV), known as ventriculoarterial discordant connection. Although the phrase complete transposition of the great arteries may properly be applied whenever this situation exists, this chapter uses TGA to denote a cardiac anomaly with atrioventricular concordant connection as well as ventriculoarterial discordant connection. Thus, the term TGA is not applicable to patients with transposed great arteries and tricuspid or mitral atresia or double inlet left or right ventricle (see Chapters 41 and 56) or atrioventricular discordant connection (congenitally corrected transposition of the great arteries; see Chapter 55).

HISTORICAL NOTE

The first morphologic description of TGA is attributed to Baillie in 1797. The term transposition of the aorta and...
pulmonary artery was coined by Farre when he described the third known case of this anomaly in 1814 using the word transposition (trans, “across”; ponere, “to place”), meaning that the aorta and pulmonary trunk were displaced across the ventricular septum. In subsequent pathologic descriptions that included attempts to explain its embryologic basis, the word transposition was used to describe an anterior position of the aorta relative to the pulmonary trunk, and by the early 1900s, it had become accepted practice to include any abnormal position of the aorta, regardless of its ventricular origin, under this heading. This broad confusing definition was clarified by Van Praagh and colleagues in 1971, when they strongly advocated return to Farre’s original definition of transposition, and introduced the useful term malposition to describe those abnormal positions of the aorta in which both great arteries fail to be displaced across the ventricular septum. This literal meaning of transposition is now accepted by most pathologists and surgeons.

Recognition of TGA during life resulted from observations of Fanconi in 1932 and Taussig in 1938. Importance of the early appearance of pulmonary vascular disease, even when the ventricular septum was intact, was described by Ferguson and colleagues in 1960 and Ferencz in 1966.

Surgery for TGA commenced in 1950 when Blalock and Hanlon at Johns Hopkins Hospital described a closed method of atrial septectomy designed to provide mixing of pulmonary and systemic venous return at the atrial level. Edwards, Barger, and Lyons modified the Blalock-Hanlon procedure in 1964 by resuturing the septum so as to connect the right pulmonary veins to the right atrium.

In 1953, Lillehei and Varco described a “partial physiologic correction” (or atrial switch) consisting of anastomosis of right pulmonary veins to right atrium, and inferior vena cava (IVC) to left atrium, a technique that became known as the “Baffes operation.” Baffes incorporated use of an allograft aortic tube to connect the IVC to the left atrium.

Palliation of TGA was revolutionized when Raskind and Miller in Philadelphia introduced balloon atrial septostomy (BAS) in 1966. However, in 1971 at Great Ormond Street Hospital in London, Tynan showed that BAS did not allow all babies with TGA to survive until repair. A modification of this procedure was introduced in 1975 by Park and colleagues with their substitution of a blade rather than a balloon at the end of the catheter.

Throughout the 1950s there were attempts to correct TGA surgically either at the atrial or the great artery levels. The concept of a physiologic correction at the atrial level by switching the atrial septum so that systemic venous return is directed to the LV and pulmonary venous return to the RV was first proposed by Albert at a meeting of the American College of Surgeons in 1954. This concept was amplified by Merendino and colleagues in 1957. The first successful operation of this type was accomplished by Senning in 1959, who refashioned the walls of the right atrium and the atrial septum to accomplish atrial-level transposition of venous return. Modifications were suggested by many, including Schumaker in 1961 and Bernard and colleagues in 1962. At the Mayo Clinic the Senning procedure was used between 1960 and 1964 with some successes (a few of these patients were still alive and well 30 years later) but with many disappointing results, related in part to the fact that most of the infants and children had a large ventricular septal defect (VSD) and varying degrees of pulmonary vascular disease.

The Mustard procedure, in which the atrial septum is excised and a pericardial baffle used to redirect systemic and pulmonary venous flow, was devised in an attempt to create larger atra than were produced by the Senning procedure and was successfully introduced at the Toronto Sick Children’s Hospital in 1963 and reported in 1964. (Actually, Wilson and colleagues described essentially the same operation in 1962. Mustard’s initial results were better than had been achieved with the Senning procedure, at least in part because he had access to a reservoir of young children with TGA and intact ventricular septum who had been palliated by a Blalock-Hanlon operation.

The Mustard technique soon was adopted in almost all cardiac surgical centers. However, a slightly modified Senning repair was reintroduced by Quaegebeur, Rohmer, and Brom in 1977, mainly because of persisting problems with baffle obstruction and arrhythmia after the Mustard procedure.

It became conventional to delay this atrial switch definitive procedure for 12 to 24 months after BAS. In occasional patients the Mustard procedure was extended to smaller infants by Dillard and colleagues in 1969, Bonchek and Starr in 1972, and Subramanian and Wagner in 1975. The first substantiated proposal that repair was necessary and possible in the first 3 months to avoid considerable pre-repair mortality was by Barratt-Boyces and colleagues.

TGA with large VSD remained a difficult problem throughout this early era because of high hospital mortality after repair and rapid development of pulmonary vascular disease in many patients. However, enough successes were obtained with the atrial switch procedures to demonstrate the value of continuing to treat patients in this subset surgically. In 1972, Lindesmith and colleagues introduced the use of a palliative Mustard procedure in which the VSD was left unclosed for patients with high pulmonary vascular resistance. The modification in which a large VSD was created in TGA with intact ventricular septum was used by Stark and colleagues in 1976.

Successes were few in patients with TGA, VSD, and important left ventricular outflow tract obstruction (LVOTO) in this early period of intracardiac surgery for TGA. Daicoff and colleagues in 1969 reported a few successful repairs by direct relief of the LVOTO associated with an atrial switch by Mustard’s technique. Later, in 1969, Rastelli and colleagues combined intraventricular tunnel repair (LV to aorta) of the double outlet RV operation (see “Intraventricular Tunnel Repair of Simple Double Outlet Right Ventricle” under Technique of Operation in Chapter 53) with a rerouting valved extracardiac conduit (RV to pulmonary trunk) and closure of the origin of the pulmonary trunk from the LV to produce an anatomic repair of TGA, VSD, and LVOTO.

Somewhat disappointing results of the atrial switch operation for TGA and large VSD continued to be a stimulus for developing an arterial switch operation, particularly because the right (systemic) ventricle sometimes failed late postoperatively in these patients. Much earlier, in 1954, Mustard and colleagues had described unsuccessful attempts to perform an arterial switch operation in seven patients, with transfer of the left coronary ostium to the pulmonary trunk and use of a monkey lung as the oxygenator. Other reports of unsuccessful operations of this general type were those of Bailey and colleagues in 1954 and Kay and Cross in 1955.
and colleagues attempted such a procedure in two patients with an intact ventricular septum in 1961 using cardiopulmonary bypass (CPB), transferring the great arteries and a ring of aorta carrying the coronary arteries. Interest then lagged in many centers, but a few groups persisted with efforts to perfect this approach. Jatene and colleagues in Brazil achieved a major breakthrough in 1975 with the first successful use of an arterial switch procedure (Jatene procedure), applying it in infants with TGA and VSD. Soon after, Yacoub and colleagues reported successful cases. An important technical modification of the original Jatene procedure was the demonstration by Lecompte and colleagues that direct anastomosis of both great arteries without interposition of a tube graft is possible when the pulmonary bifurcation is transferred in front of the distal ascending aortic arch. Aubert and colleagues successfully used intraarterial baffling and creation of an aortopulmonary tunnel to correct simple TGA by an arterial switch in 1978.

Yacoub’s attempts in London to perform an arterial switch procedure in three infants with TGA and intact ventricular septum were unsuccessful in 1972, but reports by Mauck in 1977 and Abe in 1978 with their colleagues indicated that such a repair was possible in infancy. However, most infants with TGA and intact ventricular septum did not survive arterial switching. Yacoub approached this problem of the low-pressure LV not being prepared for sustaining systemic pressure by performing pulmonary artery banding as a first stage. The matter was resolved when Radley-Smith and Yacoub in London, Quegebeur in Holland, and Castaneda in Boston with their colleagues demonstrated feasibility and safety of repair of simple TGA in the first few days of life by an arterial switch operation.

**MORPHOLOGY AND MORPHOGENESIS**

**Right Ventricle**

The RV is normally positioned, hypertrophied, and large in TGA. Its inflow and sinus portions are essentially normal in architecture. In about 90% of cases, there is a subaortic conus, and the aorta is rightward and anterior and ascends parallel to the posterior and leftward pulmonary trunk (Fig. 52-1). Such hearts also have an infundibular septum, which in the absence of a VSD, joins normally with the ventricular septum between the limbs of the trabecula septomarginalis (septal band; TSM). The infundibulum does not deviate to the left as in the normal heart, but projects directly superiorly from the sinus portion of the ventricle (Fig. 52-2).

There is less wedging of the pulmonary trunk between the mitral and tricuspid valves than in the aorta of normal hearts. As a result, a larger area of contiguity exists between the mitral and tricuspid valves than normally. These atrioventricular (AV) valves may be at virtually the same level, and the AV septum and membranous interventricular septum are then smaller than usual or (rarely) absent. The right fibrous trigone of the central fibrous body is abnormally shaped and attenuated.

In about 10% of hearts with TGA and intact ventricular septum, the subaortic conus in the RV is absent or very hypoplastic. Then the aorta is either directly anterior or anterior and to the left of the pulmonary trunk origin or (rarely) posterior. In a few cases, however, a posteriorly placed aorta is associated with a subaortic conus.

**Left Ventricle**

The LV infrequently contains a conus; typically pulmonary-mitral fibrous continuity exists, comparable with aortic-mitral fibrous continuity in the normal heart (Fig. 52-3). In about 8% of hearts with TGA, and most often in those with a VSD, a subpulmonary conus is present in the LV. The subpulmonary conus is frequently stenotic. In most of these cases, the aorta still lies anteriorly and to the right but it may be leftward or posterior.

**Ventricular Wall Thickness, Cavity Shape, and Function**

In the normal heart, the LV wall is thicker than the RV wall in utero. After birth, LV wall thickness increases progressively, whereas the RV wall becomes relatively thinner. In TGA, the RV wall is considerably thicker than normal at birth and increases in thickness with age. When the ventricular septum is intact and no important pulmonary stenosis
is present, the LV wall is of normal thickness at birth. Wall thickness remains static, however, leading to less-than-normal thickness within a few weeks of birth and a relatively thin wall by age 2 to 4 months.\textsuperscript{36,37,39,410} When a VSD is present, LV wall thickness increases slightly less than in the normal heart, but remains well within the normal range during the first year of life.\textsuperscript{318,520} With LVOTO (pulmonary stenosis) the evolution is similar, although when obstruction is severe and the ventricular septum is intact, LV wall thickness eventually exceeds RV wall thickness.\textsuperscript{6} Although not equivalent to LV work potential, LV wall thickness reflects the ventricle’s functional capacity.

In infants with TGA, the LV cavity is the usual ellipsoid in shape at birth but soon becomes banana shaped.\textsuperscript{819} Alteration in LV function accompanies this geometric change.

RV function is usually normal in TGA in the perinatal period. Thereafter, when the ventricular septum is intact, RV end-diastolic volume is increased and RV ejection fraction decreased.\textsuperscript{615,13} Depressed RV ejection fraction is unlikely to be caused by increased afterload or decreased preload and probably results from depressed RV function from relative myocardial hypoxia or the geometry of the chamber.\textsuperscript{615}

LV end-diastolic volume is increased in TGA, and LV ejection fraction is normal. RV/LV end-diastolic volume ratio, normally 1.0, is increased to 1.5 ± 0.33.

Atria

The atria are normally formed in TGA. Right atrial size is usually larger than normal, particularly when the ventricular septum is intact.

Conduction System

The AV node and bundle of His lie in a normal position, although the AV node is abnormally shaped and may be partly engulfed in the right trigone. The left bundle branch originates more distally from the bundle of His than usual and arises as a single cord rather than a sheath. Therefore, damage to the bifurcation of the bundle at VSD closure is
Great Arteries

The aorta is most often directly anterior or slightly to the right (Table 52-1). In the Taussig-Bing heart, great arteries may be side by side, with the aorta to the right (see “Taussig-Bing Heart” under Morphology in Chapter 53). Rarely the aorta is directly posterior.

Some refer to the aortic sinuses of Valsalva as “left posterior-facing” or “right posterior-facing” sinuses and “nonfacing” sinus. This becomes awkward, however, in the 25% of cases in which positions of the great arteries are different from the usual anteroposterior locations. A more universally applicable scheme is the Leiden convention, in which sinus I is on the right of an imagined observer standing in the nonfacing noncoronary aortic sinus of Valsalva looking toward the pulmonary trunk. Proceeding counterclockwise, the next sinus is sinus 2.

In 13% to 30% of patients with TGA, aortic and pulmonary commissures are not precisely aligned because of malalignment of either the aortic or mitral valve. In one study, commissural malalignment was found in nearly 40% of patients undergoing an arterial switch procedure. Recognition of commissural malalignment is important in planning the coronary transfer as well as preventing neo-aortic valve regurgitation.

Coronary Arteries

Coronary arteries in TGA usually arise from the aortic sinuses that face the pulmonary trunk, regardless of the interrelationships of the great arteries. Thus, the noncoronary sinus is usually the anterior one. Most often the left anterior descending (LAD) and circumflex (Cx) coronary arteries arise as a single trunk (left main coronary artery [LCA]) from aortic sinus 1 and distribute in a normal manner, although the Cx system is often small (Table 52-2). The right coronary artery (RCA) arises from sinus 2 and follows this artery’s usual course.

Table 52-1  Position of Great Arteries in Patients with Transposition of the Great Arteries

<table>
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<tr>
<th>Position</th>
<th>Number</th>
<th>Percent of 330</th>
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<tr>
<td>Ao anterior 0°</td>
<td>203</td>
<td>62</td>
</tr>
<tr>
<td>Ao anterior 30°R</td>
<td>54</td>
<td>16</td>
</tr>
<tr>
<td>Ao anterior 60°R</td>
<td>41</td>
<td>12</td>
</tr>
<tr>
<td>Ao-PT side-by-side 90°R</td>
<td>24</td>
<td>7</td>
</tr>
<tr>
<td>Ao anterior 30°L</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Ao anterior 60°L</td>
<td>2</td>
<td>0.6</td>
</tr>
<tr>
<td>Subtotal</td>
<td>330</td>
<td>100</td>
</tr>
<tr>
<td>Unknown</td>
<td>183</td>
<td>—</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>513</td>
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</tr>
</tbody>
</table>

Data from Kirklin and colleagues.

*Data based on 513 neonates with simple transposition of the great arteries (TGA) or TGA with ventricular septal defect undergoing arterial switch operation, 1985 to March 1, 1989, Congenital Heart Surgeons Society multinational study.

Key: Ao, aorta; L, left; PT, pulmonary trunk; R, right.

An almost infinite number of deviations from this usual pattern exist. Typical patterns are observed when both sinuses 1 and sinuses 2 give rise to a major coronary artery (Fig. 52-4). Patterns in which the Cx or LCA passes behind the pulmonary trunk deserve special attention by the surgeon (see “Arterial Switch Operation” under Technique of Operation later in this chapter).

All three main coronary arteries may arise from a single sinus (single coronary artery), most frequently, and of utmost concern to the surgeon, from sinus 2. Usually the arteries all arise from a single ostium in the center of the sinus (see Table 52-2). Alternatively, they may arise from a double-barreled ostium consisting of two ostia immediately adjacent to each other and constituting essentially a single ostium. Regardless, often these patients have an infundibular branch arising from sinus 1, making true single RCA uncommon. Coronary artery distribution in this situation has a typical pattern (Fig. 52-5). At times, however (in a pattern not shown in Fig. 52-5), the LCA or LAD passes forward between aorta and pulmonary trunk in an intramural course to emerge anteriorly. In this situation, instead of all three main coronary arteries arising from an essentially single, more or less centrally positioned, ostium, the LCA or LAD alone nearly always arises from an entirely separate ostium far to the left of the RCA ostium, adjacent to or just above the valvar commissure between sinuses 2 and sinus 1 (Fig. 52-6). An LCA or LAD arising in this
Figure 52-4  Most common patterns of circumflex coronary system when each facing sinus of Valsalva (sinuses 1 and 2) gives origin to a major coronary artery in hearts with transposition of great arteries. Key: Cx, Circumflex; L, left anterior descending coronary artery; R, right coronary artery. (From Quaegebeur.\textsuperscript{92})

Figure 52-5  Origin of all three major coronary arteries from a single ostium (or a double-barreled ostium) in sinus 2 or sinus 1 in hearts with transposition of great arteries. Key: Cx, Circumflex; L, left anterior descending coronary artery; R, right coronary artery. (From Quaegebeur.\textsuperscript{92})

location passes forward in an \textit{intramural course} (see Fig. 52-6) and entirely within the aortic wall (Fig. 52-7). It emerges from the aorta anteriorly and has the same appearance externally as when the artery originates from sinus 1.

In patients with situs inversus, the coronary arteries are a mirror image of situs solitus but seem to have a predilection for all coronary arteries to arise from a single sinus.\textsuperscript{112} Rarely the RCA may be intramural as it passes to the right and forward from its usual origin from sinus 2 in an otherwise typical pattern of “sinus 1: LAD, Cx; sinus 2: RCA” (or 1LCx-2R).

In 88 autopsy specimens, origins of coronary arteries were at or above the level of the sinutubular junction in 20%, paracommissural origin occurred in 3%, and angle of exit from the aortic wall was not orthogonal but tangential in 7%.\textsuperscript{112} Those with high takeoff were all intramural.

A \textit{conus artery} frequently arises separately and from its own ostium in sinus 1. It may supply at least a considerable part of the anterior wall of the infundibulum of the RV.

The course of the \textit{sinus node artery} may be important in the atrial switch (Mustard or Senning) operation. This artery usually arises from the RCA close to its origin and passes superiorly and rightward, usually partly embedded in the most superior portion of the limbus of the atrial septum, where it can be damaged if this portion of the atrial septum is widely excised.\textsuperscript{113} Then the sinus node artery usually passes behind or branches to form an arterial circle around the cavoatrial junction.\textsuperscript{49}
PART VII Congenital Heart Disease

Pulmonary Vascular Disease

Now that repair of simple TGA is usually performed in the first week or two of life, and repair of TGA with VSD is usually performed in the first month or two of life, pulmonary vascular disease has almost disappeared (see Natural History and Results later in this chapter), just as it has in many other types of congenital heart disease. However, it becomes important in many patients with TGA when early surgical treatment is not performed (Table 52-3). C16,F3,F4,F8,N7,V10

When pulmonary vascular disease develops in TGA, histologic changes in the pulmonary arteries are comparable with those found in isolated large VSD and can be similarly graded by the Heath-Edwards or Reid criteria (see “Pulmonary Vascular Disease” under Morphology in Section I of Chapter 35). In addition, however, pulmonary microthrombi are present in about 25% of lungs examined at autopsy N8 or on lung biopsy. W1 Pulmonary microthrombi produce a variety of intimal lesions, including eccentric cushion lesions and occlusion with recanalization of nonlamellar intimal fibrosis that can result in irregular fibrous septa within vessel lumens. These changes occur with and without laminar and circumferential changes secondary to hypertensive pulmonary vascular disease and are of uncertain etiology and importance. The changes are seldom severe enough to cause an increase in pulmonary vascular resistance (Rp) and occur with equal frequency in TGA with intact ventricular septum, large VSD, and large VSD and LVOTO N8. Using lung biopsy specimens, Wagenvoort and colleagues have also described wall thinning and dilatation of pulmonary arteries and, to a lesser extent, pulmonary veins in TGA with intact ventricular septum, particularly when the hematocrit is high. W1

Coexisting Cardiac Anomalies

About 75% of neonates presenting with TGA have no important coexisting cardiac anomaly other than a patent foramen ovale or an atrial septal defect. About 25% to 40% have a large or small VSD. Only about 5% have associated LVOTO. Some VSDs close spontaneously in the first few weeks or months of life, and some patients without LVOTO during the first few weeks of life develop obstruction later. Also, some with TGA, VSD, and LVOTO are asymptomatic as neonates and present later in life.
Table 52-3  Prevalence of Important (=Grade 3 Heath-Edwards) Pulmonary Vascular Disease at Autopsy in Patients with Transposition of the Great Arteries, Age 3 Months and Older

<table>
<thead>
<tr>
<th>Study</th>
<th>Intact Ventricular Septum</th>
<th>Large VSD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3-12 Months*</td>
<td>&gt;12 Months*</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>No.</td>
</tr>
<tr>
<td>Ferencz63</td>
<td>13</td>
<td>3</td>
</tr>
<tr>
<td>Viles et al.64</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Newfeld et al.65</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Clarkson et al.66</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>35</td>
<td>6</td>
</tr>
</tbody>
</table>

*Age at death.
+Includes patients with small ventricular septal defect.

Key: VSD, Ventricular septal defect.

Table 52-4  Types of Ventricular Septal Defect in Hearts with Transposition of the Great Arteries

<table>
<thead>
<tr>
<th>Type of VSD</th>
<th>No.</th>
<th>% of 81</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conoventricular</td>
<td>47</td>
<td>58</td>
</tr>
<tr>
<td>Without outlet septal malalignment</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>With outlet septal malalignment:</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Displaced to left</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Displaced to right</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Juxta-aortic</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Juxta-arterial</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Inlet septal (AV canal type)</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Muscular:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal (posterior, inflow)</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Midseptal</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Apical</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>81</td>
<td>100</td>
</tr>
</tbody>
</table>

*Data are based on GLH autopsy study.
+These VSDs were also juxta-tricuspid.
In 6 of the 22 hearts, VSDs were multiple.

Key: AV, Atrioventricular; VSD, ventricular septal defect.

Ventricular Septal Defect

The same types of VSD occur with TGA, and with the same definitions, as occur in hearts with a primary VSD, and they occur in about the same proportions (Table 52-4) (see “Location in Septum and Relationship to Conduction System” in Morphology in Section I of Chapter 35). Conoventricular defects of the several different varieties are most common and may not necessarily be juxtapulmonary (on LV side) (Fig. 52-8). In some hearts with conoventricular VSDs, the infundibular septum is malaligned and fails to insert within the Y of the TSM. The septum may be displaced leftward, resulting in a variable degree of LVOTO (Figs. 52-9 and 52-10), or rightward, tending to result in RV (subaortic) obstruction (Fig. 52-11). VSD with malalignment may not be juxta-tricuspid, as in tetralogy of Fallot, but the malaligned infundibular septum may be hypoplastic, varying from the usual tetralogy of Fallot (see Morphology in Section I of Chapter 38).

When the infundibular septum is displaced to the right, the pulmonary trunk may be biventricular in origin and over a juxtapulmonary VSD. Hearts with this arrangement are similar to those with double outlet right ventricle and juxtapulmonary VSD (see “Taussig-Bing Heart” under Morphology in Chapter 53) and may be associated with subaortic stenosis or aortic arch obstruction (arch hypoplasia, coarctation, or interruption). Occasionally the VSD is juxta-arterial and associated with a malaligned but nondisplaced infundibular septum. The infundibular septum may be absent or almost gone, and the VSD is then juxta-arterial (doubly committed) (Fig. 52-12).

Inlet septal defects that are also juxta-tricuspid are slightly more common in hearts with TGA than in those with a concomitant ventriculoarterial connection, in which the bundle of His passes from the AV node along the posteroinferior margin of the VSD. The juxta-aortic type of inlet septal defect, with its characteristic tricuspid straddling and abnormal AV node position, probably also occurs more often in hearts with TGA than other defects (see “Inlet Septal Ventricular Septal Defect” in Morphology in Section I of Chapter 35).

Most muscular VSDs are in the midseptum but may occur in other areas (Fig. 52-12).

Left Ventricular Outflow Tract Obstruction

Development of LVOTO, which produces subpulmonary obstruction, is part of the natural history of many patients with TGA. The obstruction may be dynamic or anatomic. LVOTO occurs in an important way at birth or within a few days in only 0.7% of patients with TGA and intact ventricular septum. Obstruction is present in about 20% of patients born with TGA and VSD. LVOTO may become apparent or develop after birth in other patients, thus reaching an overall prevalence of 30% to 35%.

Dynamic type of LVOTO, developing in patients with TGA and intact ventricular septum, is the result of leftward bulging of the muscular ventricular septum secondary to higher RV than LV pressure. Dynamic LVOTO is particularly likely to occur if the aorta lies anterior and more to the left than usual, with increased wedging of the subpulmonary area. The septum impinges against the anterior mitral leaflet in combination with abnormal systolic anterior leaflet motion (SAM). Thus, the mechanism is similar to that present.
**Figure 52-8** Specimen of transposition of great arteries with large conoventricular ventricular septal defect (VSD). A, From right ventricular side, VSD is seen to be adjacent to tricuspid valve anulus and extends inferiorly beneath it. Infundibular septum is normally aligned with trabecula septomarginalis. B, From left ventricular side, VSD is separated from pulmonary valve in part by an anomalous bulky fibrous pouch (arrow) that originates from left side of septal tricuspid leaflet and is a cause of left ventricular outflow tract obstruction. There is mitral-tricuspid continuity across floor of defect. Key: AoV, aortic valve; IS, infundibular septum; LV, left ventricle; MV, mitral valve; PV, pulmonary valve; RV, right ventricle; TSM, trabecula septomarginalis; TV, tricuspid valve.

**Figure 52-9** Specimen of transposition of great arteries with large conoventricular ventricular septal defect with leftward displacement of infundibular septum. A, From right ventricular side. B, From left ventricular side, conal septum is fused with left ventricular anterior free wall, with left ventricular outflow tract obstruction only moderate. Key: Ao, Aorta; AoV, aortic valve; IS, infundibular septum; D, ventricular septal defect; LV, left ventricle; MV, mitral valve; PV, pulmonary valve; RV, right ventricle; TSM, trabecula septomarginalis; TV, tricuspid valve.
Figure 52-10  Specimen of transposition of great arteries with large conoventricular ventricular septal defect (VSD) and leftward displacement of relatively small conal septum. A, From right ventricular side, fibrous tag (arrow), which also contributes to left ventricular outflow tract obstruction, is seen through VSD. B, From left ventricular side. Key: AoV, Aortic valve; IS, infundibular septum; LV, left ventricle; MV, mitral valve; PV, pulmonary valve; RV, right ventricle; TV, tricuspid valve; VSD, ventricular septal defect.
in hypertrophic obstructive cardiomyopathy (HOCM), but there is no asymmetric septal hypertrophy (see “Dynamic Morphology of Septum and Mitral Valve” under Morphology in Chapter 19). The gradient may be contributed to by the high velocity of blood flow produced by the usually large pulmonary-to-systemic blood flow ratio and the deformation of the LV outflow tract. When dynamic obstruction is severe, a ridge of endocardial thickening is produced on the septum at its point of contact with the mitral leaflet (Fig. 52-14). In patients with TGA and intact ventricular septum, rarely a subvalvar fibrous ridge may produce LVOTO. The ridge extends onto the anterior mitral leaflet near its hinge. This lesion is analogous to discrete subvalvar aortic stenosis occurring in otherwise normal hearts with ventriculoarterial concordant connection; it is usually localized but may be the tunnel type (see “Tunnel Subvalvar Aortic Stenosis” under Morphology in Section II of Chapter 47). LVOTO in these patients rarely may be caused by fibrous tags arising from the mitral apparatus or membranous septum. Valvar stenosis occurs infrequently in this situation, and anular hypoplasia is even less common. 

In patients with TGA and VSD, stenosis is usually subvalvar and valvar. Subvalvar stenosis is in the form of a localized fibrous ring, long tunnel-type fibromuscular narrowing, or muscular obstruction related to protrusion of the infundibular septum into the medial or anterior aspect of the LV outflow tract (Figs. 52-15 and 52-16). An important but fortunately rare form of subvalvar stenosis is attachment of the anterior mitral leaflet to the muscular outflow septum by anomalous fibrous or chordal tissue (Fig. 52-17). Other rare causes of subvalvar pulmonary stenosis are parachute mitral valve, accessory mitral leaflet tissue, and aneurysm of the membranous ventricular septum. An aneurysm may bulge as a windsock into the LV outflow tract. Its walls are thick, and the VSD is either below the aneurysm or within its sac. However, most of these “aneurysms” are examples of redundant fibrous tissue prolapsing through the VSD from the tricuspid valve (see Fig. 52-8) or accessory fibrous tags (see Fig. 52-10) in association with the anterior mitral valve leaflet.
Figure 52-12 Specimen of transposition of great arteries with large juxta-arterial ventricular septal defect (VSD). Infundibular septum is absent, and confluent aortic and pulmonary valves form upper margin of VSD. Defect is thus doubly committed. There is mild overriding of pulmonary artery and valve into right ventricle. A, From right ventricular side. B, From left ventricular side, there is pulmonary-mitral continuity. Key: Ao, Aorta; AoV, aortic valve; LV, left ventricle; MV, mitral valve; PT, pulmonary trunk; PV, pulmonary valve; TV, tricuspid valve.

Figure 52-13 Specimen of transposition of great arteries with large inlet muscular ventricular septal defect. This defect could be termed a conoventricular ventricular septal defect that is not juxtratricuspid because of a band of muscle separating it from membranous septum and tricuspid ring. A, From right ventricular side, muscle band is poorly seen (arrow). B, From left ventricular side. Key: AoV, Aortic valve; D, ventricular septal defect; LV, left ventricle; MV, mitral valve; PV, pulmonary valve; RV, right ventricle; TV, tricuspid valve.
Figure 52-14  Specimen of transposition of great arteries with essentially intact ventricular septum and dynamic muscular form of left ventricular outflow tract obstruction. Arrow points to ridge of endocardial thickening that forms at the point at which mitral leaflet touches septum during diastole. Key: LV, left ventricle; MV, mitral valve; PV, pulmonary valve.

Figure 52-15  Specimen of transposition of great arteries, ventricular septal defect (VSD), and left ventricular outflow tract obstruction. VSD is associated with infundibular septal malalignment and leftward displacement into left ventricular outflow tract. A, From right ventricular side. B, From left ventricular side, infundibular septum has fused with base of anterior mitral valve leaflet, which is cleft (arrow). Pulmonary valve ostium is displaced posteriorly and is severely stenotic. Key: AoV, aortic valve; IS, infundibular septum; MV, mitral valve; PV, pulmonary valve ostium; RV, right ventricle; TV, tricuspid valve.
Chapter 52  Complete Transposition of the Great Arteries

Valvar stenosis is caused by anular hypoplasia and when present is typically associated with subvalvar lesions. The pulmonay valve may be bicuspid. Rarely, there is a stenotic muscular subpulmonary infundibulum.

Patent Ductus Arteriosus
Patent ductus arteriosus (PDA) is more common in hearts with TGA than in hearts with ventriculoarterial concordant connection. At initial cardiac catheterization at an average age of 2 weeks, Waldman and colleagues found a PDA present in almost half the cases but it was functionally (although not necessarily anatomically) closed at 1 month. Persistence of a large PDA for more than a few months is associated with an increased prevalence of pulmonary vascular disease.

Tricuspid Valve Anomalies
The tricuspid to mitral anulus circumference ratio, normally greater than 1, is less than 1 in 46% of patients (Calder L: personal communication; 1984). This reduced ratio is most marked in hearts with associated coarctation (Fig. 52-18). Functionally important tricuspid valve anomalies are present in only about 4% of surgical patients (Table 52-5). In autopsy studies, however, a considerably higher proportion are found, particularly when there is a VSD.

Rarely, in hearts with intact ventricular septum, minor tricuspid valve anomalies may lead to severe regurgitation early in life. In hearts with TGA and VSD, anomalous chordal attachments around the edges of conoventricular VSDs are more common than in isolated VSD. These may complicate transatrial VSD closure and the construction of an intraventricular tunnel in the Rastelli operation.

The tricuspid leaflets can be redundant and dysplastic in TGA. Accessory tricuspid tissue may prolapse through the VSD and produce LVOTO (see “Left Ventricular Outflow Tract Obstruction” in previous text).

The tricuspid anulus may be dilated, resulting in some regurgitation, or in other cases the valve may be hypoplastic in association with underdevelopment of the RV sinus. Anular overriding or tensor straddling or both can occur, the latter being more common.
Figure 52-18  Ratio of tricuspid to mitral valve circumference in a series of autopsy hearts with transposition of great arteries (TGA) compared with 17 normal hearts. “Control” TGA specimens were those with a completely intact ventricular septum, with or without a small patent ductus arteriosus, atrial septal defect, or patent foramen ovale. Only unoperated specimens and those obtained within 30 days of an intracardiac repair are included. Vertical bars indicate one standard deviation. Individual P values are noted. Key: Coarct, Coarctation; PS, pulmonary stenosis; TV/MV, tricuspid to mitral valve; VSD, ventricular septal defect. (From Calder L: personal communication; 1984.)

Table 52-5  Associated Anomalies in Surgical Series of Patients with Transposition of the Great Arteries

<table>
<thead>
<tr>
<th>Anomaly</th>
<th>No.</th>
<th>% of 260</th>
</tr>
</thead>
<tbody>
<tr>
<td>No associated anomaly</td>
<td>93</td>
<td>36</td>
</tr>
<tr>
<td>Ventricular septal defect:</td>
<td>126</td>
<td>49</td>
</tr>
<tr>
<td>Small</td>
<td>31</td>
<td>12</td>
</tr>
<tr>
<td>Moderate</td>
<td>30</td>
<td>12</td>
</tr>
<tr>
<td>Large</td>
<td>65</td>
<td>25</td>
</tr>
<tr>
<td>Multiple</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>Patent ductus arteriosus*:</td>
<td>37</td>
<td>14</td>
</tr>
<tr>
<td>Small*</td>
<td>21</td>
<td>8</td>
</tr>
<tr>
<td>Moderate</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Large</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Left ventricular outflow tract obstruction*:</td>
<td>67</td>
<td>26</td>
</tr>
<tr>
<td>Essentially intact ventricular septum</td>
<td>27</td>
<td>10</td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>40</td>
<td>15</td>
</tr>
<tr>
<td>Tricuspid valve anomalies</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Mitral valve anomalies</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Coarctation (or interrupted arch)</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>Right ventricular hypoplasia</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Mild</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Moderate</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Large</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>Atrial situs inversus</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4</td>
<td>1.5</td>
</tr>
</tbody>
</table>

aData from series of 260 patients undergoing operation at GLH, 1964-1984. Totals are not cumulative.
*bStatus at time of intracardiac repair.
*cExcludes 29 patients in whom small patent ductus arteriosus was only possibly present.
*dMild in 16, moderate in 20, severe in 31.
*eRequiring closure.

Mitral Valve Anomalies

Important structural anomalies of the mitral valve are present in 20% to 30% of hearts with TGA, mostly in combination with a VSD, but the majority are not functionally important. There may be slight hypoplasia of the valve ring, often with clockwise rotation (viewed from LV apex). Mitral valve anomalies can be categorized into four groups as those affecting the:

1. Leaflets
2. Commissures
3. Chordae tendineae
4. Papillary muscles

The most important from a surgical standpoint are those of mitral valve overriding or straddling, in which the mitral valve leaflet is frequently also cleft.

Aortic Obstruction

Coexisting aortic obstruction can be discrete (coarctation or less often, interrupted aortic arch) or caused by distal arch hypoplasia. Rarely, it occurs when the ventricular septum is essentially intact, but it occurs in 7% to 10% of patients with TGA and VSD. This coexistence is more frequent when the VSD is juxtapulmonary and the pulmonary trunk is partly over the RV in association with rightward and anterior displacement of the infundibular septum and with some subaortic narrowing. (Coarctation is also common in the Taussig-Bing type of double outlet right ventricle; see “Taussig-Bing Heart” under Morphology in Chapter 53.) The ductus usually also remains patent to the aorta below the coarctation (pruductal coarctation).

When there is associated coarctation, underdevelopment of the RV sinus is more common and, as noted earlier, tricuspid to-mitral annulus circumference is less than in other TGA subsets.

Right Aortic Arch

Right aortic arch occurs in about 5% of patients with TGA. It is more common when there is an associated VSD than when the ventricular septum is intact and when there is associated leftward juxtaposition of the atrial appendages.

Leftward Juxtaposition of Atrial Appendages

Leftward juxtaposition of the atrial appendages occurs in about 2.5% of patients with TGA coming to repair. It is associated with a higher than usual prevalence of important underdevelopment of the RV sinus. Bilateral conus and dextrocardia seem more common in TGA associated with leftward juxtaposition than in TGA generally.

Right Ventricular Hypoplasia

RV hypoplasia was found to some degree in 17% of the autopsy series of TGA reported by Riemenschneider and colleagues.
Other Anomalies
Rarely, TGA coexists with congenital valvar aortic stenosis, and very rarely with total anomalous pulmonary venous connection. TGA can also coexist with complete AV septal defect (see “Complete Atroventricular Septal Defect” under Morphology in Chapter 34).

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

When the great arteries are transposed in hearts with AV concordant connection, systemic and pulmonary circulations are in parallel. Unless there is shunting between the two, this defect is incompatible with life for more than a short time. With this arrangement, pulmonary (Qp) and systemic (Qs) blood flow can vary independently, and shunting between the two circulations over more than very short periods must be equal in both directions, or eventually all the blood will be in one or the other circulation. Magnitude of bidirectional shunting is highly variable and is referred to as degree of mixing.

Symptoms and clinical presentation also depend in part on left atrial and pulmonary venous pressure. When Qp is even moderately elevated, these pressures tend to become elevated and produce symptoms. Both LV and RV failure usually result.

Clinical features and diagnostic criteria of patients with TGA fall into three groups based on these criteria, as discussed in the text that follows.

Essentially Intact Ventricular Septum (Poor Mixing)

TGA with essentially intact ventricular septum includes infants without a VSD or with a VSD 3 mm or less in diameter. A patent foramen ovale or naturally occurring atrial septal defect (ASD) is usually present. Cyanosis is apparent in half these infants within the first hour of life and in 90% within the first day and is rapidly progressive. Qp is usually increased to a pulmonary-systemic blood flow ratio (Qp/Qs) of about 2, but because of poor mixing across the small communication, this does not alleviate hypoxia. The baby becomes critically ill with tachypnea and tachycardia and dies from hypoxia and acidosis without appearance of frank heart failure. This rapid downhill course is usually obviated with a naturally occurring ASD of adequate size, because cyanosis is less severe. In surviving infants, appearance of moderate or severe dynamic LVOTO is associated with increasing cyanosis and hypoxic spells even after an adequate atrial septostomy.

Clinical signs in most newborns are unimpressive. Generally, patients are of average birth weight and in good general condition, although with severe cyanosis. Clubbing of fingers and toes is absent and generally does not appear unless the infant survives to about age 6 months. There is mild increase in heart and respiratory rates. The heart is not hyperactive, and the liver is barely palpable. A faint mid-systolic ejection-type murmur is present along the midleft sternal edge in less than half these infants. This murmur is more prominent with organic or dynamic LVOTO, first appearing at age 1 or 2 months with the dynamic form and then gradually increasing in intensity. The second heart sound is unremarkable (often apparently single or narrowly split), and the third heart sound and apical mid-diastolic flow murmur are both rare.

Chest radiography (Fig. 52-19) has three characteristic features:

1. An oval- or egg-shaped cardiac silhouette with a narrow superior mediastinum
2. Mild cardiac enlargement
3. Moderate pulmonary plethora

In the first week of life, however, the chest radiograph may be normal; occasionally cardiac enlargement may be more marked. The narrow mediastinum is caused in part by the great artery positions and by shrinkage of the thymus, usually associated with stress, and the plethora is caused by the increase in Qp. Plethora is less marked when there is important LVOTO.

The electrocardiogram (ECG) is often normal at birth, with the usual neonatal RV pattern. By the end of the first week, persistence of an upright T wave in the right precordial leads indicates abnormal RV hypertrophy, and right-axis deviation predominates. The vectorcardiogram shows a clockwise horizontal plane loop indicative of a near-normal LV systolic pressure and a dominant RV mass. When important
LVOTO is present or Rp is elevated, ECG evidence indicates biventricular hypertrophy.

Large Ventricular Septal Defect, Large Patent Ductus Arteriosus, or Both (Good Mixing)

Presentation in this TGA group generally occurs in the latter half of the first month, with mild cyanosis and signs of heart failure resulting from pulmonary venous hypertension and myocardial failure. Tachycardia, tachypnea, important liver enlargement, and moist lung bases are present. The heart is more active and usually larger than in the poor-mixing group.

A large VSD is associated with a moderate-intensity pansystolic murmur along the lower left sternal edge that may not be present initially. There is usually an apical mid-diastolic murmur or gallop rhythm and narrow splitting of the second heart sound with accentuation of the pulmonary component. With a large PDA, a continuous murmur, bounding pulses, and an apical mid-diastolic murmur are present in less than half the patients, even when the ventricular septum is intact. Sudden spontaneous closure of a large PDA when there is no VSD results in an increase in cyanosis (see Natural History later in this chapter).

Chest radiography may show more cardiomegaly, more plethora, and a wider superior mediastinum than in the poor-mixing group. Development of pulmonary vascular disease is associated with reduction in Qp and less plethora, particularly in the peripheral lung fields, as well as reduced heart size, but these features generally appear after the neonatal period.

The ECG shows biventricular hypertrophy and, when there is a persistent large VSD, a Q wave in V6. Isolated LV hypertrophy is rare and suggests RV hypoplasia with tricuspid valve overriding.

When coarctation of the aorta coexists with VSD and PDA, femoral pulses are usually normal because the coarctation is preductal and ductus arteriosus large. Rarely, differential cyanosis can occur, with cyanosis confined to the upper torso. All patients with this combination present early in life in heart failure and respond poorly to decongestive treatment. Isolated LV hypertrophy may be present on ECG because of frequent association of coarctation with RV hypoplasia.

Large Ventricular Septal Defect and Left Ventricular Outflow Tract Obstruction (Poor Mixing without High Pulmonary Blood Flow)

Large VSD with LVOTO is the least common of the three TGA groups. LVOTO is associated with a decreased Qp and poor mixing, but pulmonary venous hypertension and associated symptoms and signs do not develop because of lack of increase in Qp. Heart failure is therefore not present. Clinical findings are similar to those of tetralogy of Fallot with severe pulmonary stenosis or pulmonary atresia (see Clinical Features and Diagnostic Criteria in Section I of Chapter 38), and cyanosis is severe from birth. The heart is not overactive, and there is a pulmonary ejection murmur and often a single heart sound without an apical gallop or mid-diastolic murmur. Chest radiography shows a near normal–sized heart with normal or ischemic lung fields, and ECG shows biventricular hypertrophy.

Echocardiography

Definitive diagnosis of TGA can be made using two-dimensional (2D) echocardiography. Two-dimensional echocardiography is also particularly valuable in detecting tricuspid valve abnormalities, including overriding and straddling, and the varieties of subpulmonary stenosis, including dynamic obstruction. Echocardiographic features of dynamic LVOTO include leftward deviation of the ventricular septum, abnormal fluttering and premature closure of the pulmonary valve, SAM of the mitral leaflet (about 50% of cases), and prolonged diastolic apposition of the anterior mitral valve leaflet to the septum.

Echocardiography can also define with reasonable accuracy morphology of the coronary arteries, including number, origin, major branching pattern, and other features such as intramural course (Fig. 52-20). With two-reader methodology, the sensitivity of echocardiography to detect coronary variants is 86%, with a negative predictive value of 91% (Fig. 52-21).

Fetal echocardiography may be helpful in identifying abnormalities of the foramen ovale or ductus arteriosus, which is associated with neonatal hypoxia and death, and of the ventricular septum. Fetal diagnosis may improve perinatal care and reduce perinatal mortality and postoperative morbidity.

Cardiac Catheterization

Cardiac catheterization and cineangiography are not performed routinely, particularly in neonates, with major reliance for diagnosis placed on echocardiography. Nonetheless, knowledge of the information from these studies remains important.

A full study includes calculation of Qp and Qs and pressures, including those across the LV outflow tract. Because of intracardiac communications in patients with TGA, the Fick method is usually the only practical way of measuring Qp and Qs. Despite complexity of the circulation, standard calculations apply. Meticulous care is required in measuring oxygen consumption using a closed-box technique in infants. Equations are as follows:

\[
Q_p = \frac{V_O}{C_pO_2 - C_pO_2} \\
Q_s = \frac{V_O}{C_aO_2 - C_VO_2} \\
Q_ep = \frac{V_O}{C_pO_2 - C_VO_2}
\]

where

- \(Q_p\) = Pulmonary blood flow
- \(V_O\) = Oxygen consumption, mL · min\(^{-1}\)
- \(C_pO_2\) = Pulmonary venous oxygen content, mL · L\(^{-1}\)
- \(C_pO_2\) = Pulmonary arterial oxygen content, mL · L\(^{-1}\)
- \(Q_s\) = Systemic blood flow
- \(C_aO_2\) = Systemic arterial oxygen content, mL · L\(^{-1}\)
- \(C_VO_2\) = Mixed venous oxygen content, mL · L\(^{-1}\)
- \(Q_ep\) = Effective pulmonary blood flow

\(Q_ep\) represents flow of blood from the systemic to the pulmonary circuit at atrial, ventricular, and great arterial levels.
Flow must be equal in the opposite direction (anatomic left-to-right shunt or effective systemic blood flow), or over time one circuit would be deprived of blood.

Inherent errors occur in measuring these flows. When $Q_p$ is high and therefore pulmonary arterial oxygen saturation ($Sp_{aO_2}$) is high, the Fick calculation tends to be inaccurate. This error may be compounded by difficulties in recovering a truly mixed $Sp_{aO_2}$. Fortunately, these errors are greatest in patients with a very high $Q_p$, when concern is minimal about a high $R_p$. Calculations are more accurate when the $Q_p$ is low and $R_p$ correspondingly high. Potential for error exists if pulmonary arterial sampling is made proximal to site of entry of sizable systemic (bronchial) collaterals. Truly mixed $Sp_{aO_2}$ would then be lower than that measured, and $Q_p$ correspondingly lower, but in practice this situation is uncommon.

Thus, with careful technique, $R_p$ in patients with TGA can be calculated with reasonable accuracy. A specific problem arises, however, if hematocrit is particularly high; viscosity of the blood increases sharply when hematocrit is greater than
60%. The effect of viscosity on \( Q_p \) may then become important, and calculated \( R_p \) may be higher than that dictated by the pulmonary vascular bed alone.\(^{31}\) The only solution to this is to repeat the measurements after lowering the hematocrit by venesection.

\( Q_p \) is the flow upon which life depends. This flow is relatively fixed, typically only about 1.0 to 1.5 L \( \cdot \) min\(^{-1} \) \( \cdot \) m\(^{-2} \). This places a major constraint on oxygen supply to the patient. These relationships become evident in rewriting the Fick equation as follows:

\[
V_O_2 = Q_p (C_pO_2 - C_VO_2) = Q_p (SpvO_2 - SvO_2) \times Hb \times C_{max}O_2
\]

where

\( SpvO_2 = \) Pulmonary venous oxygen saturation
\( SvO_2 = \) Mixed-venous oxygen saturation
\( C_{max}O_2 = \) Oxygen capacity per gram of Hb
\( Hb = \) Hemoglobin concentration, g \( \cdot \) L\(^{-1} \)

On this basis, any reduction in hemoglobin will reduce oxygen uptake, and compensation for it is not possible in patients with TGA.\(^{39}\) If stress or exercise increases oxygen requirement, the difference in \( C_p \) and \( C_V \) must widen, and because \( C_p \) cannot increase, \( C_V \) (and thus tissue \( P_O_2 \)) must fall.

Cineangiography

Using appropriate views, cineangiography demonstrates the cardiac connections and great artery positions (Fig. 52-22), position and number of VSDs (Fig. 52-23), site of any LVOTO (Fig. 52-24), size and function of AV valves, size and function of both ventricles, pattern of the coronary arteries, and presence of other cardiac anomalies.

Computed Tomography and Magnetic Resonance Imaging

Although these newer modalities are more accurate than echocardiography in evaluating anatomy, particularly coronary anatomy, they are not routinely used in the neonate. Cardiac computed tomographic angiography (CTA) and image postprocessing with volume rendering can give an accurate diagnosis of the coronary pattern, even in neonates (Fig. 52-25). These modalities are used more frequently in postoperative patients in whom coronary imaging is indicated.

**NATURAL HISTORY**

Prevalence

TGA is a common form of congenital heart disease, occurring in 1:2100 to 1:4500 births\(^{1,12,14}\) and accounting for 7% to 8% of all congenital heart disease. Prevalence might be reduced more than 50% by maternal preconceptional multi-vitamin use\(^{39}\) or may be reduced by avoiding pesticides during the first trimester.\(^{1,12}\) In the Auckland area of New Zealand, prevalence over a 10-year period was 1:2400, whereas in New England (U.S.), it was 1:4000\(^{112}\) (\( P < .005 \)). Before the advent of effective treatment, at least 16% of deaths from congenital heart disease during childhood were caused by TGA.\(^{1,14}\)

Male-to-female ratio is 2:1. Male predominance increases to 3:3:1 when the ventricular septum is essentially intact and disappears in complex forms.\(^{1,14}\)

Survival

When patients with all varieties of TGA are considered, 55% survive 1 month, 15% survive 6 months, and only 10% survive 1 year (Fig. 52-26).\(^{5,8,7,8,1,12,14,7}\) Mean life expectancy is 0.65 year, rising to 4 years for those who survive to 12 months and to 6 years for the few who survive for 10 years. Thereafter, life expectancy declines rapidly (see Fig. 52-26).

Survival without treatment is different among subsets. It is particularly poor in untreated patients with *TGA and essentially intact ventricular septum*: 80% at 1 week but only 17% at 2 months and 4% at 1 year.\(^{1,14}\) Survival in this group is better when there is a true ASD (Fig. 52-27).

In patients with *TGA and important VSD*, early survival is higher: 91% at 1 month, 43% at 5 months, and 32% at 1 year.\(^{1,14}\) It is lower when the patient has a very large \( Q_p \) (see Fig. 52-27). The combination of large VSD and aortic obstruction (coarctation, interrupted arch) is particularly lethal; all patients die within a few months of birth with severe heart failure. Paradoxically, obstructive pulmonary vascular disease in patients with TGA and VSD improves early survival to 40% at 1 year, but with rapid decline thereafter and none alive by age 5 years.

In patients with *TGA, VSD, and LVOTO*, early survival is still better, reaching 70% at 1 year and 29% at 5 years, because in many patients LVOTO is only moderate initially.

Leibman and colleagues found that PDA increased risk of early death in all subsets of patients.\(^{1,14}\) This is particularly the case when the ductus is large.

Modes of Death

Poor survival in patients with *TGA and essentially intact ventricular septum* is related primarily to hypoxia. Intercurrent pulmonary infections may develop and are particularly lethal because they reduce \( Q_p \) and lead rapidly to increasing hypoxia, acidemia, and death. Death in this group may also result from cerebrovascular events, usually caused by the polycythemia and increased blood viscosity secondary to severe cyanosis, particularly in association with dehydration. However, hypoxia plus hypochromic microcytic anemia has also been implicated in the etiology of these events.\(^{116}\) Nonfatal cerebrovascular events occur in about 6% of patients treated by BAS\(^{112}\) and include cerebral abscess.

Patients with *TGA and important VSD* usually die with heart failure. Modes of death described for patients with simple transposition sometimes pertain to this group as well and include frequent intercurrent pulmonary infections.

Hypoxia is the primary cause of morbidity and mortality in patients with *TGA, VSD, and LVOTO*.

Patent Ductus Arteriosus

PDA is present at age 1 week in about half the patients with TGA, but thereafter the prevalence falls rapidly.\(^{219}\) When patent, the ductus is small (<3 mm in diameter) in about two
Figure 52-22  Cineangiograms of simple transposition of great arteries. **A-B**, Left ventricular injection, long axial view, in diastole and systole. Left ventricular outflow tract is widely open. Apparent narrowing at origin of left pulmonary artery is frequently seen and, as here, usually disappears during systole. **C-D**, Left ventricular injection, similar views and position, in another infant. Left ventricle gives origin to pulmonary trunk, and there is a long area of subpulmonary left ventricular outflow tract obstruction.
Figure 52-23  Cineangiograms of transposition of great arteries and ventricular septal defect (VSD). A, Small midmuscular VSD is demonstrated by right ventricular injection in long axial view. B, Large VSD in inflow portion of septum is demonstrated by right ventricular injection in four-chamber position. C, Large conoventricular VSD is shown with left ventricular ejection in long axial view. D, Multiple muscular VSDs are demonstrated with a right ventricular injection in long axial view. Key: Ao, Aorta; LV, left ventricle; PT, pulmonary trunk; RV, right ventricle.
Figure 52-24  Cineangiograms of transposition of great arteries, ventricular septal defect (VSD), and left ventricular outflow tract obstruction (LVOTO). A, Subvalvar LVOTO is associated with large conoventricular VSD, as shown by left ventricular injection and four-chamber view. B, Long subvalvar LVOTO is associated with large conoventricular VSD, as shown by left ventricular injection and four-chamber view. C, Discrete subvalvar LVOTO with large VSD and mild overriding of aorta onto left ventricle, as shown by left ventricular injection and four-chamber view. Key: Ao, Aorta; IS, infundibular septum; LV, left ventricle; PT, pulmonary trunk; PV, pulmonary valve; RV, right ventricle.

Figure 52-25  Computed tomography volume-rendered image showing left main coronary artery with left anterior descending and circumflex branches arising from left-facing sinus of Valsalva in infant with unrepaired S,D,D transposition of great arteries. Key: Ao, Aorta; Cx, circumflex coronary artery; L Main, left main coronary artery; LAD, left anterior descending coronary artery; LV, left ventricle PT, pulmonary trunk; RV, right ventricle.

Figure 52-26  Survival and life expectancy of 655 children with transposition of great arteries (TGA) of all types, all of whom died between 1957 and 1964; 73 living children and 14 miscellaneous deaths are excluded. Group is impure in that about 15% of the total had either single ventricle, hypoplasia of left ventricle with mitral stenosis or atresia, or hypoplasia of right ventricle with tricuspid stenosis or atresia. However, trends are representative of patients with TGA. (From Liebman and colleagues.)

1877
thirds of patients and seems to have little influence on natural history.\textsuperscript{1,14} When it is large, LV output is increased and hypoxia lessens, but heart failure becomes more severe. Under these circumstances, acute and often early closure of the ductus results in sudden increase in hypoxia and clinical deterioration.\textsuperscript{18,\textsuperscript{W2}} This is related not only to decreased mixing at the ductus level but also at the atrial level because of the fall in left atrial pressure that results from decreased pulmonary venous return.\textsuperscript{W2}

Atrial Septal Defects

In patients with TGA, the patent foramen ovale tends to close at the usual rate. This is the major cause of the time-related increase in hypoxia and death in patients with TGA and essentially intact ventricular septum without an important PDA. A true ASD, on the other hand, remains unchanged in size and palliates the patient longer.\textsuperscript{18} The same is true for those rare examples of coexisting partial anomalous pulmonary venous connections.

Ventricular Septal Defects

Large VSDs close or narrow in probably a smaller proportion (≈20\%) of patients with TGA than in patients with isolated VSD (see “Spontaneous Closure” under Natural History in Section I of Chapter 35). In most cases, however, the closing VSD is initially small and often muscular, and spontaneous closure has been documented to occur as late as the last part of the first decade of life.\textsuperscript{18} This process was rarely documented before the era of BAS, because so few patients survived beyond the first few months of life.\textsuperscript{3,13}

Left Ventricular Outflow Tract Obstruction

Dynamic LVOTO is not present at birth but can appear within several weeks. It gradually progresses in severity. Awareness of this tendency has increased since the era of BAS, after which LVOTO frequently develops. When dynamic LVOTO becomes important, hypoxia returns and life expectancy is shortened. LVOTO develops infrequently in patients with TGA and important VSD.

Pulmonary Vascular Disease

When TGA occurs as an isolated lesion (simple TGA), pulmonary vascular disease rarely develops in the first few months of life. After about 6 to 24 months, however, its prevalence increases to 10\% to 30\%.\textsuperscript{16,3,\textsuperscript{F1},\textsuperscript{F4},\textsuperscript{L3},\textsuperscript{N8}} Its development reduces Qp and increases hypoxia.

In patients with TGA and moderate or large VSD, pulmonary vascular disease develops more rapidly than in patients with simple TGA, as it does in those with persistently large PDA. Among those dying at about age 6 months, 25\% have developed severe pulmonary vascular disease (2grade 3), and 50\% of infants dying by age 12 months have developed it. These prevalences are much higher than in patients with primary VSD, and mechanisms may include hypoxemia and a prominent bronchopulmonary collateral circulation.\textsuperscript{2,\textsuperscript{F3},\textsuperscript{F4},\textsuperscript{N7},\textsuperscript{W1},\textsuperscript{W2}}

Increased Blood Flow to Right Lung

At birth in TGA, as in normal patients, slightly more blood flows to the right lung than to the left. In contrast to normal flow, however, flow to the right lung in TGA increases as age increases.\textsuperscript{4,\textsuperscript{R1},\textsuperscript{Y8}} In addition to age, magnitude of the increase is affected by the angle between takeoff of the right pulmonary artery and pulmonary trunk; the wider this angle (and thus the more the pulmonary trunk faces directly into the right pulmonary artery), the greater the blood flow to the right lung. The tendency of infants with intact ventricular septum to develop dynamic LVOTO after the first few months increases the velocity of flow, which increases the momentum effect toward the more directly aligned vessel.

Once right lung flow increases, the right vascular bed grows more and there is a relative increase in Rp and reduced compliance in the left lung, which further reduces left lung flow. It is unlikely that this phenomenon importantly affects the natural history of untreated TGA.

TECHNIQUE OF OPERATION

Currently, the arterial switch operation is advised for most patients with TGA except those with important fixed LVOTO.
An atrial switch operation (Mustard or Senning type) may be appropriate rarely, and in highly selected patients. Patients with poor mixing, typically those with intact ventricular septum and a small ASD, come to the operating room receiving an infusion of prostaglandin E2 and usually having had BAS. In current cardiology practice, septostomy is performed through transvenous access using echocardiographic guidance. These preoperative maneuvers usually result in adequate mixing and a stable patient.

Arterial Switch Operation

Simple Transposition of the Great Arteries with Usual Great Artery and Coronary Patterns

Preparation of the patient for operation, anesthesia, placement of monitoring devices, and details of the median sternotomy and initial dissection are the same as in other operations in neonates and young infants (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Positioning of the baby with extension of the neck is particularly important for exposure of the great arteries. Three general types of support systems are in use for arterial switch operation:

1. Continuous CPB, usually at 18° to 25°C, with reduced flow rate after reaching the target temperature. In some centers, mild hypothermia or normothermia is used. The IVC and superior venae cavae (SVC) are cannulated directly for venous return.

2. Near-continuous CPB at 18° to 20°C and with reduced flow rates (0.5 to 10 L·min⁻¹·m⁻²), but with a single venous cannula inserted through the right atrial appendage (see Sections III and IV in Chapter 2). Hypothermic circulatory arrest is established only for closure of the ASD, which is done through the opening in the tip of the right atrium or a small right atriotomy after removing the venous cannula. After this closure, the venous cannula is reinserted, CPB reinstituted, and full flow restored for rewarming of the patient.

3. Operation primarily is performed during hypothermic circulatory arrest after the patient has been cooled to 18°C by CPB, with rewarming also accomplished by CPB.

Preference for these methods is in the order presented.

Myocardial management is also variable among institutions achieving good results. A prevalent method is infusion into the aortic root through a large-bore needle of a cold, hyperkalemic, sanguineous solution just after clamping the ascending aorta, and no more. Another method is use of the same protocol but with an asanguineous cardioplegic solution.

The aorta and pulmonary trunk must be dissected apart and the ductus arteriosus dissected. The right and left pulmonary arteries are extensively mobilized to their lobar branches and beyond if needed. As much of this as convenient is performed before CPB, but it may be necessary to complete these steps after CPB is established. The aortic purse-string stitch is placed as far downstream as possible to facilitate work on the aortic root and ascending aorta (Fig. 52-28, A). When using two venous cannulae, purse-string sutures are placed in the superior and inferior venae cavae as they enter the right atrium. A suture ligature is placed around the aortic end of the ductus (see Fig. 52-28, A) Another purse-string stitch is placed in the right superior pulmonary vein as it enters the left atrium (not shown in Fig. 52-28, A).

After cannulation is completed, CPB is established and cooling begun. Another suture ligature is placed around the pulmonary end of the ductus and the ductus divided. If the two venae cavae have been directly cannulated, adjustable snares are placed around them and tightened, and a small (13F) angled vent catheter is placed through the purse string in the right superior pulmonary vein, positioning its tip across the mitral valve into the LV. The cardioplegic infusion needle is inserted, the aorta clamped, and infusion given.

The aorta is transected and better exposure is obtained by turning back the proximal segment to facilitate further dissecting apart the great arteries (Fig. 52-28, B). The pulmonary trunk is transected just proximal to its bifurcation (Fig. 52-28, C). The aortic button around the orifice of the LCA is excised from its sinus, and this is inserted into the left-facing sinus of the neoaorta (originally, pulmonary trunk). The aortic button around the orifice of the right coronary artery is excised and inserted into the right-facing sinus of the neoaorta (Fig. 52-28, B-D).

After the Lecompte maneuver (Fig. 52-28, E), the neoaorta is constructed by anastomosing the proximal segment of the original pulmonary trunk to the distal aortic segment. The stretched or torn foramen ovale (or ASD) is closed through an incision in the right atrium, usually with a running stitch. A patch may be used if the ASD is large. The right atrium is closed.

Separate autologous pericardial patches are used to fill in the defects in the proximal neopulmonary trunk. The neopulmonary trunk is then constructed (Fig. 52-28, F). All the latter steps involving pulmonary trunk reconstruction may be completed before removing the aortic clamp and beginning reperfusion of the heart, or reperfusion may be started at any point along the way.

A polyvinyl catheter is brought out from the left atrium through the right superior pulmonary vein or left atrial appendage if not already placed, and later, one is brought out from the right atrium. After the neonate has been rewarmed by the perfusate and proper conditions are in place, CPB is discontinued, and the remainder of operation is performed as detailed earlier (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). Use of intraoperative echocardiography to assess global and, especially, regional ventricular function is helpful in assessing adequacy of coronary translocation.

Simple Transposition of the Great Arteries with Origin of Circumflex Coronary Artery from Sinus 2

At times, the CX coronary artery arises as a branch of the RCA, the ostium of which is in sinus 2 (right-facing sinus). The CX artery then passes leftward behind the pulmonary trunk and arborizes in the usual fashion (Fig. 52-29, A). Less often the LCA arises from sinus 2 (an RCA from sinus 1) and passes leftward behind the pulmonary trunk to bifurcate in the usual manner. In both situations, particular care is required in the transfer of this coronary button from sinus 2.

Operation proceeds in the manner just described until the button of aorta containing the ostium of RCA and CX has been excised from sinus 2. A trap door opening is made in the right-facing sinus of the proximal neoaorta, cutting this
Figure 52-28  Arterial switch operation for transposition of great arteries, with aorta anterior and rightward, and usual coronary artery pattern (1LCx-2R). A, Placement of cardiopulmonary bypass (CPB) purse strings is shown in a patient who will undergo operation using continuous bypass and bicaval cannulation. Note that aortic purse string is placed as high on ascending aorta as possible to provide room for great artery manipulation. Venous purse strings are placed directly into superior and inferior venae cavae. A suture ligature has been placed around aortic end of ductus arteriosus. Tissue between great arteries is dissected prior to establishing CPB. A helpful maneuver is to place marking sutures on neoaorta for identifying sites of coronary implantation. Left and right branch pulmonary arteries are mobilized into first-order branching vessels. Cannulation proceeds in standard fashion and ductus arteriosus is immediately ligated. A separate suture ligature is placed on pulmonary artery end of ductus arteriosus and tied, and ductus is transected. A separate purse-string suture is placed in right upper pulmonary vein as it enters left atrium, and a vent catheter is introduced through purse string into left atrium, across mitral valve, and positioned into left ventricle (vent is not shown in this figure). B, After target core temperature is achieved, aorta is clamped and cardioplegia introduced into aortic root by one of standard methods. The aorta is transected just above sinutubular junction, and coronary arteries are carefully examined to confirm their positions and to rule out possibility of any unusual variations, such as eccentric coronary ostia or intramural coronary arteries. Using sharp dissection with fine scissors, coronary arteries are removed from their sinuses with at least a 1- to 2-mm cuff of sinus tissue surrounding ostia. Ligated and divided ductus arteriosus is also shown.
Coronary buttons have been completely mobilized. Pulmonary trunk is transected at its midportion and sites of coronary implantation (with help of marking sutures, if present) are identified on proximal neoaorta (dashed lines). Various techniques can be used to prepare implantation sites. Most common variation is shown here, in which implantation site is prepared by removing a horseshoe-shaped segment of pulmonary trunk wall. Implantation sites can also be prepared with a simple incision (slit) without resection of any proximal neoaortic tissue. Coronary implantation is performed sequentially using a running 8-0 or 7-0 monofilament suture. Following implantation, it is important to visualize course of coronary artery and, if any doubt remains as to its patency, a 1- to 1.5-mm probe is passed into its proximal portion to demonstrate patency.

Continued
Coronary arteries are fully implanted. Lecompte maneuver has been performed, as indicated by branch pulmonary arteries now located anterior to aorta. Anastomosis between proximal neoaorta and ascending aorta is performed end to end using a running 7-0 monofilament suture technique. After completing aortic anastomosis, coronary explantation sites on proximal neopulmonary trunk are reconstructed with individual patches of glutaraldehyde-treated autologous pericardium. Individual pericardial patches are tailored to be slightly larger than defects that resulted from coronary explantations. Proximal neopulmonary trunk is then connected to distal pulmonary trunk, end to end, using a running monofilament 7-0 suture technique. Completed great artery reconstruction is shown, along with closed CPB cannulation sites. Careful examination of proximal coronary arteries and their relation to anteriorly positioned pulmonary trunk and pericardial patches is routinely performed to ensure coronary arteries are not distorted or compressed. (Atrial septal defect [ASD] is closed using standard technique as described in text. ASD can be closed at any point in procedure. The common technique used with continuous CPB is to close ASD after aortic reconstruction is complete, but before embarking on pulmonary trunk reconstruction. In this way, ASD is closed with the aortic clamp still in place, aiding intracardiac visualization. Aortic clamp is then removed prior to performing pulmonary trunk reconstruction, minimizing myocardial ischemia time.)
Figure 52-29  Arterial switch operation for transposition of great arteries in patients with second most common coronary artery pattern (1L-2RCx). A, Aorta is anterior and slightly to right, as in the usual case. Proposed site of pulmonary trunk transection is as far distal as possible, just before bifurcation, to provide a proper implantation site on proximal neoaorta (native pulmonary trunk) for coronary button from sinus 2. Proposed aortic transection site is slightly more distal than in the case with most common coronary pattern (see Fig. 52-28), to accommodate slightly shorter distal pulmonary trunk segment at time of pulmonary reconstruction. Dashed lines show proposed transected sites of great arteries. Note circumflex coronary artery passing posterior and to left behind great arteries to distribute to its normal myocardial area. B, Using standard cardiopulmonary bypass and myocardial protection techniques, operation proceeds in standard fashion until it is necessary to reimplant coronary button from sinus 2. Coronary from sinus 1 has been reimplanted in standard fashion (see Fig. 52-28). Proximal neopulmonary trunk is retracted anteriorly, and tissue between the two great arteries at their bases is fully dissected. Dashed line shows proposed incision to create “trapdoor” flap that serves to orient sinus 2 coronary button after reimplantation such that circumflex artery is neither kinked nor stretched. Because pulmonary trunk was transected as distally as possible, reimplanted coronary also is positioned more cephalad than in usual case. This also minimizes chance of circumflex artery kinking.

Simple Transposition of the Great Arteries with Origin of All Coronary Arteries from Sinus 2

When all three major coronary arteries arise from sinus 2, they usually do so from a single ostium (see “Coronary Arteries” under Morphology earlier in this chapter). Operation is performed in the same general manner as described in the preceding text for patients in whom the Cx arises as a branch from the RCA arising from sinus 2.

When all three branches pass to the right and none passes leftward behind the pulmonary trunk, implantation can be into a simple incision in the center of the right-facing sinus.
When all three major coronary arteries arise from sinus 2, they may arise infrequently from two ostia, one of which is eccentrically located very near the valve commissure between sinus 2 and sinus 1 (Fig. 52-30, A). The LCA or only the LAD typically passes directly forward intramurally within the wall of the aorta. Unless forewarned, the surgeon may not recognize this from external examination after sternotomy, identifying it only after transecting the aorta and examining the interior of the aortic sinuses.

Several techniques have been used successfully to manage this problem.\textsuperscript{A15,A16,T2} One involves taking down the adjacent aortic (neopulmonary) valvar commissure (Fig. 52-30, B), which is resuspended subsequently on the pericardial patch used for neopulmonary trunk reconstruction. Separate aortic buttons are excised around each orifice, taking pains to include the entire intramural course of the LCA (Fig. 52-30, B and C). The buttons are inserted into the proximal neo-aortic segment in more or less the usual manner. In another technique (Fig. 52-30, D-F), both orifices are included in a single aortic button, which is inserted into the proximal neo-aortic segment by a special technique that minimizes rotation of the button.

Suzuki provides an excellent summary of different techniques of coronary transfer during the arterial switch operation.\textsuperscript{S30}

Transposition of the Great Arteries with More or Less Side-by-Side Great Arteries

The great arteries may be more or less side by side with the aorta to the right, and usually a VSD is present or the cardiac malformation is double outlet right ventricle with juxtapulmonary VSD (Taussig-Bing heart; see “Taussig-Bing Heart” under Morphology in Chapter 53). Prevalence of the various coronary artery patterns is different in this setting, one of the most common being sinus ILR-2Cx.

Operation is conveniently performed in a somewhat different manner and without the Lecompte maneuver (Fig. 52-31), although some perform the Lecompte maneuver even in this setting. Exact details of configuration and sizes of the great arteries and coronary artery positions may determine advisability of the Lecompte maneuver when more or less side-by-side great arteries are present.

Repair of Coexisting Ventricular Septal Defect

The VSD is repaired with a patch of polyester, polytetrafluoroethylene (PTFE), or autologous pericardium, with due regard for location of the conduction system (see Technique of Operation in Section I of Chapter 35). Approach may be through the right atrium, although for some VSDs access is easier through the proximal aortic (neopulmonary) segment or pulmonary (neoarterial) segment (see “Repair of Taussig-Bing Heart by Arterial Switch Repair” under Technique of Operation in Chapter 53).

Other Techniques

As in most procedures, other techniques are suitable for performing all or parts of the arterial switch operation. In one approach, after transecting the great arteries, the aortic buttons containing the coronary ostia are excised from the proximal aortic segment. Three fine sutures are placed externally on the proximal segment of the neo-arterial to mark the site of each valve commissure. The Lecompte maneuver is performed, and the two aortic segments are anastomosed to each other to construct the neo-arterial.\textsuperscript{B40,P1} The aortic clamp is released momentarily and hemostasis secured. With the clamp open and with due regard for position of commissural marking sutures, sites for implanting the coronary arteries are selected. With aorta again clamped, incisions are made, and the coronary buttons are transferred to the neo-arterial. The final steps are closure of the sites from which the coronary buttons were excised and construction of the neopulmonary artery. This method facilitates obtaining hemostasis of the neoarterial anastomosis by examining the suture line after releasing the aortic clamp momentarily and placing any needed additional stitches at that time. Also, the proximal neo-arterial is distended, facilitating selection of the site for
implanting the coronary arteries and creating incisions for receiving them.

In another alternative, the coronary buttons are implanted into incisions made proximal to the transection site. Before creating the neoaortic-aortic anastomosis, incisions into which the coronary buttons will be transferred are made, and the lower halves of the circumference of the buttons are anastomosed into this incision. The upper half is incorporated into the neoaortic-aortic anastomosis, which is made as the next step. This method puts sites of

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**Figure 52-30** Arterial switch operation for transposition of great arteries when all three major coronary arteries arise from sinus 2. In this figure, there are two separate ostia within sinus 2, with an eccentrically placed left main coronary ostium with an intramural left main coronary artery (LCA) course. **A**, Although LCA gives rise to left anterior descending (LAD) and circumflex (Cx) coronary arteries and appears from exterior inspection to be arising from sinus 1, it actually arises from sinus 2 from an eccentrically placed orifice that is distinct from nearby right coronary orifice. LCA orifice is positioned close to commissure between cusps of the two facing sinuses. Proximal aspect of LCA travels circumferentially within wall (intramurally) of neoaorta before emerging from aortic wall to become distinctly separate from it in region of left-facing sinus. Intramural component involves region of commissure between the two cusps of facing sinuses. Several important judgments must be made with this coronary pattern. First, it must be decided whether there is enough tissue separating the two ostia to be able to mobilize coronaries separately. If so, preferred method of management is to mobilize the two coronary buttons separately as shown here. **B**, The second important judgment involves managing intramural component of LCA. Right coronary button is mobilized in standard fashion. If commissure between cusps of two facing sinuses is involved with the intramural component of the LCA, then commissure is stripped away from internal aspect of sinus as shown here, leaving cusps and commissure intact. This then allows for complete mobilization of eccentrically shaped left coronary button. Eccentric shape is necessary for button to contain entire intramural component of LCA. **C**, Two completely mobilized coronary buttons are shown with remnants of commissure present on left coronary button. Each button is then reimplanted in the usual fashion. **D**, If it is determined that the bridge of tissue between the two coronary ostia is either too narrow to allow separating them or is nonexistent (true single ostium), an alternative technique of coronary implantation must be used. Shown here are separate ostia too close together to allow safe mobilization of separate buttons. Also, neither ostia shows an intramural course. In this setting, a single large button encompassing both ostia is mobilized. Proximal neoaorta is prepared for reimplantation by removing an appropriately sized segment of neoaorta wall. Distal aspect of coronary button is then sutured to implantation site. Note that coronary button is rotated minimally. **E**, Proximal neoaorta to ascending aorta anastomosis is performed, completing entire circumference except for that portion that contains coronary button. A small hemisphere-shaped segment of ascending aorta is excised in portion of ascending aorta adjacent to implanted coronary button. A roof of either glutaraldehyde-treated pericardium or pulmonary allograft arterial wall is used to create a convex roof over remaining opening in ascending aorta and remainder of free edge of coronary button. **F**, Completed aortic and coronary reconstruction. Pulmonary trunk reconstruction is performed as usual.
between sinus 1 and sinus 2 is attached at a proper level to the patch.

Finally, techniques have been described in which neopulmonary artery reconstruction is performed directly without using prosthetic material.\textsuperscript{22}

Arch obstruction in association with transposition can be managed either as a single-stage procedure, combining arch repair with the arterial switch, or in two stages, with arch repair performed via lateral thoracotomy and arterial switch performed via median sternotomy, usually within a week. In recent years, single-stage repair of both lesions has gained favor at many institutions with extensive neonatal experience.\textsuperscript{12,79}

![Figure 52-31](image)

**Figure 52-31** Arterial switch operation for transposition of great arteries with side-by-side great arteries and aorta to right, with coronary pattern of 1LR-2Cx. This coronary pattern is common with this great artery orientation. \textbf{A}, Dashed lines show proposed transection sites of great arteries. Both arteries are transected high, especially the native aorta, in anticipation of extra length needed for proximal neopulmonary trunk to meet transverse right branch pulmonary artery. \textbf{B}, Several important maneuvers required in this variant are shown. Both great arteries have been transected. Lecompte maneuver is not performed. Coronary buttons have been mobilized and coronary implant sites on proximal neoaoorta developed. Left-sided aspect of opening in distal pulmonary trunk is partially closed with a semilunar-shaped patch of autologous glutaraldehyde-treated pericardium. Right side of this opening is enlarged into right pulmonary artery as shown. This in effect shifts opening in distal pulmonary trunk to right in preparation for proximal neopulmonary trunk to distal pulmonary trunk reconstruction. This in effect reorients proximal pulmonary trunk to right side away from proximal neoaoorta and coronary reimplantation sites. Because proximal neopulmonary trunk is positioned more posterior than usual, access to coronary explantation sites for reconstruction with individual pericardial patches is more difficult. As a result, this part of operation is performed earlier than usual (i.e., before neoaorta reconstruction). Coronary explantation sites can be reconstructed with pericardial patches either before or after coronary reimplantations on proximal neoaoorta; however, this component of procedure should be performed before great artery anastomoses are performed. \textbf{C}, Completed operation. Coronary artery from sinus 2 is particularly vulnerable. Without Lecompte maneuver, proximal neopulmonary trunk is oriented somewhat posteriorly and can compress posterior reimplanted coronary artery (circumflex artery in this case) over its proximal extent. For this reason, it is critical that proximal neopulmonary trunk be implanted as far right along transverse right pulmonary artery as possible.
Atrial Switch Operation

**Senning Technique**

In the Senning type of atrial switch operation, preparations for operation and median sternotomy incision are performed as usual (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Operation may be performed during hypothermic circulatory arrest at about 18°C or, preferably, using CPB and direct caval cannulation. When CPB is used, the patient is cooled to at least 25°C; blood flow is then stabilized at 1.6 L · min⁻¹ · m⁻² or lower, and if necessary a period of 10 to 15 minutes of low flow or circulatory arrest may be employed. Myocardial management is the same as in the arterial switch operation (see preceding text).

Before CPB is established, specific measurements are made that are critical in subsequent incisions. First, circumferences of the SVC and IVC are determined (by compressing them momentarily with a clamp, measuring length of clamp occupied by compressed cava, and multiplying by 2). Position and superior and inferior extent of proposed left atriotomy are identified at the point of junction of the left atrial–right pulmonary vein wall with the most rightward aspect of the right atrial wall surface. Incision must not be extended further superiorly or inferiorly, which would necessitate its being carried leftward and behind the cavae (Fig. 52-32, A). The proposed right atriotomy incision is visualized roughly parallel to the left atriotomy incision (see Fig. 52-32, A). The superior extent is 3 or 4 mm anterior to the sulcus terminalis, thus anterior to the sinus node, and is anterior to the superior end of the proposed left atriotomy by a distance that is about two thirds of the SVC circumference. The inferior extent of the proposed right atriotomy is placed anterior to the inferior end of the proposed left atriotomy by a distance equal to two thirds of the IVC circumference. Further right-angled anterior extensions will be needed superiorly and inferiorly so that later a right atrial flap can be created (see Fig. 52-32, A).

CPB is established, preferably with direct caval cannulation or with a simple venous cannula for the hypothermic circulatory arrest technique. Initially the interatrial groove on the right side is dissected (see Fig. 52-32, A). Care is taken to keep the dissection shallow and not enter the atria.

The left atriotomy is made and pump-oxygenator sump sucker inserted if the patient is on CPB. The right atriotomy and anterior extensions are made (Fig. 52-32, B).

The atrial septal flap that will form the anterior wall of the posterior pulmonary venous compartment is fashioned (Fig. 52-32, B and C). When small, the foramen ovale is closed transversely with a few interrupted sutures, and the flap is created. When the foramen ovale is large, the flap consists solely of superior and posterior aspects of the limbus, but this is quite adequate when the maneuvers described next are used.

After making the septal flap, the coronary sinus is cut down precisely so as to leave anterior and posterior lips (Fig. 52-32, C and D). If the septal flap is particularly small, the base of the left atrial appendage can be advanced toward the right to meet the anterior superior aspect of the septal flap, and the posterior lip of the cut coronary sinus is used to connect to the anterior inferior aspect of the septal flap. The septal flap is shown being sewn into place without using the posterior coronary sinus lip in Figs. 52-32, D and E. If not used, the posterior lip may be tacked down (see Fig. 52-32, E).

The caval pathway to the mitral valve is formed posteriorly by the repositioned septal flap. The roof of the caval pathway is now completed by suturing the posterior right atrial flap anteriorly to the limbus. Interrupted sutures are used at each end to begin this (Fig. 52-32, F), placing these with great care so that the extensions of the caval wall will be undistorted. Each suture line is carried toward the midportion of the posterior margin of anterior limbus (see Fig. 52-32, F). The sutures are placed along the cut edge of the limbus anteriorly, visualizing and avoiding the position of the AV node (Fig. 52-32, G).

The pulmonary venous pathway to the tricuspid valve is now constructed. The anterior extensions of each end of the right atriotomy incision allow the right atrial flap to come to the right and posteriorly with ease (Fig. 52-32, H). Suturing is begun superiorly and is completed before beginning the inferior one. This aspect of the reconstruction may be done with 5-0 or 6-0 interrupted or continuous polypropylene sutures. This suture line passes posterior and then superior to the location of the sinus node (Fig. 52-32, I). As the superior suture line is developed, the right atrial flap is sutured to the lateral lip of the left atriotomy over the right superior pulmonary vein. A similar suture line is made inferiorly to complete this last step of the operation (Fig. 52-32, J).

Alternatively, when a near-linear right atriotomy is made and the anterior right atrial flap does not come easily to the lateral lip of left atrium, the lateral lip of the left atriotomy incision is sutured to the adjacent in situ pericardium. The anterior right atrial flap is then sutured to the pericardium at a convenient distance from the left atrial–pericardial suture line to produce a wide opening between posterior and anterior portions of the pulmonary venous compartment. In essence, the pericardium acts as an augmentation patch for the channel between posterior and anterior portions of the pulmonary venous compartments.

When CPB is used, rewarming is begun about 5 minutes before completing suturing of the right atrial flap. When suturing is completed, and with strong suction on the aortic needle vent, controlled aortic root reperfusion is begun, or the aortic clamp is released. The remainder of the procedure, including de-airing, is completed as usual (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

When hypothermic circulatory arrest is used with a single venous cannula, the cannula is reinserted through the right atrial appendage into the pulmonary venous atrium, CPB is reestablished, and rewarming is begun after removing the aortic clamp (see “Rewarming” in Section IV of Chapter 2). A small puncture may be considered in the most anterior part of the RV just below the aortic valve to allow escape of any entrapped air as the heart begins to contract. When a single venous cannula is used in this manner, pulmonary venous blood is returned to the pump oxygenator, and the circuit is in reality a systemic (right) ventricular bypass only. Thus, it is necessary to massage the heart and inflate the lungs gently to push blood through the lungs until adequate pulmonary (left) ventricular ejection returns. This is required for only a few minutes as a rule. The single venous cannula tip often partially obstructs the caval tunnels beneath the baffle so that caval pressures of 10 to 20 mmHg are usually during rewarming. They usually fall to that in the pulmonary venous atrium after the cannula has been removed. The remainder of the procedure is completed as usual.
With either technique, it is useful to leave a polyvinyl catheter through the right atrial appendage into the pulmonary venous atrium and one through the left atrial appendage into the systemic venous atrium. These catheters, plus an internal jugular catheter and a radial artery catheter placed at the beginning of the operation, allow complete monitoring of the hemodynamic state in the early postoperative period.

**Mustard Technique**
Preparations for the Mustard type of atrial switch operation and support techniques are the same as when the Senning technique is used.

The most appropriate material, configuration, and size of the atrial baffle to be inserted have been confusing and controversial. *Autologous pericardium* is considered the material of choice because of higher prevalence of baffle complications when polyester is used. If pericardium is not available at a secondary operation, however, allograft or xenograft pericardium, PTFE, or very thin knitted polyester may be used. One concept is to use a relatively small pericardial baffle and sew it snugly in place away from caval orifices in such a manner that as much of the caval pathways as possible is atrial wall rather than baffle. A different concept based on the *Toronto technique* uses a larger baffle that is sewn into place around
the caval orifices, with redundancy around the cavae to minimize the chance of narrowing SVC or IVC pathways.

Sternotomy is made, and before the pericardium is opened, it is cleared laterally to within 4 or 5 mm of each phrenic nerve, generally a distance of 5 or 6 cm in a 5-kg infant. Superiorly, the pericardium is cleared nearly to the level of the brachiocephalic vein after reflecting and partially excising the thymus. A longitudinal incision is made in the pericardium a few millimeters anterior to the right phrenic nerve; in a 5-kg infant this incision is about 6.5 cm. Next, a transverse incision is made in the pericardium along the diaphragm, extending to within 4 or 5 mm of the left phrenic nerve, a distance of about 3.5 cm in a 5-kg infant but proportionally longer in a larger patient. Superiorly, a similar but convex incision is made. A left-sided longitudinal incision is made parallel to the left phrenic nerve, but with a mild concavity in its midportion. After the pericardial patch is removed, a similar concavity is made in the midportion of the other long dimension of the rectangle (see Fig. 52-33, C inset).

After establishing CPB and aortic clamping with cold cardioplegia or establishing hypothermic circulatory arrest, the right atrium is opened through the usual oblique incision (Fig. 52-33, A). Atrial stay sutures may be placed for exposure.

Figure 52-32, cont’d  D, Atrial septal flap is now repositioned into left atrium and connected to left atrial wall, staying clear of ostia of left pulmonary veins. Suture line is brought anterior and superior to left pulmonary vein and anterior and inferior to left inferior pulmonary vein. E, In this illustration, atrial septal flap is well developed and posterior lip of cut coronary sinus is not utilized directly to augment atrial septal flap. After completing atrial septal flap suture line, unused posterior lip of coronary sinus is tacked down to anastomosis. Note position of left superior and left inferior pulmonary veins beneath septal flap (circular dashed lines). F, Posterior edge of right atrial incision is now approximated to remaining edge of atrial septum. Curved arrows show tissue manipulation required to achieve this. Most critical points in suture line are areas over orifices of superior (SVC) and inferior (IVC) venae cavae. These two aspects of suture line must be performed with great care to prevent narrowing of cavae at their transition into surgically created tunnel leading to mitral valve. Various techniques can achieve this. As shown at SVC junction, several interrupted sutures can be used to bring the two edges of tissue together over the cava. As shown at region of IVC, a “hemi–purse string” can be used to gather tissue in this area. Alternatively, interrupted simple sutures can also be used at IVC aspect of suture line. 

Continued
The atrial septum is excised, beginning by dividing the limbus superiorly with scissors, centering the cut just to the left of the midpoint of the superior limbus. The incision is carried nearly into the roof of the atrium and then posteriorly beneath the SVC and then inferiorly, removing the thick tissue from behind the SVC and in front of the right pulmonary veins. Occasionally the incision goes outside the atria, and if so, the opening is closed with fine interrupted sutures. Any remnant of the fossa ovalis is completely excised (Fig. 52-33, B).

The center of the free wall of the coronary sinus is divided downward with scissors for 7 to 10 mm, exactly as described for the Senning procedure (see Fig. 52-33, B). This transfers the coronary sinus opening into the left atrium and widens the area that will be the extension of the IVC toward the mitral valve.

A double-armed 4-0 or 5-0 polypropylene suture is passed through the pericardial baffle, and through the left atrial wall anterior to and between the left superior and inferior pulmonary veins (see Fig. 52-33, C). The superior suture line is

Figure 52-32, cont’d  
G, Remainder of suture line is performed with running monofilament suture to complete systemic venous to mitral valve pathway. Note positions of sinoatrial and atrioventricular nodes. H, Anterior edge of right atrial incision is then advanced posteriorly and attached to lateral free edge of left atrial incision. It is critical to utilize the length of anterior cut edge of right atrial incision appropriately such that underlying venae cavae are not constricted. Stay sutures shown here are positioned to allow appropriate length of right atrial flap overlying the two venae cavae. I, Suture line has been developed along both its superior and inferior aspects, crossing both cavoatrial junctions, and is completed along lateral edge of left atrial incision. Note that sinoatrial node now lies inside heart within wall of superior limb of systemic venous–to–mitral valve tunnel. Superior limb of the external suture line runs superior to sinoatrial node along superior cavoatrial junction.
Chapter 52  Complete Transposition of the Great Arteries

Figure 52-33  Atrial switch operation by Mustard technique (see text). Cardiopulmonary bypass and myocardial protection are similar to those used for Senning technique. A, Dashed line indicates proposed atrial incision. B, Entire atrial septum is excised as shown, and coronary sinus is cut down similar to Senning procedure (dashed line). C, Pericardial patch used to create intra-atrial baffle is shown in inset. Shape of this patch is generally that of an oval, with a gradual waist created in its midportion along long axis. Dimensions of patch will vary depending on size of infant. For a newborn infant weighing less than 5 kg, an initial oval patch measuring approximately 7 cm × 3.5 cm will be adequate, and may need to be tailored substantially. Width of patch at waist should be roughly 2.5 cm. Patch is sewn into place, beginning within left atrium, as shown, anterior to left-sided pulmonary veins.

Continued

made, but as the point just superior to the left superior pulmonary vein is reached, the suture line is carried superiorly to the posterolateral border of the orifice of the SVC and then up around the lateral and anterior margin of the caval orifice (Fig. 52-33, D). A larger distance is left between bites on the patch than between those around the caval orifice so as to avoid “purse-stringing” this orifice and to bring a redundant amount of pericardial patch into the area. The inferior suture line is made using the anterior lip of the incised coronary sinus (Fig. 52-33, D). The baffle is then sutured to the remnant of atrial septum anteriorly (Fig. 52-33, E).

The right atriotomy incision is closed primarily. Alternatively, if there is concern about patency of the pulmonary venous–to–tricuspid valve pathway, the right atrial free wall can be augmented with a patch of pericardium or PTFE.

Repair of Left Ventricular Outflow Tract Obstruction

This discussion refers primarily to the atrial switch operation for TGA with essentially intact ventricular septum, because direct relief of LVOTO is not usually possible in TGA, VSD, and LVOTO.

When obstruction is dynamic and LV systolic pressure is similar to or less than that in the right (systemic) ventricle, nothing is done directly to LVOTO. When LV systolic pressure is considerably higher, surgical relief of LVOTO is
D, Suture lines are developed superiorly and inferiorly around orifices of left pulmonary veins and toward superior and inferior caval orifices on their posterior, lateral, and then anterior aspects as shown. Suture line is then transitioned from caval orifices onto cut edge of atrial septum. Eustachian valve (if well developed) and anterior cut lip of coronary sinus can be used to enlarge pathway from inferior vena cava to mitral valve. 

E, Baffle is shown after suture lines are completed. The four pulmonary veins are visible: right-sided pulmonary veins completely, and left-sided ones partially. All pulmonary veins are unobstructed by baffle. Atrial incision, shown here still open, is closed with a running monofilament suture. If pathway from posteriorly positioned pulmonary veins to anteriorly positioned tricuspid valve appears to be narrowed in its midportion as it passes around baffle, right atrial incision can be augmented with pericardial or polytetrafluoroethylene patch.

**Figure 52-33, cont’d**

- Generally required. This may be in the form of resection of muscle, but in extreme cases a valved extracardiac conduit may be needed (see text that follows).
- When the LVOTO is in the form of localized or diffuse fibromuscular obstruction, the obstructive tissue is resected. One approach is through the mitral valve after creating the septal flap (Senning repair) or excising the atrial septum (Mustard repair). Alternatively, resection is performed through the pulmonary trunk and valve. In the uncommon circumstance of valvar obstruction, valvotomy through the pulmonary trunk is performed.
- When LVOTO is severe and cannot be relieved by resection, placing an LV–pulmonary trunk allograft valved conduit is required. (See “Double Outlet Right Ventricle and Pulmonary Stenosis” under Technique of Operation in Section II of Chapter 55 for additional details about placing left ventricular to pulmonary artery conduits.) After the first part of the atrial switch procedure has been completed, a longitudinal incision is made along the left side of the pulmonary trunk; if necessary, the incision is carried onto the left pulmonary artery. The proposed left ventriculotomy, between or beyond the diagonal branches of the LAD and along the anterolateral aspect of the LV near the apex, is marked with 5-0 sutures. The heart is allowed to fall back against the pericardium, and position on the pericardium of the proposed ventriculotomy is noted. Then, with the heart retracted upward and to the right, the proper length of the conduit can be estimated from the curving course between the pulmonary arteriotomy and the designated points on the pericardium. The conduit is trimmed to a proper length. It is cut short (about 5 mm beyond the aortic valve commissures) distally and beveled proximally. The conduit is sewn into position exactly as is done for other ventriculopulmonary trunk conduits (see “Rastelli Operation” later in text). After completing this, the last stages of the atrial switch operation are carried out.
Intraventricular Repair

In hearts with TGA and large VSD, occasionally a completely intraventricular repair can be done by the intraventricular tunnel technique. Its applicability depends on the relationship of the VSD to the great arteries and tricuspid valve. Techniques for doing this are variable and may require enlarging the VSD, but operation is essentially the same as the intraventricular repair that may occasionally be possible in Taussig-Bing heart (see “Intraventricular Tunnel Repair of Taussig-Bing Heart” under Technique of Operation in Chapter 53). In some cases the tunnel may be made superior to the pathway to the pulmonary trunk rather than inferior to it.

A partially intraventricular repair associated with placing a valved extracardiac conduit between the RV and pulmonary trunk has been described, but in the largest reported series, hospital mortality was high.

Rastelli Operation

Usual preparations for operation are made when performing the Rastelli operation for TGA, VSD, and LVOTO. A conduit is prepared using an estimate of the largest size of extracardiac conduit that can be comfortably placed within the patient’s thorax. A valved conduit is preferred, and options include pulmonary or aortic valved allografts and composite grafts using either woven polyester or PTFE conduits with bioprosthetic valves (see Appendix A in Chapter 12 and Technique of Operation in Section II of Chapter 38). A median sternotomy incision is made, and if stenoses are present at the pulmonary trunk bifurcation or in proximal portions of right or left pulmonary arteries, a piece of pericardium is removed and set aside. Pericardial stay sutures are placed. The pulmonary trunk in most patients with this anomaly is posterior and to the left of the ascending aorta. Therefore, to avoid conduit compression between the right-sided and anterior ascending aorta and sternum, preparations are made for routing the conduit so that it approaches the pulmonary trunk from the patient’s left side. The pulmonary trunk and its bifurcation are dissected completely free of the ascending aorta, and the first portions of left and right pulmonary arteries are also mobilized. Purse-string sutures are placed appropriately (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Any previously made systemic–pulmonary arterial anastomotic operations are dissected and closed just after establishing CPB (see “Repair of Tetralogy of Fallot after a Blalock-Taussig or Polytetrafluoroethylene Interposition Shunt” under Technique of Operation in Section I of Chapter 38).

After CPB is established and moderate hypothermia achieved, the aorta is clamped and cold cardioplegia is established (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). The left side of the heart is decompressed using a vent catheter placed through a purse-string suture in the right superior pulmonary vein and positioned across the mitral valve into the left ventricular cavity.

The infundibular free wall of the RV is opened by a moderate-sized vertical ventriculotomy that avoids major coronary artery branches. The incision may have to extend to the midportion of the RV free wall (Fig. 52-34, A). Appropriate stay sutures are placed on the ventriculotomy edge (Fig. 52-34, B). Origins of the aorta from the RV and pulmonary trunk from the LV are confirmed. It has already been determined by preoperative imaging study that the VSD is a conoventricular perimembranous type in the outflow portion of the ventricular septum, but this is now confirmed visually. The tricuspid valve and its tensor apparatus are usually well away from the pathway between the VSD and aorta, but if not, special measures are required. They may involve detachig tricuspid valve chords, with reattachment onto the intraventricular tunnel material (Hanley FL: personal communication; 2002) or using the conal flap method. Unless the VSD is clearly large and nonrestrictive, it is enlarged by excising the septum anterior to the defect (see dashed line in Fig. 52-34, B). Care is taken that the excision is in the inteventricular septum and not the ventricular free wall. Generally this provides considerable enlargement of the VSD, but care should be taken to not injure the septal coronary artery branches.

Intraventricular tunnel repair is now done similarly to that described for simple double outlet right ventricle (see “Intraventricular Tunnel Repair for Simple Double Outlet Right Ventricle” under Technique of Operation in Chapter 53). The LV ejects into the aorta through this tunnel (Fig. 52-34, C and D).

The pulmonary trunk is divided, and the proximal stump is oversewn at the valve level (see Fig. 52-34, C). The distal portion of the trunk and proximal left and right pulmonary arteries are mobilized, allowing the pulmonary trunk to be reoriented for a straightforward end-to-end anastomosis (see Fig. 52-34, D). Proximal anastomosis of the conduit to the right ventriculotomy is made (Fig. 52-34, E and F).

Remainder of the operation includes controlled reperfusion and de-airing procedures (see Chapters 2 and 3). The foramen ovale may be left open; as with tetralogy of Fallot (see Section I of Chapter 38) the right-to-left shunting across it in the early postoperative period augments cardiac output, although at the expense of systemic arterial desaturation. If a true ASD is present, however, it should be closed. Depending on the patient’shemodynamic status, transesophageal echocardiography findings, and surgeon preference, polyvinyl recording catheters may be placed in the right atrium, left atrium, and pulmonary artery for postoperative monitoring.

Lecompte Operation

The alternative method of managing TGA, VSD, and LVOTO, the Lecompte intraventricular repair, is also applicable to other types of ventriculoarterial discordant connections (see “Lecompte Intraventricular Repair” under Technique of Operation in Chapter 53). Other techniques for reconstructing the RV outflow tract have been described.

Aortic Root Translocation (Nikaidoh)

For patients with TGA and LVOTO with or without VSD, aortic root translocation has been adopted by some surgeons because of concerns about long-term outcomes of the Rastelli procedure. In this procedure, the aortic root is detached from the RV along with the coronary arteries and translocated posteriorly after making a septal incision or enlarging the VSD, then patching it, thereby relieving the LVOTO.
Figure 52-34  Rastelli operation for transposition of great arteries, ventricular septal defect (VSD), and left ventricular outflow tract obstruction. A, After standard median sternotomy incision, pulmonary trunk and left and right pulmonary arteries are completely dissected away from aorta and surrounding structures. Dashed line shows site of proposed right ventricular infundibular incision, which is in line with most anterior aspect of aorta. B, Standard cardiopulmonary bypass and myocardial protection techniques are used. Right ventricular infundibular incision is made and retraction sutures placed. Through this incision, rightward and anterior ascending aorta can be seen immediately, and leftward and posterior pulmonary valve can be visualized through VSD. Dashed line on rim of VSD shows site of incision on ventricular septum where VSD is enlarged in preparation for left ventricular to aortic baffle. This incision is necessary only when VSD is small (less than 60% aortic diameter). Dashed line on pulmonary trunk indicates proposed site of transection at sinutubular junction. C, Pulmonary trunk has been transected and proximal pulmonary trunk oversewn at level of valve. An alternative technique is to close pulmonary valve from within heart, working through infundibular incision and VSD. Using this method, if pulmonary valve anulus is small, it may be closed primarily; otherwise a circular patch is placed around immediately subvalvar tissue. VSD, which has been enlarged by incision, is shown with tunnel from left ventricle to aorta partially constructed. Material for tunnel is fashioned from a tube of polyester with a diameter approximately the size of ascending aorta. After tailoring, this results in a naturally curved baffle that is positioned with convex aspect of baffle facing into right ventricle. Lower aspect of baffle is sewn around rim of VSD, taking standard precautions with respect to inlet valves and conduction system (see “Location in Septum and Relationship to Conduction System” under Morphology in Section I of Chapter 35). Upper aspect of baffle is sewn into place by transitioning suture line away from rim of VSD as patch approaches aortic valve anulus on each side. Baffle is then sewn to immediately subaortic region along lateral aspects, and then finally anterior aspect, of circumference of aorta. A running technique, using nonabsorbable monofilament suture, is used. D, Left ventricular to aortic baffle is shown with suture line completed. A valved allograft conduit (or other composite conduit) is used to reconstruct right ventricular outflow tract. Conduit is tailored to appropriate length and is sewn end to end to pulmonary trunk as shown with a running monofilament technique.
sternotomy, and the usual limited dissection is made (see “Secondary Median Sternotomy” in Section III of Chapter 2) without freeing the front and leftward aspect of the heart. Tapes are passed around the cavae beyond the caval-atrial junctions, and they are cannulated directly. CPB is commenced and conducted as usual. The aorta is clamped and cold cardioplegic solution infused into the aortic root. The right atrium is opened with a centrally placed transverse or oblique incision.

When obstruction involves only the pathway from the SVC, this portion of the baffle may be enlarged. The baffle is incised vertically at its midpoint with a knife and the incision carried upward to open widely the pathway from the SVC. When this is totally occluded, the SVC–right atrial junction, which is always still patent beneath the baffle, is defined by inserting the tip of a curved forceps through a stab wound in the SVC (avoiding the sinus node area) and cutting down onto the tip of the instrument as it tents the baffle toward the right atrial cavity (pulmonary venous compartment). Alternatively, it may be possible to use the tip of a curved forceps to bluntly dissect the area of obstruction from above downward so that the tip appears below it. The baffle is opened at the point at which it joins the right atrial wall in front of the SVC junction, and fibrous thickening is excised to recontour the baffle and floor of the new tunnel. An elliptical PTFE or polyester patch is now sewn into the baffle incision with continuous 4-0 polypropylene suture to create a new roof to the pathway. The patch must not compromise the pulmonary venous channel.

To avoid kinking or stretching of the coronary arteries, modifications of this procedure with transfer of one or two coronary buttons akin to the arterial switch have been reported (Fig. 52-35). The pulmonary outflow tract is then reconstructed with an allograft valved conduit or a valveless patch.

Pulmonary Trunk Banding

Pulmonary trunk banding is discussed in detail in Chapter 35 (see “Pulmonary Trunk Banding” under Technique of Operation in Section I), including the Trusler rules for patients with transposition and large VSDs, and in Chapter 41 (see “Pulmonary Trunk Banding” under Technique of Operation in Section II).

Systemic–Pulmonary Arterial Shunting Procedures

Systemic–pulmonary arterial shunting techniques are described in detail in Chapter 38 (see “Technique of Shunting Operations” in Section I), and in Chapter 41 (see “Systemic–Pulmonary Arterial Shunt” under Technique of Operation in Section II). The same guidelines are followed concerning the size and type of shunt as in tetralogy of Fallot and in univentricular hearts.

Caval Obstruction

With caval obstruction after the Mustard procedure, usual preparations for operation through a median sternotomy are made, although others have preferred a right anterolateral thoracotomy. An oscillating saw is used for the secondary sternotomy, and the usual limited dissection is made (see “Secondary Median Sternotomy” in Section III of Chapter 2) without freeing the front and leftward aspect of the heart.

Tapes are passed around the cavae beyond the caval-atrial junctions, and they are cannulated directly. CPB is commenced and conducted as usual. The aorta is clamped and cold cardioplegic solution infused into the aortic root. The right atrium is opened with a centrally placed transverse or oblique incision.

When obstruction involves only the pathway from the SVC, this portion of the baffle may be enlarged. The baffle is incised vertically at its midpoint with a knife and the incision carried upward to open widely the pathway from the SVC. When this is totally occluded, the SVC–right atrial junction, which is always still patent beneath the baffle, is defined by inserting the tip of a curved forceps through a stab wound in the SVC (avoiding the sinus node area) and cutting down onto the tip of the instrument as it tents the baffle toward the right atrial cavity (pulmonary venous compartment). Alternatively, it may be possible to use the tip of a curved forceps to bluntly dissect the area of obstruction from above downward so that the tip appears below it. The baffle is opened at the point at which it joins the right atrial wall in front of the SVC junction, and fibrous thickening is excised to recontour the baffle and floor of the new tunnel. An elliptical PTFE or polyester patch is now sewn into the baffle incision with continuous 4-0 polypropylene suture to create a new roof to the pathway. An opened, preclotted, knitted or woven double-velour polyester graft of appropriate diameter is used for the patch because it contours toward the pulmonary venous atrium.
Figure 52-35  Aortic root translocation for transposition of great arteries and left ventricular outflow tract obstruction. A, Ventricular and aortic incisions required for aortic autograft excision are shown. Note that infundibular incision is circumferential just below aortic anulus, and as shown in inset depicting cross-section through ventriculoarterial junction, incision is slightly oblique. Coronary ostia are excised as circular buttons from respective sinuses of Valsalva. B, Once aortic autograft is excised and coronaries mobilized, pulmonary trunk is transected and an incision is extended across pulmonary valve anulus and septum connecting to ventricular septal defect (VSD), if present. Enlargement of left ventricular outflow tract is then accomplished by inserting a triangular-shaped VSD patch. C, Aortic autograft is reinserted into left ventricular outflow tract. It is then rotated 180 degrees so that defects from coronary buttons face anteriorly. Coronaries are then reimplanted. Before reestablishing ascending aortic continuity, branch pulmonary arteries are mobilized and brought anterior to aorta (Lecompte maneuver) in preparation for right ventricular outflow reconstruction. D, Right ventricle (RV) to pulmonary trunk continuity is achieved by inserting an interposition allograft connecting RV infundibulum to pulmonary trunk.
Alternatively, the baffle can be removed entirely. When the entire baffle is grossly thickened and distorted, especially if it contains folded polyester and the pathway from the IVC is obstructed, the entire baffle must be excised. A new baffle is inserted using pericardium, if enough is available, or PTFE or polyester. The remainder of the operation is completed as usual.

As a final alternative for isolated SVC obstruction, a bidirectional superior cavopulmonary anastomosis can be created (see Technique of Operation in Section III of Chapter 41).

**Pulmonary Venous Obstruction**

With pulmonary venous obstruction after Mustard repair, initial stages of operation and establishing CPB and cold cardioplegia are as described earlier. A transverse incision is made through the right atrial wall and into the anterior pulmonary venous compartment. Incision is carried posteriorly through the waist between anterior and posterior pulmonary venous compartments and directly between the right superior and right inferior pulmonary veins. Excess fibrous tissue surrounding the open stenosis is excised without breaching the baffle. One technique for repair involves closing the transverse atriotomy with continuous 4-0 polypropylene suture to create a vertical atrial suture line in much the same manner as described by Dillard and colleagues as part of the Mustard baffle technique in 1969. Instead, a V-atrial flap may be created from the lateral right atrial wall anterior to the stenotic site, with the apex of the V advanced posteriorly as a V-Y atrialplasty. Alternatively, a properly sized and shaped precut double-valve woven polyester gusset cut from a tube to create a convex contour is sutured into the atriotomy. This approach has the potential disadvantage that the stenosis may recur as the patch thickens, but this has not yet been reported. The remainder of the operation is completed as usual.

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Postoperative care is as usual for patients undergoing all types of intracardiac operations (see Chapter 5), with special considerations after some types of procedures.

When an arterial switch operation has been performed, particularly in a neonate, left atrial (or pulmonary artery) diastolic pressure should remain low, less than about 12 mmHg. Because restlessness or agitation increases metabolic demands and cardiac output, neonates and infants are usually kept intubated and sedated for 24 to 48 hours after operation. If cardiac output is less than optimal, particularly when 2D echocardiographic study indicates poor LV function, catecholamine support is used rather than further increasing LV filling pressure. Careful study shows that cardiac output profile occurs independently of the perfusion technique used at operation and occurs with and without associated VSD.

When an atrial switch operation has been done, positive end-expiratory pressure (PEEP) is not used because it tends to obstruct the SVC. Infants are nursed in a slightly head-up position. Atrial pressures are kept as low as is compatible with an adequate cardiac output; low-dose (2.5 to 5 mg·kg⁻¹·min⁻¹) dopamine during the early postoperative hours is helpful.

**RESULTS**

Simple Transposition of the Great Arteries and Transposition of the Great Arteries with Ventricular Septal Defect Using Arterial Switch Operation

**Early (Hospital) Death**

Currently, in institutions properly prepared for the arterial switch operation in neonates, early (hospital) mortality in both simple TGA and TGA with VSD is about 2% to 7%, a considerable improvement compared with about 15% reported in earlier eras.

**Time-Related Survival**

Instantaneous risk of death (hazard function) is extremely low by 6 to 12 months after arterial switch repair, and survival declines minimally after that time (Fig. 52-36). Thus, overall 5-year survival, including hospital mortality, has been 82% among a heterogeneous group of patients operated on in different institutions. In Williams’s group, 15-year survival was 81%. This intermediate-term survival is predicted to
Coronary Arteries

**Figure 52-37** Predicted survival after arterial switch repair in neonate with simple TGA and transposition of great arteries with ventricular septal defect, operated on in an institution of proven competence (“low risk”) in arterial switch repair. Depiction is a specific solution of the multivariable equation described in Appendix 52A, Table 52A-1. Birth weight was entered at 3.4 kg, with usual coronary anatomy (1LCx-2R) and no important coexisting cardiac or noncardiac anomalies. Key: TGA, Transposition of great arteries. (From Kirklin and colleagues.)*

Long-term (20-year) survival after the arterial switch operation is about 90% in patients operated on in the most experienced institutions.

**Modes of Death**

Mode of death is usually acute or subacute cardiac failure secondary to ventricular dysfunction resulting from imperfect transfer of coronary arteries to the neoaorta.\(^{19}\) This applies to deaths after hospital discharge as well as those during postoperative hospitalization. In the Congenital Heart Surgeons Society’s multistitutional study, five of six patients dying 6 or more months after the arterial switch operation died with severe ventricular (usually LV) dysfunction.\(^{41,12,74,76}\)

In one single-institution study, postmortem examination revealed severe proximal coronary artery stenosis caused by fibrocellular intimal thickening in six patients dying after the perioperative period.\(^{14}\)

The only other important mode of death occurs with RV dysfunction secondary to severe pulmonary vascular disease, which was not present at operation in a neonate with simple TGA. This mode has occurred in less than 1% of patients.\(^{42}\)

**Patient-Related Incremental Risk Factors for Death**

**Coronary Arterial Pattern** This has been the most important patient-related risk factor for death, based on multistitutional experience during the first decade after introduction of the arterial switch procedure in neonates, with two specific coronary patterns increasing risk. Risk of death is increased when the LCA or either of its branches arises from sinus 2, and risk is further increased when the LCA or LAD passes anteriorly between the two great arteries, a situation typically accompanied by an intramural course of the artery in the aortic wall (see “Coronary Arteries” under Morphology earlier in this chapter) (Fig. 52-38). As is usually the case, these risk factors are particularly strong in situations in which the overall risks are increased. Other unusual coronary patterns, some introduced more recently, have been identified as risk factors for death.*12,4,74,76*

Coronary arterial pattern is not an immutable risk factor and has been overcome, at least in some institutions, by appropriate techniques of coronary transfer (see “Arterial Switch Operation” under Technique of Operation earlier in this chapter).\(^{42}\) Nevertheless, a recent report of a large single-institution experience cautions that intramural coronary arteries remain associated with increased morbidity and mortality following the neonatal arterial switch operation (Fig. 52-39).\(^{42}\)

**Multiple Ventricular Septal Defects** Multiplicity of VSDs increased the risk of arterial switch repair in the first decade following the procedure’s introduction (Fig. 52-40). This risk factor may be neutralized by technical advances,\(^{4,46}\) but this is less certain than in the case of unusual coronary artery patterns. In some studies, presence of a single VSD increases risk of death compared with TGA and intact ventricular septum.\(^{41}\)

**Older Age at Repair** During the initial decade of the neonatal arterial switch experience, the younger the neonate at arterial switch repair, the safer the operation (Fig. 52-41). This age effect was particularly strong in patients with simple TGA and correlated with the magnitude of age-related differences in wall thickness characteristics of the LV of the normal neonatal heart and those of the heart with TGA. This age effect may be neutralized in current practice.\(^{4,37}\)

Arterial switch has been successfully performed beyond the neonatal period—up to age 9 months—in patients with TGA and intact septum, but such patients are more likely to require postoperative mechanical support.\(^{42}\)
Coexisting Cardiac and Noncardiac Congenital Anomalies
These anomalies may increase the risk of arterial switch repair, but are fortunately infrequent in patients undergoing repair. The most notable coexisting cardiac anomaly is aortic arch obstruction or interruption.

Operative Support and Procedural Incremental Risk Factors for Death
The support technique (CPB vs. hypothermic circulatory arrest) has not been a risk factor for death in the experience of some, but duration of circulatory arrest has been found to increase risk by others. However, longer global myocardial ischemic times have increased probability of death, suggesting that improved methods of myocardial management may improve results of operation. Even in institutions with substantial neonatal experience, CPB time is still a risk factor for early death.

Transection of the aorta or the pulmonary trunk at a site different from that described earlier in this chapter under Technique of Operation has been shown to be a risk factor for death. Inferences from various multivariable analyses support the method of management described there.

Growth of Arteries
All currently available information indicates that aortic, pulmonary, and coronary arterial anastomoses grow at a rate comparable with growth of the child. In one study, the neoaortic root was usually enlarged but with a growth pattern comparable with the normal population. Growth of the neopulmonary anulus was between the fifth and fiftieth percentile of a normal body surface area–matched population. These relationships reflect the normal disparity between pulmonary and aortic roots (see Chapter 1).
Patients with TGA and either intact ventricular septum or VSD treated by the arterial switch operation have been free of supraventricular rhythm disturbances that many patients have after atrial switch procedures. Arensman and colleagues report that this is true whether or not a right ventriculotomy has been made for repair of the VSD.\textsuperscript{113}

Only 3% of patients with simple TGA had arrhythmias after arterial switch repair in one study, compared with 57% after atrial switch repair.\textsuperscript{11,12} This continues to be the case even in more recent reports of longer-term follow-up.\textsuperscript{17} This casts doubt on the supposition that rhythm disturbances are an inherent part of the malformation of TGA.

**Coronary Blood Flow**

Positron emission tomography evaluation of coronary blood flow has revealed significantly lower coronary flow reserve in arterial switch patients compared with control subjects,\textsuperscript{816} although these findings are controversial.\textsuperscript{819} Other studies document exercise-induced perfusion defects and reduced coronary flow reserve at late follow-up;\textsuperscript{610} abnormal autonomic innervation, especially in children undergoing arterial switch at older age;\textsuperscript{814} and small-caliber left coronary systems.\textsuperscript{816,817}

**Coronary Artery Lesions**

Coronary artery obstruction has been documented in a disturbingly high number of asymptomatic TGA patients evaluated prospectively by angiography at 5- to 10-year follow-up. One study showed that 6 of 105 patients (5.7%; 95% CL 1.2%-10.2%) had important coronary lesions.\textsuperscript{813} In patients with perioperative ischemia that subsequently resolved before discharge after arterial switch, coronary obstruction was found in only 1 of 27 patients, whereas in those patients in whom perioperative ischemia persisted, all 10 patients demonstrated coronary obstruction.\textsuperscript{813} In general, coronary patterns involving a major coronary vessel passing behind the pulmonary trunk and operations using unusual techniques of coronary reimplantation demonstrate an increased risk of coronary obstruction.\textsuperscript{813} In other studies, coronary occlusion or stenosis was found in 3.0% to 7.8% of patients at follow-up.\textsuperscript{814,76}

Coronary artery stenosis continues to be higher in complex coronary patterns and in patients with evidence of ischemia.\textsuperscript{826} Also, asymptomatic coronary stenosis remains an ongoing finding with a prevalence similar to earlier reports. Results of both surgical revascularization and percutaneous transluminal angioplasty are acceptable. However, whether or not asymptomatic coronary obstruction with normal ventricular function should be treated remains controversial.\textsuperscript{810,812,11,19,8,13}

Both CTA and magnetic resonance imaging are useful non-invasive modalities to detect coronary abnormalities and myocardial perfusion defects.\textsuperscript{816,818} In a recent study using intracoronary ultrasound in 20 patients at 5 to 22 years after arterial switch, Pedra and colleagues found that a disturbingly high proportion of coronary arteries (89%) displayed a variable degree of proximal eccentric intimal proliferation.\textsuperscript{814} All children had coronary artery lesions, with 50% having moderate to severe intimal thickening (>0.3 mm). No risk factors for such abnormalities were encountered, including age, coronary artery pattern, hemodynamics, and follow-up duration. The authors speculate that this suggests early development of arteriosclerosis in reimplanted coronary arteries, which may play a role in the genesis of late coronary events.

**Functional Status**

Essentially all surviving patients are fully active and without limitations.\textsuperscript{812,811} However, decreased exercise capacity has been documented in patients who have undergone an arterial switch procedure as neonates. Residual RV outflow tract obstruction seems to have an effect on exercise capacity. Impaired chronotropic effect also appears to be an important contributor to reduced exercise capacity.\textsuperscript{811,814,819,820,821}

**Ventricular Function**

LV function is usually normal after an arterial switch operation. In a study of 12 patients, Borow and colleagues found normal contractility and normal dimensions and wall thickness in 10 of 12 patients studied between 2 and 7 years postoperatively (83%; CL 65%-94%).\textsuperscript{836} However, Hausdorf and colleagues identified 1 patient of 14 studied (7%; CL 2%–19%) late after arterial switch operation in whom LV stiffness was severely increased,\textsuperscript{815} and Okuda and colleagues reported three patients with reduced ejection fractions associated with neoaoortic valve regurgitation.\textsuperscript{814} Massin and colleagues found reduced LV function in only 1 of 71 patients at catheterization 1 year after an arterial switch operation, and that patient had had a coronary complication at the time of the arterial switch.\textsuperscript{814} Ventricular function after the arterial switch appears to remain normal at midterm follow-up (mean 3.8 years, maximum 10 years) in a large study,\textsuperscript{819} and with 20-year follow-up, LV dimensions and fractional shortening are within normal limits.\textsuperscript{811}

Interestingly, preoperative dynamic LVOT obstruction, even with a gradient of up to 120 mmHg, disappears after the arterial switch procedure.\textsuperscript{815,811}

In a comparative study between the arterial and atrial switch, Backer and colleagues found late postoperatively that systemic ventricular ejection fraction was within the range of normal in 98% of patients with simple TGA undergoing arterial switch repair,\textsuperscript{811} but in 79% of those who underwent an atrial switch repair.

**Rhythm Disturbances**

Patients with TGA and either intact ventricular septum or VSD treated by the arterial switch operation have been free of supraventricular rhythm disturbances that many patients have after atrial switch procedures. Arensman and colleagues report that this is true whether or not a right ventriculotomy has been made for repair of the VSD.\textsuperscript{113}

Only 3% of patients with simple TGA had arrhythmias after arterial switch repair in one study, compared with 57% after atrial switch repair.\textsuperscript{81,82} This continues to be the case even in more recent reports of longer-term follow-up.\textsuperscript{817} This casts doubt on the supposition that rhythm disturbances are an inherent part of the malformation of TGA.
Neurodevelopmental Status
At 8-year follow-up in one patient cohort, overall physical and psychosocial health status was similar to that of the general population, according to the Mean Physical Health Summary and the Mean Psychosocial Summary scores; however, increased problems with attention, learning, speech, and developmental delay were reported by parents.\textsuperscript{195} Neurologic testing at age 8 years in this cohort revealed that neurodevelopmental status was below expectation in many respects, including academic achievement, fine motor function, visualspatial skills, working memory, hypothesis generating and testing, sustained attention, and higher-order language skills.\textsuperscript{113} Earlier evaluation in this cohort at age 2.5 years suggested increased problems with expressive language and problem behavior if hypothermic circulatory arrest had been used for the repair.\textsuperscript{117} Others have shown reduced neurologic status in 21% of patients evaluated at age 3.0 to 4.6 years after neonatal arterial switch using circulatory arrest.\textsuperscript{119} In a recent study of 193 late survivors who underwent arterial switch more than 15 years previously, 98% were either attending school or working.\textsuperscript{185} It is important to realize that the neurodevelopmental alterations in these studies may have as much or more to do with CPB management as they do with the fact that these children had TGA.

Right Ventricular Outflow Tract Obstruction
Right ventricular outflow tract obstruction (RVOTO) was observed as a postoperative complication of arterial switch soon after this technique was introduced.\textsuperscript{227,4} Whether this is an immutable complication or can be prevented is still not certain.

RVOTO has occurred with sufficient severity to require reintervention in about 10% of patients and in one multi-institutional experience had a peak incidence about 6 months after the arterial switch operation (Fig. 52-43). Others have reported that RVOTO has become evident later after operation.\textsuperscript{4,3} In one analysis, freedom from reintervention was 94% (95% CL 64%-99%) at 1 year, and 79% (95%; CL 64%-94%) at 5 years.\textsuperscript{111} Subsequently, others reported much lower need for reintervention, and it is generally believed that this complication occurs less frequently in current practice.\textsuperscript{112} In one large cohort of patients from a single institution, reoperation for RVOTO was 1.5%.\textsuperscript{111} In general it is agreed that adequate mobilization of the branch pulmonary arteries during the Lecompte procedure is necessary to minimize supravalvar pulmonary stenosis. However, there is no consensus on whether a single vs. double patch technique, or use of a certain type of patch material, increases the risk of RVOTO. Smaller neo-PT or complex coronary patterns requiring larger coronary buttons may predispose patients to later RVOTO. Although reintervention for RVOTO shows a declining trend with experience, there still remains a larger number (up to 24%) of patients with mild RVOT gradients who do not necessarily qualify for reintervention, but may have reduced physical performance because of this.\textsuperscript{842}

Usually, obstruction is in the pulmonary trunk. Less frequently, RVOTO is at the bifurcation of the pulmonary trunk, and some have thought that stenosis at this area is the result of the Lecompte maneuver. In a careful analysis of a two-institution experience, however, the Lecompte maneuver could not be identified as a risk factor (Williams WG, Lincoln CL: personal communication; 1992). Occasionally the obstruction is at the RV–pulmonary trunk junction or in the RV infundibulum.

Neoaortic Valve Regurgitation
The neoaortic valve (pulmonary valve at birth) is competent in about 60% of patients studied several years after the arterial switch operation; mild regurgitation has been found in about 35% of patients and moderate or severe regurgitation in 5% or fewer.\textsuperscript{1,19,8,6,16,111} Risk factors for neoaortic regurgitation include older age at time of arterial switch, prior pulmonary trunk banding, presence of VSD, larger discrepancy between neoaortic root and ascending aorta, LVOTO, Taussig-Bing morphology, use of trap door techniques for coronary reimplantation, and implantation of coronary buttons compromising the integrity of the sinutubular junction of the neoaortic root.\textsuperscript{1,19,59,72,16,1,8,1,2,3,12,23,22,57} Prevalence of neoaortic valve regurgitation in patients at late follow-up is appreciable and progressive over time.\textsuperscript{19,72,1,8,1,2,3,22,57} However, need for
valve reintervention is less than 2% at current follow-up.\textsuperscript{22}\textsuperscript{22,33,57} Neoaoartic root dilatation and abnormalities in its distensibility have been documented.\textsuperscript{22,33,57}

Neopulmonary Valve Regurgitation

Neopulmonary valve regurgitation occurs after an arterial switch operation, but prevalence of important regurgitation has not been well documented. Obstruction at this level is more common, especially in patients with associated aortic coarctation.\textsuperscript{10}\textsuperscript{10}

Reoperation

Reinterventions are mainly for RVOTO and LVOTO\textsuperscript{11} after arterial switch. Freedom from reintervention was 75% at 20 years in one large study, with 58% of reoperations involving RVOTO at various levels and 43% involving LVOTO (Fig. 52-44 and Table 52-6). Over a 10-year period, Serraf and colleagues reported that for supravalvular pulmonary stenosis was necessary in 2.1% of patients, whereas all other indications showed a prevalence of less than 1%.\textsuperscript{22}\textsuperscript{22,24,12} Some reports document an increase in late reinterventions for coronary artery lesions.\textsuperscript{22,24,12} Mortality of reintervention has been low unless reoperation is early following initial operation.

Simple Transposition of the Great Arteries with Atrial Switch Operation

Early (Hospital) Death

Hospital mortality after an atrial switch ranges from 0% to 15%.\textsuperscript{22,33,45,12,20,35,41,73,57} \textsuperscript{1} Variability in prevalence of risk factors and degree of institutional competence with atrial switch repair are the determining factors.

Atrial switch operations are usually delayed for a few weeks to a few months after birth, in contrast to arterial switch operations, which are usually performed within a few days of birth. Thus, in addition to mortality early after the atrial switch operation, deaths that occur before operation must also be considered (Table 52-7). About 10% of uncorrected patients with simple TGA die by age 30 days despite adequate

![Figure 52-44](image-url) Freedom from reoperation among survivors of initial hospitalization after corrective operations for transposition of great arteries, stratified by type of operation.

Table 52-6 Reoperations Among 874 Survivors Through Hospitalization after the Mustard, Senning, or Arterial Switch Operation

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Mustard</th>
<th>Senning</th>
<th>Arterial Switch</th>
</tr>
</thead>
<tbody>
<tr>
<td>All reoperations</td>
<td>37</td>
<td>38</td>
<td>69</td>
</tr>
<tr>
<td>No. of reoperations</td>
<td>30</td>
<td>33</td>
<td>52</td>
</tr>
<tr>
<td>Closure of baffle leak</td>
<td>7 (19%)</td>
<td>11 (29%)</td>
<td>0</td>
</tr>
<tr>
<td>Enlargement of systemic venous pathway</td>
<td>24 (65%)</td>
<td>10 (26%)</td>
<td>0</td>
</tr>
<tr>
<td>Enlargement of pulmonary venous pathway</td>
<td>18 (49%)</td>
<td>8 (21%)</td>
<td>0</td>
</tr>
<tr>
<td>Enlargement of subvalvular pulmonary stenosis</td>
<td>0</td>
<td>0</td>
<td>10 (14%)</td>
</tr>
<tr>
<td>Enlargement of valvular pulmonary stenosis</td>
<td>1 (2.7%)</td>
<td>2 (5.3%)</td>
<td>5 (7.2%)</td>
</tr>
<tr>
<td>Enlargement of supravalvular pulmonary stenosis</td>
<td>0</td>
<td>0</td>
<td>16 (23%)</td>
</tr>
<tr>
<td>Enlargement of pulmonary arterial stenosis</td>
<td>0</td>
<td>0</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Enlargement of left ventricular outflow tract and aortic arch</td>
<td>3 (8.1%)</td>
<td>13 (34%)</td>
<td>19 (28%)</td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>0</td>
<td>1 (2.6%)</td>
<td>11 (16%)</td>
</tr>
<tr>
<td>Banding or debanding of pulmonary artery</td>
<td>2 (5.4%)</td>
<td>7 (18%)</td>
<td>3 (4.3%)</td>
</tr>
<tr>
<td>Arterial switch and atrial redirection</td>
<td>0</td>
<td>5 (13%)</td>
<td>0</td>
</tr>
<tr>
<td>Tricuspid valve procedure</td>
<td>5 (14%)</td>
<td>4 (10%)</td>
<td>4 (5.8%)</td>
</tr>
<tr>
<td>Closure of residual ventricular septal defect</td>
<td>5 (14%)</td>
<td>3 (7.9%)</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (5.4%)</td>
<td>2 (5.3%)</td>
<td>5 (7.2%)</td>
</tr>
</tbody>
</table>

Data from Horer and colleagues.\textsuperscript{22}\textsuperscript{22} Percentages refer to percentage of total number of operations in group.

Table 52-7 Category of Death in Infants with Simple Transposition of the Great Arteries Who Died Before Atrial Switch Repair\textsuperscript{a}

<table>
<thead>
<tr>
<th>Category</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA class V on admission and death in continuing hypoxia</td>
<td>4</td>
</tr>
<tr>
<td>Cerebral death after late (&gt;12 days old) referral in NYHA class V</td>
<td>6</td>
</tr>
<tr>
<td>Associated large PDA and NYHA class IV</td>
<td>3</td>
</tr>
<tr>
<td>Intercurrent respiratory infection</td>
<td>1</td>
</tr>
<tr>
<td>\textit{Escherichia coli} sepsis</td>
<td>1</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>1</td>
</tr>
<tr>
<td>Accident at balloon septostomy</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>17</strong></td>
</tr>
</tbody>
</table>

\textsuperscript{a}Data from study of 188 patients with simple transposition of great arteries admitted to GLH, 1970-1984.

\textsuperscript{b}Three of the 17 patients died before balloon septostomy.

Key: NYHA, New York Heart Association; PDA, patent ductus arteriosus.
Survival after the atrial switch operation is strikingly lower in patients with TGA and VSD than in those with simple TGA (Table 52-9). Currently, there are few risk factors for death after repair of simple TGA by the atrial switch operation (Table 52-9).

**Younger Age at Repair** Younger age has often been found in the past to be a risk factor for death after atrial switch repair. However, some institutions have achieved good results with the Senning atrial switch repair even when performed in the first 2 weeks of life, with hospital mortality in 4 of 26 patients (15%; CL 8%-26%). Several single-institution studies attest to the likelihood that young age can no longer be considered a risk factor for death after atrial switch repair in institutions properly prepared for this type of surgery.

“Older age” at repair (i.e., >3 years) has been shown to be a risk factor for late death, as have RV dysfunction and presence of active dysrhythmias.

**Lower Birth Weight** As with almost all operations for congenital heart disease, very low birth weight is a risk factor for death after atrial switch repair.

**Ventricular Septal Defect or Pulmonary Stenosis** In Senning’s long-term follow-up study, late systemic RV failure was three times more common in patients with VSD than in those with simple TGA, and systemic RV failure was found to be the most common cause of late death.

**Electrophysiologic Disturbances** Although much of the information about electrophysiologic disturbances after atrial switch operations comes from patients undergoing the Mustard technique, no evidence indicates that these disturbances are different with the Senning technique.
The morphologic basis of conduction and rhythm disturbances are understood to some extent. Histologic examination of the sinus node region reveals that the sinus node itself, sinus node artery, and paranodal tissues are frequently abnormal after the Mustard operation. B26,E4,E6 Acute changes include compression of the sinus node artery by sutures or, less often, intimal thickening or thrombus formation and suture compression, necrosis, or infarction of the sinus node itself with interstitial hemorrhage and edema of nodal tissue and adjacent myocardium. Edwards and Edwards found that in nine patients with sinus node artery compression, the sinus node showed acute infarction in seven. E4 Chronic changes include marked fibrosis in the node and paranodal tissue, such that in some cases the sinus node can no longer be identified. Surgical maneuvers responsible for this damage include incorrect techniques for SVC cannulation (e.g., too close to the node such that the purse-string suture damages it, use of crushing clamps in this region), damage to the sinus node

Figure 52-47 Effect of type of transposition of great arteries on mortality after atrial switch operation. Depictions are as in Fig. 52-43. A, Survival after Mustard atrial switch. B, Instantaneous risk of death (hazard function) after Mustard atrial switch. C, Survival after Senning atrial switch. D, Instantaneous risk of death (hazard function) after Senning atrial switch. Key: TGA, Transposition of great arteries; VSD, ventricular septal defect. (Congenital Heart Surgeons Society data: personal communication; 2011.)

Figure 52-48 Mortality after atrial switch operation for simple transposition of great arteries according to type of operation. Depiction is as in Fig. 52-43. A, Survival. B, Instantaneous risk of death (hazard function). (Congenital Heart Surgeons Society data: personal communication; 2011.)
artery by overzealous excision of the limbus and reendothelialization of the bare area so created, and placing suture lines too close to the sinus node.

Although these abnormalities are associated with dysrhythmias and are present in many individuals with late sudden death, it is uncertain whether they explain all late benign arrhythmias after the Mustard and Senning operations. Extensive suture lines within the atria, combined with excision of virtually all the atrial septum, may be related factors. Although it is no longer believed that atrial conduction occurs through discrete, well-defined internodal tracts (see “Internodal Pathways” under Conduction System in Chapter 1), preservation of the anterosuperior portion of the limbus may decrease prevalence of dysrhythmia. In contrast, division of the free wall of the coronary sinus is not detrimental.

Functional rhythm becomes progressively more prevalent as the years pass (Fig. 52-50). Usually sinus rhythm is present on standard ECG tracings at hospital discharge after the atrial switch operation for simple TGA. About 10% of such

![Figure 52-49](image1)

![Figure 52-50](image2)

**Table 52-8** Modes of Hospital Death in Patients with Simple Transposition of the Great Arteries

<table>
<thead>
<tr>
<th>Major Association with Death</th>
<th>Age at Operation</th>
<th>Other Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>High pulmonary vascular resistance</td>
<td>6, 7, 21 mo</td>
<td></td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>3, 3, 2 mo</td>
<td>NYHA class V in two Escherichia coli enteiritis in one</td>
</tr>
<tr>
<td>Baffle obstruction</td>
<td>19 days</td>
<td></td>
</tr>
<tr>
<td>Respiratory complications</td>
<td>11 days</td>
<td>NYHA class V heart failure, large PDA</td>
</tr>
<tr>
<td>Arrhythmia (at 27 days postop)</td>
<td>5 mo$^d$</td>
<td></td>
</tr>
<tr>
<td>Chyl Omar pericardium (at 26 days postop)</td>
<td>10 mo$^d$</td>
<td></td>
</tr>
</tbody>
</table>

$^d$Data from study of 10 hospital deaths after 141 atrial switch operations for simple transposition of the great arteries at GLH, 1970-1984.

$^e$Preoperatively, 8.3, 14, 22 μ m$^{-2}$. All showed grade 4 Heath-Edwards changes at autopsy.

$^f$Senning repair.

Key: mo, Months; NYHA, New York Heart Association; PDA, patent ductus arteriosus; postop, postoperatively.

**Table 52-9** Incremental Risk Factors for Hospital Death after Atrial Switch Operation

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Coefficient ± SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate or large VSD</td>
<td>2.2 ± 0.44</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>PDA$^b$</td>
<td>0.96 ± 0.49</td>
<td>.05</td>
</tr>
<tr>
<td>Age ≤ 30 days</td>
<td>2.3 ± 0.79</td>
<td>.003</td>
</tr>
<tr>
<td>Intercept</td>
<td>2.9</td>
<td></td>
</tr>
</tbody>
</table>

$^b$Sex, race, and ethnicity–matched general population.

$^c$Small, moderate, or large.

Key: PDA, Patent ductus arteriosus; SD, standard deviation; VSD, ventricular septal defect.
patients are in a varying sinus junctional rhythm, and only a few show a pure benign-type junctional rhythm (Table 52-10). Thereafter, there is a gradual decrease in prevalence of sinus rhythm after Mustard-type repair as follow-up continues.\(^{210,219,239}\) Besides the apparent slight increase in risk of sudden death when a benign junctional rhythm is present, this rhythm appears to have no other importance. In some normal subjects in sinus rhythm, heart rate can fall below 40 beats · min\(^{-1}\) during sleep, and rhythm is then usually junctional.\(^{315,58,521}\)

In patients with slow junctional rhythm there is a relatively normal rate response to exercise, often with reversion to sinus rhythm.\(^{109}\) Occasionally rapid (accelerated) junctional rhythm can occur. This rhythm, and occasionally supraventricular tachycardias or atrial flutter, can lead to a malignant arrhythmia that reduces cardiac output and requires active measures for control.\(^{56}\) Sinus node recovery time after atrial switch operations may be abnormal.\(^{357,54,450}\) Also, even when in sinus rhythm, maximal exercise heart rate response and postexercise recovery rate may be abnormal.\(^{109}\)

Twenty-four-hour Holter monitoring after both the Mustard and Senning procedures may reveal dysrhythmias that are infrequent enough to be overlooked on standard ECGs, even when these are repeated on many occasions.\(^{512}\) This technique allows frequency of rhythm disturbances to be assessed, as well as their categorization as a normal or probably abnormal variant. Holter studies that fail to make this latter differentiation overstate dysrhythmia prevalence.\(^{510}\)

Before a postoperative dysrhythmia can be categorized as resulting from the surgical procedure, it is necessary to know that the abnormal rhythm was not present on a preoperative Holter monitor recording.\(^{522}\) Using these criteria, dysrhythmias do not occur often before atrial switch procedures. Thus, 24 patients with TGA aged 1 to 10 months had preoperative monitoring; using the criteria in Table 52-11, only one was abnormal (frequent atrial premature beats), although five patients showed abnormalities within the normal range.\(^{522}\)

Postoperative Holter monitoring reveals additional dysrhythmias (Table 52-12), particularly when the patient is in junctional rhythm. If standard ECG always shows sinus rhythm, however, in about two thirds of patients the Holter study is normal. Rarely is an important abnormality in rhythm disclosed for the first time on Holter monitoring. Dysrhythmias that predispose to sudden death in this context are as yet unknown.

Rhythm monitoring during maximal exercise testing may provide additional information, although at present its prognostic implications are also unknown. Mathews and colleagues noted that of 15 patients in sinus rhythm at rest who underwent exercise testing a mean of 9 years after Mustard repair, nine developed either premature atrial or ventricular contractions or junctional rhythm during exercise.\(^{316}\) This finding contrasted with a control group, none of whom developed a dysrhythmia.\(^{516}\)

Sudden death may well be related to some of these dysrhythmias. This complication was emphasized during early

---

### Table 52-10 Cardiac Rhythm after Mustard Atrial Switch Repair in Patients with Simple Transposition of the Great Arteries

<table>
<thead>
<tr>
<th>Rhythm</th>
<th>Prevalence at Hospital Discharge</th>
<th>Rhythm at Last Review</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Sinus</td>
<td>88</td>
<td>79</td>
</tr>
<tr>
<td>Junctional</td>
<td>9(^{a})</td>
<td>8</td>
</tr>
<tr>
<td>Sinus/junctional</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Uncertain</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>100</td>
</tr>
</tbody>
</table>

\(^{a}\)Data from study of 112 hospital survivors at GLH, 1964-1982; longest follow-up was 17 years.

\(^{b}\)Among the 28 patients in junctional rhythm, only 4 (19%) later converted to sinus rhythm.

\(^{c}\)Among the 88 patients in sinus rhythm at discharge, 28 (32%) later converted to junctional rhythm.

\(^{d}\)Temporary CHB postoperatively.

\(^{e}\)One known to be present preoperatively.

\(^{f}\)One with a PR interval of 0.27.

Key: CHB, Complete heart block.

---

### Table 52-11 Criteria of Normality and Abnormality of Arrhythmias Observed on 24-Hour Ambulatory Electrocardiographic Monitoring in Normal Infants and Children

<table>
<thead>
<tr>
<th>Arrhythmia</th>
<th>Normal Criteria</th>
<th>Abnormal Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Junctional (nodal)</td>
<td>Rare, unsustained</td>
<td>Frequent, sustained</td>
</tr>
<tr>
<td>Accelerated junctional (&gt;100 · min(^{-1}))</td>
<td>Unsustained (&lt;6 beats)</td>
<td>Prolonged, repetitive</td>
</tr>
<tr>
<td>Tachycardias/bradycardias</td>
<td>Occasional</td>
<td>Frequent episodes</td>
</tr>
<tr>
<td>Sinus pauses</td>
<td>50%-99% duration(^{a})</td>
<td>50%-99% duration when ≥10 · h(^{-1})</td>
</tr>
<tr>
<td></td>
<td>Infrequent (&lt;10 · h(^{-1}))</td>
<td>≥100% duration, total pause ≥1800 ms</td>
</tr>
<tr>
<td>Premature beats</td>
<td>Infrequent (&lt;10 · h(^{-1}))</td>
<td>≥10 · h(^{-1})</td>
</tr>
<tr>
<td>Atrial bi/trigeminy</td>
<td>Infrequent (&lt;3 episodes)</td>
<td>Repetitive</td>
</tr>
<tr>
<td></td>
<td>Unsustained (&lt;6 beats)</td>
<td>Sustained</td>
</tr>
<tr>
<td>Supraventricular tachycardia(^{a})</td>
<td>Unsustained (&lt;6 beats)</td>
<td>Sustained, chaotic, repetitive</td>
</tr>
</tbody>
</table>

\(^{a}\)PP (or RR) interval length of sinus pause beat compared with preceding normal beat.

\(^{b}\)Some are caused by atrial flutter.
Table 52-12  Arrhythmias on 24-Hour Ambulatory Electrocardiographic Monitoring of Patients after Mustard Atrial Switch Procedurea

<table>
<thead>
<tr>
<th>Rhythm on Holter Monitor</th>
<th>Persistent SR</th>
<th></th>
<th>Persistent JR</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>No.</td>
<td>% of 19</td>
<td>Normal</td>
</tr>
<tr>
<td>SR</td>
<td>16</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>JR</td>
<td>0</td>
<td>3</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>Accelerated JR</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Tachy/bradycardias</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sinus pauses4:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50%-99%</td>
<td>5</td>
<td>6</td>
<td>32</td>
<td>4</td>
</tr>
<tr>
<td>≥100%</td>
<td>0</td>
<td>3</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>≥1800 ms</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>APBs</td>
<td>9</td>
<td>2</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>VPBs</td>
<td>3</td>
<td>1</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Bi/trigeminy</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>SVT</td>
<td>0</td>
<td>1</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL ARRHYTHMAs8</td>
<td>18</td>
<td>13</td>
<td>42</td>
<td>16</td>
</tr>
<tr>
<td>TOTAL PATIENTS</td>
<td>11</td>
<td>8</td>
<td>42</td>
<td>CL 29%-57%</td>
</tr>
</tbody>
</table>

aData from a study at GLH, 1970-1984. Criteria are given in Table 52-11.
See Table 52-11.
Excluding junctional rhythm.
Key: APBs, Atrial premature beats; CL, 70% confidence limits; JR, junctional rhythm; SR, sinus rhythm; SVT, supraventricular tachycardia; VPBs, ventricular premature beats.

Development of the atrial switch operation by Aberdeen.3 Sudden death occurs in about 5% of hospital survivors over 10 to 20 years. Sudden death is rare in patients who remain in sinus rhythm postoperatively and when pacemaker recovery times are normal.4,5,6 Risk of sudden death in patients in junctional rhythm is 7%. No other risk factors for sudden death could be identified in a collaborative study of 372 patients. In a prospective 8-year study of 100 Senning and Mustard patients, progressive loss of a stable sinus rhythm was noted in more than 60% of patients at a mean follow-up of 7 years. However, rhythm disturbance identified by ECG or Holter monitoring did not identify patients at risk for sudden death.8

Changes in P-wave amplitude and contour are virtually constant after Mustard repair.4,6 Postoperatively, the P wave is greatly diminished in amplitude and is frequently bifid in shape. The mean frontal plane P-wave axis, however, is unchanged.

At late follow-up (23 years post-Mustard procedure), prevalence of atrial fibrillation or flutter is approximately 20% and seems to be a marker of reduced RV function.4,6,7 Episodes of supraventricular tachycardia occur in 3% to 5% of hospital survivors of the Mustard-type atrial switch procedure. In a 27-year follow-up of survivors of Senning procedures, 78% were in sinus rhythm, and freedom from pacemaker implantation for hospital survivors was 81 ± 5.9% at 25 years.8 In the 20-institution study of the Congenital Heart Surgeons Society, 94% and 91% of patients were free of pacemaker insertion 5 and 9 years after atrial switch repair, with risk factors being TGA and VSD vs. simple TGA and Senning versus Mustard type of repair.8

Growth and Functional Status

Most patients appear to be asymptomatic after an atrial switch procedure, although at 9 to 12 years of follow-up in a large multinstitutional study, only 60% were in New York Heart Association (NYHA) class I, and most of the rest in class II.9 However, graded exercise testing has shown that up to 80% have reduced exercise capacity associated with lower maximal oxygen consumption values compared with normal.3,4 Functional capacity may be better in patients receiving the Senning rather than the Mustard type of atrial switch procedure; Bjornstad and colleagues found atrial function to be superior with the Senning operation.5,6,10 Abnormal lung function has been implicated in reduced exercise capacity.11

Height and weight increase considerably after an atrial switch repair, particularly in those with importantly decreased height and weight preoperatively.11 Return to normal height and weight may be achieved within 2 years of operation.

Coronary Arteries

Abnormalities in the caliber of proximal coronary arteries have been noted in patients after the atrial switch procedure. Diameter of the RCA is larger and that of LCA smaller in
symptomatic patients compared with either asymptomatic or non-TGA patients.\(^\text{47}\)

**Venous Pathway Obstruction**

The complex problem of obstructed venous pathway is discussed in detail under Special Situations and Controversies later in this chapter.

**Right Ventricular Function**

Ventricular function after atrial switch repair of transposition is often discussed by analogy with function of the ventricles in congenitally corrected TGA. Contrary to traditional beliefs, right (systemic) ventricular function is demonstrably abnormal only during stress, and then only mildly (see “Ventricular Function” under Natural History in Chapter 55). This finding suggests that more severe abnormalities in ventricular function found after an atrial switch repair are related primarily to abnormalities in ventricular filling patterns and other post–atrial switch effects.\(^\text{21}\)

RV systolic function, usually studied by measuring ejection fraction at rest or during exercise or another form of stress, is usually reduced after atrial switch repair in patients with simple TGA.\(^\text{B14,B18,D13,G14,H15,M36}\) However, at least some patients have reduced ejection fraction preoperatively, and it is uncertain whether further reduction postoperatively is common.\(^\text{G14}\) When RV systolic function decreases after an atrial switch procedure, it is usually associated with increased RV end-diastolic volume.\(^\text{H13}\)

During exercise, RV ejection fraction may increase, remain unchanged, or decrease; patient age at operation, time of study, and the postoperative interval are not predictive of the change.\(^\text{B37,M36,P8,R4}\) In a group of patients averaging 10 years of follow-up after an atrial switch operation, cardiac output response to submaximal exercise was abnormally reduced compared with non-TGA subjects.\(^\text{P2}\) Other reports support this finding.\(^\text{M17}\) Limitation in cardiac output may have complex etiologies. Dobutamine-induced increases in systemic RV contractility may not be attended by increased stroke volume, possibly because of limited ventricular filling caused by rigid atrial baffle or decreased RV compliance caused by hypertrophy.\(^\text{P2,T15}\) More recent studies examining this stroke volume effect suggest that, in fact, atrial transport is responsible.\(^\text{T14}\)

Further evidence about a possible decrease in RV function after atrial switch repair was obtained by Borow and colleagues.\(^\text{M37}\) The systemic RVs in patients in whom the procedure was performed during the first year of life responded to afterload stress (methoxamine infusion) with a smaller increase in minute work index than did ventricles in normal patients or patients after repair of isolated VSD or tetralogy of Fallot. Parrish and colleagues found a similar impairment of systemic RV response in patients with congenitally corrected transposition.\(^\text{F8}\) The reasons for this finding are not entirely evident. Myocardial fiber arrangement in the RV may differ from that in the LV, which may render it less able to function systemically.\(^\text{S27}\) Possibly the RV cannot benefit from the septal component of ejection because of bellowslike action of the ventricular free wall.\(^\text{B17}\) Benson and colleagues suggest that a mismatch may exist between RV coronary blood supply and demand.\(^\text{B17}\) In a study of 22 patients at a mean of 15 years post–atrial switch, all showed evidence of either fixed or reversible perfusion defects in the RV.\(^\text{M28}\)

In any event, progressive deterioration of RV function is uncommon after the atrial switch procedure in patients with simple TGA, although serial evaluations of RV function suggest worsening of function over time.\(^\text{H19}\) Thus, obvious RV failure with marked hypokinesis and increased end-diastolic volume and signs and symptoms of heart failure\(^\text{F14}\) is rare.\(^\text{C15,P8}\) Frank RV dysfunction is more common in patients with associated large VSD that also requires repair.\(^\text{G14,P8}\) In a 27-year single-institution follow-up of 314 survivors of the Senning operation (82 with VSD), freedom from reoperation for systemic RV failure at 25 years was 96% ± 1.2%.\(^\text{H11}\)

**Left Ventricular Function**

LV function at rest is often normal late after atrial switch operations.\(^\text{H11}\) In some patients, however, LV ejection fraction fails to increase with exercise.\(^\text{M36}\)

**Tricuspid Valve Regurgitation**

Important (moderate or severe) tricuspid regurgitation occurs infrequently after the atrial switch procedure for simple TGA. Exceptional patient groups with a prevalence of up to 15% have been reported,\(^\text{R4}\) but reasons for this variability are not evident. Trivial and mild regurgitation occasionally occur.\(^\text{C15,G9,M3,M34}\)

**Left Ventricular Outflow Tract Obstruction**

When an atrial switch procedure is performed for patients with simple TGA and dynamic LVOTO (see Morphology earlier in this chapter), obstruction rarely progresses thereafter.\(^\text{P4}\) In fact, LVOTO usually regresses to some degree, whether or not a myotomy or myectomy is performed (Fig. 52-51).

Results of direct relief of the other types of LVOTO are also reasonably good (Fig. 52-52). When direct relief has not been possible, bypassing the obstruction with an LV–pulmonary trunk valved conduit provides good relief.\(^\text{C23}\)

![Figure 52-51 Preoperative, intraoperative, and late postoperative (mean 35 months) pressure measurements in patients with simple transposition of great arteries and dynamic type of left ventricular outflow obstruction undergoing an atrial switch procedure (GLH, 1964-1984). Follow-up time is 23 to 134 months (mean 56 months). When myotomy or myectomy was performed, approach was through pulmonary trunk. Key: Intraop, Intraoperative; LV/RV, left ventricular/right ventricular; Postop, postoperative; Preop, preoperative.](image-url)
Residual Atrial Shunting

Trivial leaking at the baffle suture line occurs in about a fourth of patients (26%; CL 24%-29% in 390 collected cases).\textsuperscript{A12,C9,G13,H2,M3,M34,P4,S29,T1,T13}

Severe leaks requiring reoperation are uncommon, occurring in 12 (3%; CL 2%-4%) of the 390 collected cases. Leaks are most common in the trabeculated upper portion of the atrium.

Pulmonary Vascular Disease

When an atrial switch operation is performed in the first 3 months for patients with TGA and essentially intact ventricular septum, new and progressive pulmonary vascular disease is uncommon; Mahoney and colleagues found no instances (0%; CL 0%-7%) in 28 patients undergoing operation during the first 100 days of life.\textsuperscript{M3} However, when repair is done after age 3 months, some patients (5%-10%) with normal Rp preoperatively develop pulmonary vascular disease postoperatively (Table 52-13).\textsuperscript{N8,R16} The disease often progresses and causes death.\textsuperscript{B20} More recent studies confirm that pulmonary hypertension can develop and progress in patients documented as having normal pulmonary artery pressure postoperatively.\textsuperscript{R11}

Infants with simple TGA with evidence of elevated Rp preoperatively to levels less than about 12 U \cdot m\(^2\) may experience a satisfactory fall in resistance late postoperatively.\textsuperscript{C16} Some of this fall is related to reduction in hematocrit that occurs postoperatively.\textsuperscript{C16,D12,H5} In some patients, however, preexisting pulmonary vascular disease may progress postoperatively and be a cause of late mortality (Table 52-14).\textsuperscript{M5} The occasional neonate with TGA who manifests evidence of pulmonary vascular disease may have antenatal constriction of the ductus arteriosus.\textsuperscript{K17}

Transposition of the Great Arteries, Ventricular Septal Defect, and Left Ventricular Outflow Tract Obstruction

Early (Hospital) Death

In the early years of their use, early mortality after both the Rastelli and Lecompte operations (see “Lecompte Intravenous Repair” under Technique of Operation in Chapter 53) was high: 20% to 30%.\textsuperscript{H38,L6} In more recent times, however, mortality after both types of repairs has been reduced to less than 5%.\textsuperscript{K15,V13} Contemporary early mortality after Rastelli, Lecompte, or Nikaidoh operations are comparable.\textsuperscript{H15}

Time-Related Survival

Including early in-hospital mortality, 10-year predicted survival of patients undergoing surgery during the 1980 to 1991

### Table 52-13 Pulmonary Vascular Resistance after Atrial Switch Operation*a

<table>
<thead>
<tr>
<th>Preoperative Study</th>
<th>Operation</th>
<th>Postoperative Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>Rp (u \cdot m(^2))</td>
<td>Age (months)</td>
</tr>
<tr>
<td>---------------------</td>
<td>-----------------</td>
<td>--------------</td>
</tr>
<tr>
<td>3</td>
<td>2.0</td>
<td>4</td>
</tr>
<tr>
<td>3\textsuperscript{b}</td>
<td></td>
<td>21</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>9.2</td>
</tr>
<tr>
<td>35</td>
<td>103</td>
<td>8.9</td>
</tr>
<tr>
<td>24</td>
<td>44</td>
<td>8.1</td>
</tr>
<tr>
<td>43</td>
<td>102</td>
<td>7.7</td>
</tr>
<tr>
<td>4</td>
<td>1.6</td>
<td>4</td>
</tr>
<tr>
<td>45</td>
<td>98</td>
<td>7.2</td>
</tr>
<tr>
<td>38</td>
<td>47</td>
<td>6.2</td>
</tr>
<tr>
<td>26</td>
<td>45</td>
<td>4.2</td>
</tr>
<tr>
<td>46\textsuperscript{c}</td>
<td></td>
<td>78</td>
</tr>
</tbody>
</table>

*aData are from patients with simple transposition of great arteries operated on at age 3 or more months; GLH, 1964-1984. Patients for whom no data are available preoperatively are presumed to have then had normal resistance.

*bMild fibrous left ventricular outflow tract obstruction.

*cMild dynamic left ventricular outflow tract obstruction.

Key: PDA, Patent ductus arteriosus; PVD, pulmonary vascular disease; Rp, pulmonary vascular resistance.
period was 80% to 85%, with no difference attributed to whether the Rastelli or Lecompte operation was done. Predicted 10-year survival for patients operated on in the latter part of that period was even higher—about 95% (Fig. 52-54). Recently, 15- and 20-year follow-ups have been reported after the Rastelli operation. In this experience, 10-year follow-up was comparable with that just described, but 15- and 20-year survival dropped to 68% and 52%, respectively. Based on very small numbers, late survival appears to be similar for the Nikaidoh operation.

**Incremental Risk Factors for Death**

Few if any patient-related risk factors for death have been identified for TGA, VSD, and LVOTO repair, but advanced disability has been (Table 52-15), probably in part because it is usually associated with severe cyanosis, polycythemia, advanced ventricular hypertrophy, and heart failure. Young age at operation has not been found to be a risk factor with the Lecompte operation; Vouhe and colleagues reported no deaths (0%; CL 0%-21%) among infants undergoing this operation, although the youngest patient was 4 months old. Straddling tricuspid valve has been identified as a risk factor for early death in at least one series.

*Earlier date of operation* has been a risk factor for death after repair, but results have been better in recent years (see Table 52-15).

**Procedural risk factors** for premature death have not yet been identified. Survival is similar after the Rastelli and Lecompte procedures. Reports on the Nikaidoh procedure or modifications thereof have yielded comparable early results, although numbers are small.

**Functional Status**

Functional status of most patients undergoing repair of TGA, VSD, and LVOTO by either the Rastelli or Lecompte method is good. Vouhe and colleagues report that 98% of patients undergoing these operations were in NYHA class I or II.

---

**Table 52-14** Pulmonary Vascular Resistance in Patients with Preoperatively Moderate or Severe Pulmonary Vascular Disease

<table>
<thead>
<tr>
<th>Preoperative Study</th>
<th>Postoperative Study (or Autopsy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months)</td>
<td>Operation</td>
</tr>
<tr>
<td>5</td>
<td>(HD) Gr4 PVD</td>
</tr>
<tr>
<td>6</td>
<td>(HD) Gr4 PVD</td>
</tr>
<tr>
<td>10</td>
<td>(HD) Gr4 PVD</td>
</tr>
<tr>
<td>57</td>
<td>(HD) Gr4 PVD</td>
</tr>
<tr>
<td>19</td>
<td>(HD) Gr4 PVD</td>
</tr>
<tr>
<td>30</td>
<td>(HD) Gr4 PVD</td>
</tr>
<tr>
<td></td>
<td>Rp, pulmonary vascular resistance</td>
</tr>
</tbody>
</table>

*Data from patients with simple transposition of great arteries who were aged 3 months or older at time of an atrial switch operation at GLH, 1964-1984.

*Small patent ductus arteriosus.

*Moderate patent ductus arteriosus.

Key: Gr, Grade; HD, hospital death; PVD, pulmonary vascular disease; Rp, pulmonary vascular resistance.

---

**Table 52-15** Incremental Risk Factors for Premature Death after Rastelli Operation for Transposition of the Great Arteries, Ventricular Septal Defect, and Left Ventricular Outflow Tract Obstruction

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Single Hazard Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Earlier date of operation (months since 1/1/67)</td>
<td>Coefficient ± SD</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td>0.6 ± 0.42</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.112</td>
</tr>
</tbody>
</table>

*Analysis is of 57 patients (22 deaths, including hospital and later deaths) operated on at UAB, 1967-1984. See Appendix 52C for variables entered into analyses.*

Key: NYHA, New York Heart Association; SD, standard deviation.
**Complete Heart Block**

Complete heart block may occur with slightly greater frequency than after repair of simple primary VSD. Vouhe and colleagues report one such patient (2%; CL 2%-5%) among 62.\(^{11,13}\)

**Reoperation**

Reoperation is in general ultimately inevitable when an extracardiac conduit is used. When the Rastelli operation is properly performed, however, placing the conduit to the left of the ascending aorta rather than to the right as originally described by Rastelli,\(^{88}\) reoperation occurs with the same prevalence as when it is used in other operations (see “Reoperation and Other Reinterventions for Right Ventricular Outflow Problems” in Section I of Chapter 38).

Patients have not been entirely free of reoperation for RVOTO after the Lecompte operation for TGA, VSD, and LVOTO; 7% (CL 2%-15%) of 30 surviving patients had reoperation over a 5-year period.\(^{11,13}\) However, the proportion of patients having either reoperation for this problem, or the problem itself but as yet without reoperation, was lower in those undergoing the Lecompte operation (26%) than in those undergoing the Rastelli operation (67%; \(P = .005)\).\(^{11,13}\)

Reoperation for obstruction in the subaortic region within the surgically created tunnel between the LV and aorta may occur in as many as 35% to 40% of patients undergoing the Rastelli operation or one of its variants.\(^{110}\) Risk factors are not clearly defined but may include small VSD size and early age at operation. Other factors such as surgical technique and ventricular geometric changes may also be important. At medium term, the need for intervention for LVOTO may be higher after the Rastelli operation compared with the Lecompte and Nikaidoh operations; however, again the numbers are very small.\(^{11,18}\) Resection of the infundibular septum and adequate enlargement of the VSD may be the reason for this. Nevertheless, mortality with reintervention is currently far better than previously reported. Although the Nikaidoh operation has theoretical advantages, concern about developing translocated aortic valve regurgitation is very high.

**INDICATIONS FOR OPERATION**

**Simple Transposition of the Great Arteries in Neonates**

Presence of the malformation is an indication for operation. If cyanosis and symptoms are severe, BAS is performed as soon as possible. A less attractive alternative is immediate arterial switch.

When indicated, an arterial switch operation should be performed within the first week of life, and at least within the first 30 days of life. Increased Rp at this stage is not a contraindication to repair.\(^{57}\) LVOTO, which is typically dynamic in this setting, is also not a contraindication regardless of its imaged appearance.\(^{11,95}\) Risk of operation is probably lowest when it is performed in the first week of life (see Fig. 52-41), and there is the additional advantage of minimizing exposure time of the brain to the hypoxia of uncorrected TGA.\(^{11,66}\)

Excellence of results to date favors the arterial switch over the atrial switch operation (see Fig. 52-37).

**Simple Transposition of the Great Arteries Presenting after Age 30 Days**

Primary arterial switch operation may carry a higher risk for infants with simple TGA who are beyond age 1 month, because by then the LV has usually become morphologically adapted to supporting the low-pressure pulmonary circulation. Davis and colleagues have taken exception to this and, based on their favorable experience, recommend a primary arterial switch operation unless the infant is older than age 8 weeks.\(^{118}\) Arterial switch has been successfully performed beyond the neonatal period and up to 9 months of age in patients with intact septum, but such patients are more likely to require postoperative mechanical support.\(^{11,2}\) Based on these experiences and similar observations by others, there is a willingness in most cases to perform primary arterial switch in infants younger than 8 weeks of age, and in some cases even in older infants with persisting large PDA, as long as mechanical assistance can be provided (see “Temporary Ventricular Assistance” in Section I of Chapter 5). If mechanical assistance is not available, or if primary arterial switch is not undertaken for some other reason, the options are:

- Pulmonary trunk banding with concomitant systemic–pulmonary artery shunting, followed within 1 or 2 weeks by arterial switch operation\(^{11,2,17,3}\)
- Atrial switch operation

Because the first approach appears to carry only slightly more risk than a primary atrial switch operation in a neonate in institutions properly prepared for this surgery, it is the more desirable of the two procedures.\(^{17}\)

When arterial switch operation is delayed for a month or more after banding, risk of postoperative death may be considerably increased,\(^{11,12}\) although others have shown no increased risk in waiting up to 4 months after banding.\(^{11,3}\) In institutions not well prepared for this type of surgery, an atrial switch operation may be more appropriate.

**Transposition of the Great Arteries with Ventricular Septal Defect**

TGA with VSD is an indication for arterial switch operation and repair of the VSD. It is indicated at the time the patient is first seen, with the procedure performed within the first few weeks of life.

**Transposition of the Great Arteries with Ventricular Septal Defect and Left Ventricular Outflow Tract Obstruction**

Diagnosis of TGA with VSD and LVOTO is an indication for operation, but type and timing of the definitive procedure remain controversial.

Many babies born with TGA, VSD, and LVOTO are not sufficiently cyanotic in early life to require urgent surgical intervention. Although the youngest age at which the Lecompte operation can be performed is not certain, it can be performed in infants older than age 6 months with a reasonably low mortality. The Lecompte procedure is probably the indicated operation in patients with this anomaly who appear for surgical repair between age 6 months and 4 to 5 years. When cyanosis and symptoms are important before age 6 months, either a systemic–pulmonary artery shunt, followed by a Lecompte operation within 6 to 18 months, or a primary
Lecompte operation, is indicated. The choice is best made in individual institutions according to their capabilities and experience.

In children age 3 to 5 years, either the Lecompte or Rastelli operation provides good results. In special situations, the Nikaidoh procedure may be considered as an alternative to the Rastelli or Lecompte operation.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Arterial Switch Repair**

*Transposition of the Great Arteries with Posterior Aorta*

The unusual posterior aorta variant of TGA, described in 1971 by Van Praagh and colleagues, had been considered a contraindication to the arterial switch operation until a successful case was reported by Tan, Murphy, and Norwood. They repaired the conoventricular VSD through the aorta after transecting the great arteries, and transplanted the coronary ostia just as in the routine approach. Switch of the great arteries was accomplished without the Lecompte maneuver. Benatar and colleagues had previously reported treating a patient with this morphology by an arterial switch repair, but the patient died on the fifth postoperative day.

*Straddling Atrioventricular Valves*

Serraf and colleagues have shown that straddling AV valves, either tricuspid or mitral, do not represent a contraindication to two-ventricle repair in TGA. When appropriate, the arterial switch operation can be combined with AV valve repair in most patients, with good outcome.

*Other Techniques*

Current surgical techniques for the arterial switch operation (see Technique of Operation earlier in this chapter) have evolved from original descriptions of Jatene and of Yacoub, in which a synthetic tube was used to aid in reconstruction of the neopulmonary artery. This approach is now rarely necessary.

The Damus-Kaye-Stansel type of arterial switch procedure has also been used in patients with TGA and large VSD. The pulmonary trunk is transected near its bifurcation and the proximal end anastomosed end-to-side to the ascending aorta. A valved extracardiac conduit is placed between the RV and distal pulmonary trunk and the VSD closed. RV systolic pressure falls to about 30 mmHg, and aortic pressure, which is above 100 mmHg, keeps the aortic valve closed. Mortality in this relatively simple and theoretically attractive operation has been considerable; Ceithaml and colleagues from the Mayo Clinic report 10 deaths (53%; CL 38%-66%) among 19 patients. However, if patients younger than 1 year of age or those with severe pulmonary vascular disease or LV systolic pressure less than two-thirds systemic are excluded, hospital mortality was 1 in 7 patients (14%; CL 2%-41%). Patients have been clinically well after repair. Over time, an increasing prevalence of regurgitation of the original aortic valve has been observed. The Damus-Kaye-Stansel repair is now rarely used for patients with TGA and VSD.

**Atrial Switch Complications**

*Superior Vena Caval Obstruction*

SVC pathway obstruction appears late postoperatively in 5% to 10% of survivors of the Mustard type of atrial switch procedure (Table 52-16). Prevalence appears to be unrelated to age at repair, although Cobanoglu and colleagues reported that freedom from reoperation was 59% in patients younger than 7 months of age at operation, compared with 95% in those older than 1 year. A Congenital Heart Surgeons Society multiinstitutional study found that the highest hazard for reintervention (operative or percutaneous intervention) for pathway obstruction was in the first 6 months after repair, followed by a constant low risk of 0.018% per year thereafter. At 1 and 9 years, freedom from such reinterventions was 97% and 95%, respectively.

SVC obstruction is maximal at the site of excision of the superior remnant (limbus) of the atrial septum beneath the

**Table 52-16  Incidence of Superior Vena Caval (Upper Systemic Venous Compartment) Obstruction after Mustard Operation**

<table>
<thead>
<tr>
<th>Age at Operation</th>
<th>Hospital Survivors</th>
<th>SVCO (Moderate/Severe)</th>
<th>Reoperation No.</th>
<th>Late Death No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ Months</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>No.</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3</td>
<td>12</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>7</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>12</td>
<td>24</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>18</td>
<td>11</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>166</td>
<td>7</td>
<td>9</td>
<td>4 (2%)</td>
</tr>
</tbody>
</table>

*Data from analysis based on 166 hospital survivors of Mustard operation for transposition of great arteries of all types at GLH, 1964 to July 1981.

*Pressure gradients ranged between 9 and 22 mmHg.

*One patient had associated significant lower venous compartment obstruction.

*Two of these three deaths occurred without reoperation (one from associated severe pulmonary venous compartment obstruction, the other from noncardiac causes).

Key: SVCO, Superior vena caval obstruction.
upper baffle compartment, and thus lies within the right atrium rather than at the SVC–right atrial junction. This location was first described by Mazzei and Mulder in 1971. The venous pathway may be totally occluded for over 1 cm or more in this area, or there may be only a localized zone of narrowing. Baffle shape, size, and composition are each important in its production, as is the position of suture lines within the atrium. Because it has proven impossible to eliminate this problem after the Mustard procedure, despite intense study, the exact mechanism is not understood.

Prevalence of late SVC obstruction after a Senning operation is probably lower than after a Mustard operation, although some have found no difference. Geometry of the pathway is, on average, better with the Senning-type repair, and the entire compartment is composed of viable atrial wall. Chin and colleagues, however, found SVC obstruction present in 2 of 28 (7%; CI 2.4%-16%) recatheterized patients after Senning repair.

Clinical Features The patient may be asymptomatic. Venables and colleagues found that although symptoms could be present with an SVC mean pressure as low as 10 mmHg, they were not constant until it rose above 16 mmHg.

The least conspicuous clinical feature, but one that suggests diagnosis, is ruddiness of the cheeks. Puffiness of the eyelids, face, and neck can mask fixed distention of the jugular veins. Tortuous subcutaneous venous collaterals can occur but are uncommon. A bilateral or right-sided pleural effusion may be present, sometimes chylous. On chest radiograph, there may be bilateral cervical and axillary lymphadenopathy and paramediastinal densities caused by tortuous collaterals. Less common features are increasing head circumference and hydrocephalus associated with widening of the cranial sutures in children younger than age 18 months (the upper age limit for normal closure of the cranial sutures), which is a response to increased intracranial venous pressure. Children older than age 3 may develop pseudotumor cerebri. There may also be protein-losing enteropathy, presumably caused by interference with the normal return of intestinal lymph to the venous system secondary to a high venous pressure (this is more common with IVC obstruction).

Time of Onset SVC obstruction is usually apparent within 12 months of operation, although asymptomatic patients may not be discovered until they are investigated later. The appearance between 12 and 18 months after operation of a new stenosis has not been convincingly documented, although slow progression of a mild to severe stenosis has been. Prevalence is 9% at 4 years, with no further events up to 17 years postoperatively (Fig. 52-55). Late postoperatively (Fig. 52-57), nor is there necessarily a gradient, but they are common. When SVC obstruction is mild, the striking feature is the damped waveform in the SVC tracing.

Obstruction severe enough to become apparent clinically is associated with an SVC mean pressure above about 15 mmHg and an SVC–systemic venous atrium gradient of at least 10 mmHg. In 19 patients with severe obstruction, Silove and Taylor recorded a mean gradient of 17 ± 9.0 mmHg. SVC pressure tends to be higher when there is also IVC obstruction. Occasionally the SVC tracing may show tall a waves caused by contraction of the right atrial appendage (when it lies above the site of stenosis); in this situation the blood refluxes up the SVC (see Fig. 52-56).

Angiography shows either complete obstruction or severe stenosis.

Treatment When symptoms are present, reoperation is indicated (see Technique of Operation earlier in this chapter). Reoperation is also indicated in any child who shows progressive increase in head size beyond the normal range. Balloon expandable stents delivered using interventional cardiologic techniques have been successful in relieving some obstructions. Alternatively, if Rp is acceptably low, a bidirectional superior cavopulmonary anastomosis can be performed.

Inferior Vena Caval Obstruction Although an important occurrence of IVC pathway obstruction was reported in the early series of Stark and associates and Venables and colleagues using polyester baffles, current prevalence is low (1%-2%). This complication

Figure 52-55 Freedom from superior vena caval obstruction in hospital survivors of Mustard-type atrial switch operation (GLH, 1964-1981). Time of appearance of obstruction is taken as time of postoperative catheterization (n = 10) or recognition of an increase in head circumference (>2 SD of expected mean for age) at 6 and 9 months postoperatively. Obstructions documented as appearing after 1 year postoperatively were either without symptoms or at an earlier stage or, in one patient, had serial cardiac catheterization showing progression of a mild stenosis. Of 166 patients, 94 had late postoperative cardiac catheterization. Each closed circle up to 4 years is an event, vertical bars represent 68% confidence limits, and numbers are traced patients.
Figure 52-56 Data from postoperative cardiac catheterization in patient who had undergone Mustard repair and developed severe obstruction to superior vena caval (SVC) flow into systemic venous atrium (SVA). A, Phasic withdrawal pressures from SVA to SVC. Mean pressures were 5 and 20 mmHg, respectively. Note dominant a wave in SVC tracing, caused by contraction of portion of right atrial appendage that lies above site of obstruction. B, Cineangiogram after injection into SVC, in 20-degree left anterior oblique projection. Heavy arrow marks site of obstruction. Fine dotted lines (small arrows) outline that portion of original right atrial appendage that lies in upper venous compartment beneath baffle and above site of obstruction. There is retrograde flow into azygos vein. Key: A, Azygos vein; LAA, left atrial appendage; LV, left ventricle. (From Clarkson and colleagues.\textsuperscript{15})

can be minimized when at the atrial switch procedure, the coronary sinus is opened down into the left atrium (see Technique of Operation earlier in this chapter).

Postoperative IVC obstruction, as with SVC obstruction, occurs within the heart at about the midpoint of the lower portion of the systemic venous compartment adjacent to the coronary sinus ostium. Patients with important IVC obstruction usually are symptomatic, with liver enlargement, ascites, and leg edema. A protein-losing enteropathy may occur more frequently than with SVC obstruction,\textsuperscript{315} and particularly when combined with some degree of SVC obstruction, there may be low cardiac output and premature late death.

Diagnostic techniques used in obstructed IVC are similar to those for SVC obstruction. Pressure gradients are also similar, averaging $18 \pm 8.8$ mmHg in the series reported by Silove and Taylor.\textsuperscript{318}

Reoperation with insertion of a new baffle is always indicated for IVC obstruction (see Technique of Operation earlier in this chapter). Balloon expandable stents have been used for IVC as for SVC obstruction.\textsuperscript{48,50}

Pulmonary Venous Obstruction
Pulmonary venous obstruction is a less common but more lethal type of venous pathway obstruction. It is more common
hypertension and usually an elevation of the calculated Rp are present. Normal pulmonary artery and LV systolic pressures argue against important stenosis. On cineangiography, narrowing of the pulmonary venous atrium waist can be seen best in lateral projection. Diagnosis is also possible using 2D echocardiography.

Treatment Urgent reoperation is indicated.

Palliative Operations for Patients with Severe Pulmonary Vascular Disease

Palliative operations may be indicated when Rp is elevated beyond about 10 U · m². However, more recent experience suggests that full repair can be achieved with good long-term outcome, including regression of pulmonary hypertension, even when initial Rp calculations show levels of 10 to 20 U · m².2 Thus, in the current era, with general improvements in preoperative and postoperative care and the availability of pulmonary vasoactive agents such as nitrous oxide, palliative procedures are rarely indicated. Palliation consists of an atrial (or preferably an arterial) switch procedure without closing an existing VSD or creating a VSD when one is not present.

Technique of Operation

When the ventricular septum is essentially intact, a large VSD is created in the apex of the ventricular septum through a limited apical left ventriculotomy. After the ventriculotomy is made, a finger is inserted through the tricuspid valve through the previously made right atriotomy to tent the ventricular septum toward the left, and a limited opening is made with a knife onto the finger. The opening is then progressively enlarged (up to 20 mm) using the knife, avoiding damage to the inferior papillary muscle. (Hegar dilators are used to measure the size of the created defect.) The ventriculotomy is closed, and the switch procedure completed.
Special Features of Postoperative Care

SaO₂ in TGA depends on the relative proportions of systemic venous and pulmonary venous blood reaching the aorta, and on SvO₂. After palliative switch repair, the effective systemic flow is greatly increased, with the ratio usually changing from 1:3 to approximately 2:1. Decrease in the proportion of systemic venous blood entering the aorta is also influenced by the rise in systemic arteriolar resistance that follows the rise in SaO₂, because the increase in systemic vascular resistance decreases the right-to-left shunting of systemic venous blood through the open VSD. Finally, doubling of effective systemic flow results in an important increase in SvO₂ despite concomitant reduction in hemoglobin concentration. As a result of these complex interactions, there is an absolute increase in SaO₂ of approximately 20% in most patients after a palliative switch operation; the increase ranged from 6% to 48% (mean = 24%) in the report by Byrne and colleagues. The only preoperative variable that correlates with postoperative SaO₂ is pulmonary arteriovenous oxygen difference: A higher arteriovenous oxygen difference is associated with a higher postoperative SaO₂.

Results

Hospital mortality after a palliative switch operation has been surprisingly low. Lindsey and colleagues report no deaths in 10 patients with VSD. Byrne and colleagues report no deaths in 23 patients (20 with VSD, 3 with created VSD), and Benhard and colleagues report one death in 8 patients.

Staged Conversion of Atrial Switch to Arterial Switch for Systemic Right Ventricular Failure

Late failure of the systemic RV occurs in up to 10% of patients after the atrial switch procedure. Because ample evidence suggests lesser degrees of RV dysfunction in a much greater percentage of patients with the atrial switch procedure, it seems likely that late RV failure will become an increasingly common problem as longer follow-up is obtained.

When the systemic RV fails, treatment options include lesion-specific surgical intervention (e.g., tricuspid valve repair or replacement), medical management, transplantation, and conversion from atrial to arterial switch. Escalation of medical management may be effective in the short term, but this form of therapy should be seen as limited in a young individual with progressive systemic RV failure. Nevertheless, this form of therapy, followed by cardiac transplantation when end-stage ventricular failure develops, represents an effective therapeutic plan. Tricuspid valve repair is difficult when the valve is in the systemic position and is generally not indicated. Valve replacement is indicated in highly selected patients who have good systemic RV function. An alternative plan is to intervene earlier in the course of systemic RV failure by performing a staged conversion to the arterial switch. Indications for embarking on the staged conversion are not clearly defined; however, it is generally accepted that the process should begin well before end-stage heart failure is present. Relative indications include worsening functional status, progressive loss of RV function, and progressive tricuspid valve regurgitation. Besides end-stage heart failure, biventricular dysfunction and severe rhythm disturbances are contraindications.

There are two general controversies related to this topic. First, the choice of management between (1) medical management followed by transplantation and (2) staged conversion; and second, if staged conversion is considered, the timing of the intervention in the gradual course of progressive RV dysfunction. The conversion process carries substantial risk. Initiation of the process too late in the course of progressive failure results in unacceptable outcome, whereas initiation of the process at the first signs of RV dysfunction or tricuspid regurgitation, although effective in minimizing the risk of the conversion process, may be premature. Adding to the uncertainty, only limited experience and data are available to define the ideal interval between pulmonary trunk banding and the arterial switch, or the preferred methodology for determining when the LV is adequately prepared. The subject of LV training and conversion to arterial switch in atrial switch patients with failing RV is discussed in more detail under “Transposition of the Great Arteries” in Chapter 29. Pulmonary trunk banding alone as a treatment for isolated progressive tricuspid valve regurgitation has resulted in a decrease in regurgitation in some cases, but the evidence is only anecdotal. In one study, banding did not improve the severity of regurgitation at follow-up, but did improve symptoms in a cohort of patients.

Occasionally, LV-to-pulmonary trunk obstruction is already present. If LV peak pressure is greater than 75% of systemic pressure, it is possible to proceed with conversion immediately. It should be emphasized that the biomechanics of the unconditioned LV are poorly appreciated.

Technical details of the staged conversion have been described and outcomes reviewed. Operative mortality was 12.5% (CL 4%-27%) and 1-year survival 80% (CL 62%-92%) in one series. In that series, age younger than 16 years was thought to increase the chance of successful conversion. In another study, early mortality was 33% (2 of 6 patients). In the experience of Winlaw and colleagues, of 31 patients entering a banding protocol, 52% met criteria to proceed to conversion. Survival after conversion was 75% at mean follow-up of 5 years. Age at banding did not influence outcome. The experience of Winlaw and colleagues was similar. Nine of 20 banded patients (45%) underwent conversion, with 6 successful midterm outcomes (67%). Another study suggests that conversion may be more appropriate for Mustard than for Senning patients; however, most studies show no difference based on the type of former atrial procedure. Important differences in outcome among these studies is not surprising, considering the small number of patients, lack of consensus regarding patient selection, and lack of a universal protocol for LV training.
Multivariable Risk Factor Equations for Death after Arterial Switch Operation for Simple Transposition of the Great Arteries and Transposition of the Great Arteries with Ventricular Septal Defect

### Table 52A-1
Congenital Heart Surgeons Society Equation for Death after Arterial Switch Repair Incorporating Patient-Related Risk Factors and “High-Risk” vs. “Low-Risk” Institutions and Institutional Experience (in Years)\(^a\)

<table>
<thead>
<tr>
<th>Incremental Risk Factors</th>
<th>Single Hazard Phase P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient</strong></td>
<td></td>
</tr>
<tr>
<td>(Lower) Birth weight(^b)</td>
<td>.05</td>
</tr>
<tr>
<td>LCA, LAD, or Cx arising from sinus 2(^c)</td>
<td>.007</td>
</tr>
<tr>
<td>Intramural course of LCA or LAD(^d)</td>
<td>.07</td>
</tr>
<tr>
<td>Coexisting cardiac anomalies (including multiple VSDs)</td>
<td>.07</td>
</tr>
<tr>
<td>Coexisting noncardiac anomalies</td>
<td>.07</td>
</tr>
<tr>
<td>PT banding &gt; 1 month previously(^e)</td>
<td>.009</td>
</tr>
<tr>
<td><strong>Institutional</strong></td>
<td></td>
</tr>
<tr>
<td>(Lesser) Interval since first switch operation(^f):</td>
<td></td>
</tr>
<tr>
<td>In “low-risk” institutions</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>In “high-risk” institutions</td>
<td>.0004</td>
</tr>
</tbody>
</table>

---

Data from Kirklin and colleagues.\(^{12}\)

*Only patient and institutional (“high-risk” vs. “low-risk” and experience) potential risk factors were analyzed; \(n = 513\) patients with simple TGA or TGA with VSD.

\(^a\)Active only in simple TGA in “low-risk” institutions.

\(^b\)Active only in “high-risk” institutions.

\(^c\)Applies only to arteries without or with an intramural course.

\(^d\)Active only in “high-risk” institutions; added an increment of risk to “origin from sinus 2.”

\(^e\)Active only in “low-risk” institutions.

\(^f\)In this equation, “interval since the first arterial switch repair” was specific for each patient.

Key: Cx, Circumflex artery; LAD, left anterior descending coronary artery; LCA, left coronary artery; PT, pulmonary trunk; VSD(s), ventricular septal defect(s).

### Table 52A-2
Congenital Heart Surgeons Society Equation for Death after Arterial Switch Repair Incorporating Patient-Related Risk Factors and “High-Risk” and “Low-Risk” Institutions and Institutional Experience (in Number of Cases)\(^a\)

<table>
<thead>
<tr>
<th>Incremental Risk Factors</th>
<th>Single Hazard Phase P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient</strong></td>
<td></td>
</tr>
<tr>
<td>(Older) Age at operation(^b)</td>
<td>.06</td>
</tr>
<tr>
<td>LCA, LAD, or Cx arising from sinus 2:</td>
<td></td>
</tr>
<tr>
<td>In “low-risk” institutions</td>
<td>.09</td>
</tr>
<tr>
<td>In “high-risk” institutions</td>
<td>.0007</td>
</tr>
<tr>
<td>Intramural course of LCA or LAD(^d)</td>
<td>.002</td>
</tr>
<tr>
<td>Coexisting cardiac or noncardiac anomalies</td>
<td>.06</td>
</tr>
<tr>
<td>PT banding &gt; 1 month previously(^e)</td>
<td>.002</td>
</tr>
<tr>
<td><strong>Institutional</strong></td>
<td></td>
</tr>
<tr>
<td>Number of cases since first switch operation(^f):</td>
<td></td>
</tr>
<tr>
<td>In “low-risk” institutions</td>
<td>.001</td>
</tr>
<tr>
<td>In “high-risk” institutions</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

---

Data from Kirklin and colleagues.\(^{12}\)

*Only patient and institutional (“high-risk” vs. “low-risk” and experience) potential risk factors were entered into analysis for this parsimoniously derived equation; \(n = 513\) patients with simple TGA or TGA with VSD. The experience was in terms of number of arterial switch operations performed on CHSS patients.

\(^a\)Active only in “high-risk” institutions.

\(^b\)Active only in “low-risk” institutions.

\(^c\)Active only in “low-risk” institutions.

\(^d\)Active only in “low-risk” institutions.

\(^e\)In this equation, “number of cases since the first arterial switch repair” was specific for each patient.

Key: Cx, Circumflex artery; LAD, left anterior descending coronary artery; LCA, left coronary artery; PT, pulmonary trunk; TGA, transposition of great arteries; VSD, ventricular septal defect.
Table 52A-3  Congenital Heart Surgeons Society Equation for Death after Arterial Switch Repair, Incorporating Only Patient-Related Risk Factors

<table>
<thead>
<tr>
<th>Incremental Risk Factors for Death</th>
<th>Single Hazard Phase P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Older) Age at repair(\d)</td>
<td>.08</td>
</tr>
<tr>
<td>In simple TGA(\d)</td>
<td>.07</td>
</tr>
<tr>
<td>LCA, LAD, or Cx arising from sinus 2(\d)</td>
<td>.05</td>
</tr>
<tr>
<td>Without an intramural course of LCA or LAD(\d)</td>
<td>.02</td>
</tr>
<tr>
<td>With an intramural course of LCA or LAD(\d)</td>
<td>.02</td>
</tr>
<tr>
<td>Coexisting noncardiac anomalies</td>
<td>.02</td>
</tr>
<tr>
<td>PT banding &gt; 1 month previously</td>
<td>.097</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues.\(^{6,12}\)

\(^{a}\)Only patient potential risk factors were entered into the parsimonious analysis \((n = 513\) patients with simple TGA or TGA with VSD).

\(^{b}\)The ratio between size of the pulmonary trunk and that of the ascending aorta was not entered into the analysis because the value was available in only 140 patients, but univariable ratios of <1.2 and >2.3 were associated with lower survival \((P = .09)\).

\(^{c}\)This variable was active only in patients without pulmonary trunk banding >1 month previously.

\(^{d}\)An increment in risk was added when the patient had simple TGA (an interaction term) rather than TGA and VSD.

\(^{e}\)Among the 12 patients classified as having an “intramural course,” in 1 the artery to the left system arose from the midpoint of sinus 2 and juxtaposed to the right coronary artery. The left artery coursed anteriorly between aorta and pulmonary trunk but could possibly not have had an intramural course.

\(^{f}\)These are mutually exclusive variables.

Key: \(\text{Cx, circumflex artery; LAD, left anterior descending artery; LCA, left coronary artery; PT, pulmonary trunk; TGA, transposition of great arteries; VSD, ventricular septal defect.}\)

Table 52A-4  Congenital Heart Surgeons Society Equation for Death after Arterial Switch Repair, Incorporating Patient-Related and Support Technique Risk Factors

<table>
<thead>
<tr>
<th>Incremental Risk Factors for Death</th>
<th>Single Hazard Phase P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Older) Age at repair(\d)</td>
<td>.31</td>
</tr>
<tr>
<td>In simple TGA(\d)</td>
<td>.02</td>
</tr>
<tr>
<td>LCA, LAD, or Cx arising from sinus 2(\d)</td>
<td>.10</td>
</tr>
<tr>
<td>Without an intramural course of LCA or LAD(\d)</td>
<td>.06</td>
</tr>
<tr>
<td>With an intramural course of LCA or LAD(\d)</td>
<td>.02</td>
</tr>
<tr>
<td>Coexisting noncardiac anomalies</td>
<td>.01</td>
</tr>
<tr>
<td>PT banding &gt;1 month previously</td>
<td>.23</td>
</tr>
<tr>
<td>Multiple VSDs</td>
<td>.02</td>
</tr>
<tr>
<td>(Longer) Myocardial ischemic time</td>
<td>.001</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues.\(^{6,12}\)

\(^{a}\)Patient-specific and support risk factors were entered into the nonparsimonious analysis of \(513\) patients as described for Appendix Tables S2A-1, S2A-2, and S2A-3. Risk factors identified in the previous analyses in this sequential series were forced to remain in the equation, even though the \(P\) value was >.1.

\(^{b}\)This variable was active only in patients without PT banding >1 month previously.

\(^{c}\)An increment in risk was added when the patient had simple TGA (an interaction term) rather than TGA and VSD.

Key: \(\text{CA, coronary artery; Cx, circumflex artery; LAD, left anterior descending artery; LCA, left coronary artery; PT, pulmonary trunk; TGA, transposition of great arteries; VSD, ventricular septal defect.}\)

Table 52A-5  Congenital Heart Surgeons Society Equation for Death after Arterial Switch Repair, Incorporating Patient-Related and Procedural Risk Factors

<table>
<thead>
<tr>
<th>Incremental Risk Factors</th>
<th>Single Hazard Phase P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
<td></td>
</tr>
<tr>
<td>LCA, LAD, or Cx arising from sinus 2(\d)</td>
<td>.099</td>
</tr>
<tr>
<td>Without intramural course of LCA or LAD</td>
<td>.02</td>
</tr>
<tr>
<td>Multiple VSDs</td>
<td>.01</td>
</tr>
<tr>
<td>Coexisting noncardiac anomalies</td>
<td>.09</td>
</tr>
<tr>
<td>PT banding &gt;1 month previously</td>
<td>.7</td>
</tr>
<tr>
<td>(Older) Age at repair(\d)</td>
<td>.11</td>
</tr>
<tr>
<td>In simple TGA(\d)</td>
<td>.21</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
</tr>
<tr>
<td>Aorta transected distally</td>
<td>.002</td>
</tr>
<tr>
<td>PT transected proximally or at midpoint</td>
<td>.06</td>
</tr>
<tr>
<td>No Lecompte maneuver</td>
<td>.0003</td>
</tr>
<tr>
<td>Coronary implantation not at transection site</td>
<td>.05</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues.\(^{6,12}\)

\(^{a}\)Patient-related and procedural risk factors were entered into nonparsimonious analysis as in Table 52A-4. Risk factors identified in the previous analyses in this sequential series were forced to remain in the equation, even though \(P >.1\).

\(^{b}\)Active only in patients without PT banding >1 month previously.

\(^{c}\)Increment in risk was added when the patient had simple TGA (an interaction term) rather than TGA and VSD.

Key: \(\text{Cx, circumflex artery; LAD, left anterior descending coronary artery; LCA, left coronary artery; PT, pulmonary trunk; TGA, transposition of great arteries; VSD(s), ventricular septal defect(s).}\)
Table 52A-6  Congenital Heart Surgeons Society Equation for Death after Arterial Switch Repair, Incorporating Patient-Related, Support, and Procedural Risk Factors

<table>
<thead>
<tr>
<th>Incremental Risk Factors</th>
<th>Single Hazard Phase P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient</strong></td>
<td></td>
</tr>
<tr>
<td>LCA, LAD, or Cx arising from sinus 2:</td>
<td></td>
</tr>
<tr>
<td>Without intramural course of LCA or LAD</td>
<td>.15</td>
</tr>
<tr>
<td>With intramural course of LCA or LAD</td>
<td>.03</td>
</tr>
<tr>
<td>Multiple VSDs</td>
<td>.01</td>
</tr>
<tr>
<td>Coexisting noncardiac anomalies</td>
<td>.03</td>
</tr>
<tr>
<td>PT banding &gt;1 month previously</td>
<td>.9</td>
</tr>
<tr>
<td><strong>(Older) Age at repair</strong>:</td>
<td>.5</td>
</tr>
<tr>
<td><strong>(Longer) Support</strong></td>
<td></td>
</tr>
<tr>
<td>Myocardial ischemic time</td>
<td>.0005</td>
</tr>
<tr>
<td><strong>Procedural</strong></td>
<td></td>
</tr>
<tr>
<td>Aorta transected distally</td>
<td>.0006</td>
</tr>
<tr>
<td>PT not transected proximally or at midportion</td>
<td>.09</td>
</tr>
<tr>
<td>No Lecompte maneuver</td>
<td>.001</td>
</tr>
<tr>
<td>Coronary implantation not at transection site</td>
<td>.08</td>
</tr>
</tbody>
</table>

Data from Kirklin and colleagues.12

*Patient-related, support, and procedural risk factors were entered into the nonparsimonious analysis as in Table 52A-4. Risk factors identified in the previous analyses in this sequential series were forced to remain in the equation, even though $P > .1$.

*Active only in patients without PT banding >1 month previously.

*Increment in risk was added when the patient had simple TGA (an interaction term) rather than TGA with VSD.

Key: Cx, Circumflex artery; LAD, left anterior descending coronary artery; LCA, left coronary artery; PT, pulmonary trunk; TGA, transposition of great arteries; VSD(s), ventricular septal defect(s).

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**Multivariable Analysis of Risk Factors for Death after Atrial Switch Operation**

Variables entered into the multivariable logistic regression analysis of hospital deaths in patients with TGA at Green Lane Hospital between 1970 and 1984 after atrial switch repair were as follows:

- Age at operation
- Date of operation
- Atrial septal defect creation (none, septostomy, repeat septostomy, septectomy)
- Other palliation (Blalock-Taussig, Waterston, banding, ductus ligation, coarctation repair)
- Atrial septal defect size at repair (none, small, moderate, large)
- Ventricular septal defect size (small, moderate, large)
- Additional ventricular septal defects (yes/no)
- Left ventricular outflow tract obstruction (yes/no) and type (valvar, fibrous, muscular)
- Coarctation (yes/no)
- Right ventricular size (moderate or severe hypoplasia: yes/no)
- Urgency of operation (elective, New York Heart Association class IV, semi-urgent, urgent)
- Type of operation (standard Mustard, V-Y Mustard, Senning)
- Technique of cardiopulmonary bypass (standard/profound hypothermia; circulatory arrest)
- Preoperative pulmonary vascular resistance (or lung histology) in patients aged 3 months or older
Early reoperation (for bleeding, baffle obstruction, baffle leak, infection)

Discharge electrocardiogram (sinus, junctional, complete heart block)

Patent ductus arteriosus (absent/small, moderate, large in various combinations)

Operation (baffle repair) at age 30 days or younger (yes/no)

Early operation (repair or palliation) at age 30 days or younger (yes/no)

Preoperative growth patterns (normal, third percentile, well below third percentile, always below third percentile but steady, always below third percentile but declining, and various combinations)

Addition variables considered in Cox’s proportional hazard model for late mortality in the same data set are as follows:

- Upper systemic venous compartment obstruction (none/mild, moderate, severe)
- Lower systemic venous compartment obstruction (same criteria)
- Pulmonary venous compartment obstruction (same criteria)
- Baffle leak (same criteria)
- Residual left ventricular outflow tract obstruction
- Residual ventricular septal defect (yes/no)

Risk factors entered into the multivariable analysis of death, in the hazard function domain, after Rastelli operation (UAB experience) are as follows:

- Demographic: gender, age at operation, body surface area
- Clinical: New York Heart Association functional class, hematocrit
- Morphology: juxtaposition of atrial appendages
- Surgical: cardioplegia; aortic clamp time in cardioplegic group; type of valved conduit; enlargement of ventricular septal defect

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Chapter 52 Complete Transposition of the Great Arteries


Chapter 52 Complete Transposition of the Great Arteries


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U


V


### Definition 1932

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  - Subaortic Ventricular Septal Defect 1933
  - Subpulmonary Ventricular Septal Defect 1934
  - Doubly Committed Ventricular Septal Defect 1934
  - Noncommitted or Remote Ventricular Septal Defect 1935

**Infundibulum 1935**

**Great Arteries 1935**

**Pulmonary Stenosis 1939**

**Conduction System 1939**

**Coronary Arteries 1939**

**Associated Anomalies 1939**

**Morphologic Syndromes of Double Outlet Right Ventricle 1940**

**Simple Double Outlet Right Ventricle 1940**

**Taussig-Bing Heart 1940**

**Double Outlet Right Ventricle with Doubly Committed Ventricular Septal Defect 1941**

**Double Outlet Right Ventricle with Noncommitted Ventricular Septal Defect 1941**

**Double Outlet Right Ventricle with L-Malposition 1941**

**Double Outlet Right Ventricle with Complete Atrioventricular Septal Defect 1941**

**Double Outlet Right Ventricle with Superior-Inferior Ventricles 1941**

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**Intraventricular Tunnel Repair of Double Outlet Right Ventricle with Noncommitted Ventricular Septal Defect 1953**

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  - Complex Intraventricular Tunnel Repair 1956
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**Complications of Intraventricular Tunnel Repair 1956**

**Complications after Taussig-Bing Repair 1957**
Double outlet right ventricle (DORV) is a congenital cardiac anomaly in which both great arteries arise wholly or in large part from the right ventricle. It is a type of ventriculoarterial connection (see “Cardiac Connections” under Terminology and Classification of Heart Disease in Chapter 1).

In this chapter, DORV with atriovenous (AV) concordant connection is discussed in detail. DORV also occurs in other settings (Fig. 53-1), but when the AV connection is discordant, that becomes the surgically more important feature, and patients with this combination (commonly called congenitally corrected transposition of the great arteries) are better considered along with others with AV discordant connection (see Chapter 55). DORV may also occur in patients with univentricular AV connections (see “Ventriculoarterial Connections” under Morphology in Chapter 56). It is a frequent occurrence in patients with atrial isomerism (see “Ventriculoarterial Connections” under Morphology in Chapter 58).

One or both great arteries may directly overlie the ventricular septal defect (VSD) and thus arise biventricularly. For purposes of categorization, the great artery so arising is assigned to the ventricle it overlies by more than 50% on morphologic examination. Thus, when one great artery arises wholly or nearly so from the right ventricle (RV) and the other more than 50% from it, the condition is termed DORV. Uncommonly, both great arteries arise biventricularly in association with a doubly committed juxta-arterial VSD (see Chapter 35, Figs. 35-8 and 35-9). One option is to arbitrarily assign each great artery to the ventricle above from which more than 50% arises and categorize the anomaly accordingly; the alternative is to term the malformation double outlet both ventricles.

Tetralogy of Fallot is an entity characterized by a variable amount of dextroposition of the aorta. When the aorta arises more than 50% from the RV, the anomaly may be categorized as tetralogy of Fallot with DORV or as DORV with pulmonary stenosis. Edwards uses different criteria for distinguishing between these two conditions. Taurig-Bing heart (see description under Morphology later in this chapter) is an entity with variability in the origin of the pulmonary artery. This diagnosis may be made when the pulmonary artery arises wholly or nearly so from the RV (in which case, it is a type of DORV), equally from right and left ventricles, or more than 50% but not entirely from the left ventricle (LV; in which case, it is not a type of DORV). When it arises entirely or essentially so from the LV, the assignment is to transposition of the great arteries with VSD.

Because of this differing terminology, surgical reports must clearly describe the entities under discussion.

HISTORICAL NOTE

When Kirklin performed the first repair of DORV (which was of the simple type with a subaortic VSD) in May 1957 at the Mayo Clinic, the anomaly was virtually unknown, and the preoperative diagnosis was large VSD with high pulmonary blood flow. Diagnosis was correctly made at operation, the term double outlet right ventricle or origin of both great vessels from the right ventricle coined in the operating room, position of the His bundle deduced, and intraventricular tunnel repair performed in much the same manner as is done today. An identical sequence occurred at GLH in September 1958. Earlier, in 1952, Braun and colleagues reported what was clearly a case of DORV with pulmonary stenosis and used the phrase double outlet ventricle, but the title of their paper was confusing, and it escaped notice. About the time of the first repair, the first morphologic paper with the title “Double Outlet Right Ventricle” was published by Witham; subsequently, other early descriptions of the morphology appeared. In 1963, Redo and colleagues also reported repair of this entity.

Taurig-Bing heart was described in 1949, but its place in the spectrum of DORV was not recognized until later. Many early papers understandably referred to it under the heading Transposition. Levy and colleagues recognized it as a form of DORV with subpulmonary VSD. They and earlier workers did not clearly state, however, that Taussig-Bing heart is different from the heart with classic DORV with...
subaortic VSD, not only with respect to relationships of the VSD but also with respect to position and interrelations of great arteries and infundibular (outlet) septum.\textsuperscript{A4,A7,W2}

Early reports of successful surgical treatment were published in 1967 and 1969.\textsuperscript{D1,H2} Other early reports were by Patrick and McGoon in 1968 and by Kawashima and colleagues in 1971.\textsuperscript{K3,P3}

The other types of DORV with AV concordant connection began to be clarified in the classic paper by Lev and colleagues in 1972.\textsuperscript{L4} Successful correction of unusual forms was reported in the 1970s and early 1980s.\textsuperscript{K6,P6,S13}

**MORPHOLOGY AND MORPHOGENESIS**

Although controversies developed concerning categorization of hearts with DORV and their basic morphologic features, these are now straightforward because of numerous detailed morphologic and clinical studies. The basic categorization of Lev and colleagues forms the basis of most surgical thought about this anomaly, but the terms they used, such as “sub-aortic” and “subpulmonary,” are relational ones.\textsuperscript{L4} Confusion arises when their terms are used as morphologic ones for actual location of the VSD (see “Location in Septum and Relationship to Conduction System” under Morphology in Section I of Chapter 35).

Actual categorization of DORV and related conditions (specifically, Taussig-Bing heart, transposition of the great arteries with VSD, and double outlet left ventricle) is less important than a generalized surgical plan for their management.\textsuperscript{S1} Even so, development of a valid body of knowledge concerning surgical methods and outcomes requires accurate categorization of morphologic details and other patient characteristics. Even with the goal of accurate morphologic categorization and description, problems remain. Although a conus (or infundibulum) is easy to define as the presence of a muscle strip between a semilunar and AV valve, the muscle strip may vary from a few millimeters to a few centimeters wide. An aorta that is to the right and side by side with the pulmonary trunk may seem essentially normal in position to one observer or in D-malposition to another. These matters complicate categorization accuracy and precision.

**Morphogenesis**

Complex categorization points to a unifying hypothesis of morphogenesis put forth in a series of papers by the Van Praaghs, summarized recently by Richard Van Praagh.\textsuperscript{V2} He hypothesizes that “the distal or subsemilunar part of the infundibulum or conus arteriosus performs an arterial switch during cardiogenesis,” with the development stage similar to the Taussig-Bing heart. The developmental steps that avoid double outlet right ventricle relate to asymmetric conal free wall enlargement. Van Praagh proposes that failure of this morphologic step leads to such entities as double outlet right ventricle with subaortic ventricular septal defect (VSD). There is a prominent subaortic conus and a well-developed infundibular septum separating pulmonary valve (PV) from aorta, tricuspid valve (TV), and VSD. Key: AR, Aortic root (conus); RT, right. (From Kirklin and colleagues.\textsuperscript{L5,4})

In most DORV hearts, the VSD is conoventricular, lying between the limbs of the trabecula septomarginalis (TSM; septal band).\textsuperscript{C1,71} However, such defects vary in their relationships with the great arteries. Therefore, the VSD is discussed in relational categories.\textsuperscript{S5,14}

**Subaortic Ventricular Septal Defect**

The subaortic VSD and TSM lie more posteriorly in the ventricular septum than subpulmonary and doubly committed VSDs, and are tucked beneath the infundibular (conal) septum (Fig. 53-2). Distance between the VSD and aortic valve varies, depending on presence and length of the subaortic conus (infundibulum); this determines whether the aorta overrides the VSD and hence whether the VSD is juxtaaortic.

When there is aortic-mitral fibrous continuity, absence of a subaortic conus, and a typical juxtaaortic VSD, the posteroseptal margin of the VSD is formed by the left aortic cusp or base of the anterior mitral leaflet, depending on degree of overriding. The ventriculoinfundibular fold and rightward posterior division of the TSM may form the posterior margin of the VSD. Alternatively, the VSD may reach the tricuspid anulus (opposite the anteroseptal leaflet commissure), resulting in mitral-tricuspid continuity, and the VSD is perimembranous\textsuperscript{H4,W2} (see “Perimembranous Ventricular Septal Defect” under Morphology in Section I of Chapter 35). In this event, the rightward posterior division of the trabecula septomarginalis is deficient, and the bundle of His lies along the posteroinferior border of the VSD and is at risk during surgical repair\textsuperscript{A4,A5} (Fig. 53-3). Occasionally

![Figure 53-2 Autopsy specimen of simple double outlet right ventricle with subaortic ventricular septal defect (VSD). There is a prominent subaortic conus and a well-developed infundibular septum separating pulmonary valve (PV) from aorta, tricuspid valve (TV), and VSD. Key: AR, Aortic root (conus); RT, right. (From Kirklin and colleagues.\textsuperscript{L5,4})](image-url)
The VSD and TSM lie more superiorly and anteriorly in the ventricular septum, directly beneath the pulmonary conus and valve, than they do in subaortic VSD with right-sided aorta, but in a position similar to that of subaortic VSD with aortic L-malposition. If there is a subpulmonary conus, infundibular (conal) muscle forms the superior margin of the defect. If there is no subpulmonary conus, there is pulmonary-mitral and occasionally pulmonary-tricuspid continuity, and the VSD is juxtapulmonary with the pulmonary valve over-riding it (Fig. 53-5). The infundibular septum inserts behind left anterior division of TSM, and its leftward end contributes to the interventricular septum in front of the VSD. The posterosuperior margin of the VSD is formed by the zone of fibrous continuity or by the pulmonary cusps, depending on degree of pulmonary valve over-riding, or by the subpulmonary conus if present. As with subaortic VSD, the defect may extend to the tricuspid anulus posteroinferiorly and be perimembranous (see Fig. 53-5), but often it does not. The infundibular septum is usually sagittally oriented and is then not a part of the interventricular septum.

The VSD and TSM lie more superiorly and anteriorly in the ventricular septum, directly beneath the pulmonary conus and valve, than they do in subaortic VSD with right-sided aorta, but in a position similar to that of subaortic VSD with aortic L-malposition. If there is a subpulmonary conus, infundibular (conal) muscle forms the superior margin of the defect. If there is no subpulmonary conus, there is pulmonary-mitral and occasionally pulmonary-tricuspid continuity, and the VSD is juxtapulmonary with the pulmonary valve over-riding it (Fig. 53-5). The infundibular septum inserts behind left anterior division of TSM, and its leftward end contributes to the interventricular septum in front of the VSD. The posterosuperior margin of the VSD is formed by the zone of fibrous continuity or by the pulmonary cusps, depending on degree of pulmonary valve over-riding, or by the subpulmonary conus if present. As with subaortic VSD, the defect may extend to the tricuspid anulus posteroinferiorly and be perimembranous (see Fig. 53-5), but often it does not. The infundibular septum is usually sagittally oriented and is then not a part of the interventricular septum.

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Subpulmonary Septal Defect
Taussig-Bing heart is the typical example of DORV and subpulmonary VSD. It may be considered a form of DORV in which the VSD is subpulmonary and associated with malalignment of the infundibular septum.

Doubly Committed Ventricular Septal Defect
In doubly committed VSD, an uncommon variant, the VSD and TSM lie more superiorly in the septum than subaortic or
subpulmonary VSDs. This, plus absence (or severe hypoplasia) of the infundibular septum and consequent confluence of the aortic and pulmonary valves, place the defect in a juxtaarterial position. The semilunar valves are related to posterior and superior boundaries of the defect. Anterior and inferior boundaries are formed by the TSM and its left anterior division; posteroinferior boundaries are formed by the posterior division. This muscle band usually separates the VSD from the tricuspid valve anulus. There is usually no conus, but if present it is very narrow, and there may be aortic-tricuspid and pulmonary-mitral continuity (Fig. 53-6).

The VSD and its relationships resemble those of isolated juxtaarterial VSD (see Chapter 35), tetralogy of Fallot with juxtaarterial VSD (see Chapter 38), and some types of double outlet left ventricle (see Chapter 54). Both semilunar valves usually lie over the RV, but it can be difficult to decide whether this is the case or whether they lie mostly over the LV. At times, they may arise equally over both ventricles, a condition that can be called double outlet both ventricles.

Noncommitted or Remote Ventricular Septal Defect

Trabecular VSDs are not related to the TSM and its divisions, as are VSDs of most hearts with DORV, and they are clearly away from the semilunar valves. However, an inlet septal VSD (see Morphology in Section I of Chapter 35) may be sufficiently remote from the great arteries as to be considered noncommitted (Fig. 53-7).

Infundibulum

In general, hearts with DORV may have bilateral conuses, one beneath the aortic valve and one beneath the pulmonary valve, or a single conus beneath either semilunar valve, or no conus. About three fourths of hearts with subaortic VSD have bilateral conuses, and about one fourth have only a subpulmonary conus (Table 53-1). An operative experience, however, may reflect a nonrepresentative prevalence of morphologic features. For example, in 350 patients operated on at Madras Medical Mission, the distribution of conal morphology was weighted far more toward absent conus (86%); prevalence of subaortic VSD was 57% (KM Cherian; personal communication, 2000) (Table 53-2). Hearts with subpulmonary VSD (Taussig-Bing hearts) have either bilateral conus or a single conus beneath the aortic valve, in about equal proportions. Hearts with doubly committed VSDs may have a single common conus beneath the two semilunar valves (“doubly committed”), or there may be fibrous continuity between one of the semilunar valves and one of the AV valves, associated with absence of a conus.

There is a pattern of relations between conus and position of the great arteries (Table 53-3). As a general rule, presence of conus beneath a semilunar valve tends to result in an anterior position of the valve and great artery. Absence of conus links semilunar valve and artery to the mitral valve with fibrous continuity, resulting in a posterior position of valve and artery. As a result, degree of conal development beneath the aortic and pulmonary valves fairly well predicts position and relationship of the great arteries. This can be inferred from the Madras experience (see Table 53-2), in which there is a high prevalence of normally related great arteries and subaortic or absent conus. Anterior position (D-malposition) of the aorta is uncommon (26%) when there are bilateral conuses, but common (67%) when there is only a subaortic conus. An anterior position has not been observed to occur with only subpulmonary conus or with no conus. An aorta side by side with or posterior to the pulmonary trunk occurs in all conal patterns.

Great Arteries

Both great arteries may lie over the RV in their entirety in the rare instances of DORV with intact ventricular septum and noncommitted VSD. This is often the situation as well when the VSD is subaortic. When the VSD is doubly

Figure 53-4  Specimen of double outlet right ventricle (RV) with bilateral conus and subaortic ventricular septal defect (VSD) in a patient with a pulmonary trunk band. A, Right ventricular outflow tract has been opened as has aortic valve (AoV) and aorta (Ao). VSD (arrow) is only just visible, because it is partly overlaid by anomalously attached chordae from the tricuspid valve (TV), which may interfere with placing an intraventricular tunnel patch. B, Infundibular (conal) septum (CS) displaced to right to reveal pulmonary valve (PV) and extensive subpulmonary conus. Infundibular septum inserts posteriorly and is unrelated to interventricular septum. In some respects, this VSD is intermediate between a subaortic and a subpulmonary defect and illustrates the difficulties of accurate and precise categorization. (From Barratt-Boyes and Calder.)
Figure 53-5 Specimen of double outlet right ventricle (RV) with subpulmonary ventricular septal defect (VSD) (Taussig-Bing heart). A, Right ventricular outflow tract, aortic valve (AoV), and aorta (Ao) have been opened. The subaortic conus separates aortic from tricuspid valve (TV). Rightward aspect of infundibular (conal) septum is visible. B, Infundibular septum and adjacent portion of free wall are displaced toward aorta to reveal opened RV outflow tract, pulmonary valve (PV), and pulmonary trunk (PT). Infundibular septum lies in a sagittal plane and has no attachment to the ventricular septum; moreover, it separates VSD from aortic valve. VSD lies directly above trabecula septomarginalis (TSM), but because the rightward posterior division of the TSM is deficient, it reaches the tricuspid anulus and is perimembranous. PV overrides VSD onto left ventricle (LV). There is no subpulmonary conus. Aorta is to the right and slightly anterior to pulmonary trunk. C, View from opened LV. Overriding PV is in direct fibrous continuity with anterior leaflet of mitral valve (MV). (From Barratt-Boyes and Calder.22)
committed or subpulmonary, there is usually a variable degree of overriding of one or both great arteries over the VSD.

Positional interrelationships of the great arteries are variable in hearts with DORV. Interrelationships are normal or near-normal in most patients with DORV, with the aorta located rightward and posterior relative to the pulmonary trunk. Less often, the great arteries are side by side, with the aorta to the right. D-malposition may be present in hearts with DORV, with the aorta anterior and to the right of the pulmonary trunk or at times directly anterior. Rarely, it is anterior and to the left. Occasionally there is L-malposition, with the aorta to the left but side by side with the pulmonary trunk.

Although in 77% of hearts with subaortic VSD the aorta is to the right and either side by side or posterior to the pulmonary trunk (more or less normally related), it is anterior (D-malposition) in 23% of cases (see Table 53-4). Furthermore, more or less normally related great arteries are not unique to hearts with subaortic VSD; those with subpulmonary VSD have normally related great arteries in similar frequency (P for difference = .8).

Only in hearts with noncommitted VSD is the frequency of more or less normally related great arteries less (33%) (P for difference = .06; see Table 53-4). Although D-malposition of the aorta may be considered characteristic of ordinary transposition (see “Great Arteries” under Morphology in Chapter 52) and by implication Taussig-Bing heart, hearts with DORV and subpulmonary VSD are associated with typical D-malposition in a minority of cases (see Table 53-4).
### Table 53-1  Relationship of Ventricular Septal Defect and Conus Pattern in Double Outlet Right Ventricle

<table>
<thead>
<tr>
<th>Relationship of VSD</th>
<th>Type of Conus</th>
<th>Bilateral</th>
<th>Subpulmonary Only</th>
<th>Subaortic Only</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No.</td>
<td>% of n</td>
<td>Conus</td>
<td>No.</td>
</tr>
<tr>
<td>Subaortic</td>
<td>22</td>
<td>17</td>
<td>77</td>
<td>64-7</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(63)</td>
<td>51-74</td>
<td>(100)</td>
<td>68-100</td>
<td>(0)</td>
</tr>
<tr>
<td>Subpulmonary</td>
<td>11</td>
<td>5</td>
<td>45</td>
<td>27-65</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>(19)</td>
<td>11-29</td>
<td>(0)</td>
<td>0-32</td>
<td>(67)</td>
</tr>
<tr>
<td>Doubly committed</td>
<td>3</td>
<td>2</td>
<td>67</td>
<td>24-96</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(7)</td>
<td>2-17</td>
<td>(0)</td>
<td>0-32</td>
<td>(0)</td>
</tr>
<tr>
<td>Noncommitted</td>
<td>6</td>
<td>3</td>
<td>50</td>
<td>24-76</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>(11)</td>
<td>5-21</td>
<td>(0)</td>
<td>0-32</td>
<td>(33)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>42</td>
<td>27</td>
<td>64</td>
<td>55-73</td>
<td>5</td>
</tr>
</tbody>
</table>

*P*(χ²)

Note: In parentheses are percentages and confidence limits of various VSD locations within each type of conus.

Data based on study at GLH of 42 autopsy specimens. Specimens with atrial isomerism or L-malposition of the aorta are excluded.

*P* values along bottom of table refer to difference in prevalence of type of conus within the various relationships of the VSD.

Key: CL, 70% confidence limits; VSD, ventricular septal defect.

### Table 53-2  Cardiac Morphology of 350 Patients with Double Outlet Right Ventricle

<table>
<thead>
<tr>
<th>VSD Position</th>
<th>No.</th>
<th>%</th>
<th>Conus</th>
<th>No.</th>
<th>%</th>
<th>Position of Aorta in Relation to Pulmonary Trunk</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subaortic</td>
<td>199</td>
<td>57</td>
<td>Subaortic</td>
<td>32</td>
<td>9.1</td>
<td>Normal</td>
<td>232</td>
<td>66</td>
</tr>
<tr>
<td>Subpulmonary</td>
<td>37</td>
<td>11</td>
<td>Subpulmonary</td>
<td>6</td>
<td>1.7</td>
<td>D-Malposed</td>
<td>51</td>
<td>15</td>
</tr>
<tr>
<td>Doubly committed</td>
<td>21</td>
<td>6</td>
<td>Bilateral</td>
<td>10</td>
<td>2.9</td>
<td>L-Malposed</td>
<td>29</td>
<td>8.3</td>
</tr>
<tr>
<td>Noncommitted</td>
<td>93</td>
<td>27</td>
<td>Noconus</td>
<td>302</td>
<td>87</td>
<td>Anteroposterior</td>
<td>38</td>
<td>11</td>
</tr>
</tbody>
</table>

*Data from study of 350 patients with double outlet right ventricle operated on at the Institute for Cardiovascular Disease, Madras Medical Mission, 1989-2000.

(Cherian KM; personal communication, 2000.)

Key: VSD, Ventricular septal defect.

### Table 53-3  Type of Conus and Position of Great Arteries in Double Outlet Right Ventricle

<table>
<thead>
<tr>
<th>Type of Conus</th>
<th>n</th>
<th>No.</th>
<th>% of n</th>
<th>CL</th>
<th>Side by Side or Posterior</th>
<th>No.</th>
<th>% of n</th>
<th>CL</th>
<th>Anterior</th>
<th>No.</th>
<th>% of n</th>
<th>CL</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral</td>
<td>27</td>
<td>20</td>
<td>74</td>
<td>63-83</td>
<td>(69)</td>
<td>58-79</td>
<td>(54)</td>
<td>36-71</td>
<td>.3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subpulmonary only</td>
<td>5</td>
<td>5</td>
<td>100</td>
<td>68-100</td>
<td>(17)</td>
<td>10-28</td>
<td>(0)</td>
<td>0-14</td>
<td>.14</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subaortic only</td>
<td>9</td>
<td>3</td>
<td>33</td>
<td>15-56</td>
<td>(10)</td>
<td>5-20</td>
<td>(46)</td>
<td>29-64</td>
<td>.009</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1</td>
<td>1</td>
<td>100</td>
<td>15-85</td>
<td>(3)</td>
<td>0-11</td>
<td>(0)</td>
<td>0-14</td>
<td>.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>42</td>
<td>29</td>
<td>69</td>
<td>60-77</td>
<td>13</td>
<td>31</td>
<td>23-40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data and presentation are as described for Table 53-1.

*Side by side or posterior refers to aorta being to the right and beside or slightly posterior to pulmonary trunk, with the great arteries more or less normally interrelated.

*Anterior refers to D-malposition, with aorta anterior and more or less to the right.

*P*-value column refers to difference in occurrence of the given VSD position in the two great artery positions.

Key: CL, 70% confidence limits.
Hearts with doubly committed VSD tend to have more or less normally related great arteries. Observing great artery position at cineangiography or operation does not permit a reasonably accurate inference as to the position and category of the VSD (see Table 53-4). There is no greater certainty that the VSD is subaortic when the great arteries are more or less normally interrelated than when in D-malposition (\( P = .2 \)). When the aorta is in D-malposition, there is no greater certainty that the VSD will be subpulmonary than subaortic (\( P = .8 \)).

### Pulmonary Stenosis

Pulmonary stenosis is common in hearts with a subaortic VSD. It is most often infundibular (Fig. 53-8), but it may be valvar, with or without a small pulmonary valve ring. Thus, all types of pulmonary stenosis observed in hearts with tetralogy of Fallot may be seen in DORV. Rarely, infundibular stenosis may be of the isolated low-lying variety, producing a two-chambered RV.\(^{15,334}\)

Pulmonary stenosis is also common in hearts with doubly committed VSD (five of five in the GLH experience). It is uncommon in association with Taussig-Bing heart and in hearts with a noncommitted VSD.\(^{14,19}\)

### Conduction System

The AV node is in its normal position in the AV septum, and the bundle of His penetrates the right fibrous trigone in the usual way. Thus, the course of the bundle of His relative to the VSD is the same as in primary VSD and in tetralogy of Fallot (see Chapters 35 and 38). The bundle is at risk of damage during repair when the defect reaches the tricuspid anulus (and becomes perimembranous). This is true whether the defect is subaortic or subpulmonary and whether the ascending aorta is right or left sided.\(^{45,69,18}\) However, as in other conditions with clockwise rotation and dextroposition of the aorta, the bundle is more on the LV side of the septum than usual.\(^{88}\) Furthermore, the trigone is often attenuated in DORV when there is a subaortic conus, which removes the aortic anulus from the central fibrous skeleton of the heart.

When a complete AV septal defect coexists, the node and bundle course are altered accordingly (see “Conduction System” under Morphology in Chapter 34).

### Coronary Arteries

Coronary artery pattern depends on position of the great arteries. In most varieties of DORV, it is similar to normal except that the aortic sinuses are rotated in a clockwise direction (viewed from below), such that the right coronary arises anteriorly and the left coronary posteriorly.\(^{12,13,17}\) When the aorta is anterior and rightward, the pattern is usually similar to that in transposition of the great arteries (see “Coronary Arteries” under Morphology in Chapter 52), with the right coronary artery arising from sinus 2 (right posterior facing sinus).\(^{1,2,12}\) In 15% of cases, a single coronary ostium may arise either anteriorly or posteriorly that supplies left and right sides of the heart.\(^{1,2,12}\) The branching pattern is also usually normal, except for occasional origin of the left anterior descending from the right coronary artery, with this vessel crossing the RV outflow from right to left as in tetralogy of Fallot (see Chapter 38). This anomaly was found in 25% of the DORV hearts reported in the early Mayo Clinic series, but it was not encountered in 42 GLH autopsy cases.\(^{62}\)

When the aorta is to the left in L-malposition, the right coronary artery passes to the right from the anterior sinus of the leftward anterior aorta to reach the AV groove in front of the pulmonary trunk. Its position prohibits extensive anterior patching across the pulmonary “anulus.”

### Associated Anomalies

Major associated cardiac anomalies, in addition to pulmonary stenosis of the tetralogy of Fallot type, may coexist. Coarctation of the aorta may be present, particularly in Taussig-Bing...
variant, and may require repair in the neonatal period; rarely, discrete subvalvar aortic stenosis may coexist. Various other cardiac anomalies coexist in about 30% of patients coming to intracardiac repair of DORV with a subaortic or doubly committed VSD (Tables 53-5 and 53-6).

Morphologic Syndromes of Double Outlet Right Ventricle

**Simple Double Outlet Right Ventricle**

The phrase *simple DORV* connotes the commonly occurring and easily repaired type of DORV in which the VSD is subaortic and the aorta is to the right, usually by the side of the pulmonary trunk or slightly posterior to it, or which in about 20% of cases is somewhat anterior to the pulmonary trunk (see Table 53-4). The aorta may spiral around the pulmonary trunk as it leaves the heart, or the great arteries may course parallel to each other. Usually there is a conus (infundibulum) beneath both the aorta and pulmonary valve, but in some cases there may be no subaortic conus (see Table 53-1). Coronary arterial anatomy is normal.

![Figure 53-8 Specimen of double outlet right ventricle (RV) with subaortic ventricular septal defect (VSD) and infundibular pulmonary stenosis. A, Right ventricular outflow tract is opened to aortic valve (AoV) and aorta (Ao). A subaortic conus separates aortic and tricuspid valves (TV). Poorly expanded subpulmonary conus narrows outflow tract. B, Infundibular (conal) septum is displaced to reveal opened pulmonary outflow tract. Pulmonary valve (PV) is bicuspid, and it and the pulmonary trunk (PT) are smaller than normal. Aorta is slightly anterior to pulmonary trunk. A probe passes through VSD and into aorta. Key: PT out, Pulmonary outflow. (From Barratt-Boyes and Calder.)](image)

**Table 53-5** Associated Cardiac Anomalies (Exclusive of Pulmonary Stenosis and Atrioventricular Septal Defect) in Patients Undergoing Surgical Correction of Double Outlet Right Ventricle with Subaortic or Doubly Committed Ventricular Septal Defect

<table>
<thead>
<tr>
<th>Associated Cardiac Anomalies</th>
<th>No.</th>
<th>Percentage of Total (n = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple VSDs</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Patent ductus arteriosus</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Pulmonary artery distribution deficiencies or post-shunt stenoses</td>
<td>9</td>
<td>13</td>
</tr>
<tr>
<td>Pulmonary atresia</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>LV hypoplasia + MV hypoplasia or regurgitation</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Congenital mitral stenosis</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Subaortic stenosis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Tricuspid regurgitation (severe)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Unroofed coronary sinus syndrome</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Azygos continuation of IVC</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Right aortic arch</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Aberrant right subclavian artery</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Origin of right coronary from left coronary artery</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Juxtaposed atrial appendages</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>Situs inversus totalis (Van Praagh S,L,L)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>No associated anomalies</td>
<td>41</td>
<td>59</td>
</tr>
</tbody>
</table>

*Data combine the experience at UAB (1967-1982; n = 42) and GLH (1958-1984; n = 28). Because some patients had multiple anomalies, total is not cumulative, nor is list mutually exclusive. Key: IVC, Inferior vena cava; LV, left ventricular; MV, mitral valve; VSD, ventricular septal defect.*

In borderline cases, this type of DORV merges with the type in which a perimembranous VSD demonstrates inlet extension and appears to be noncommitted and, on the other hand, the type in which the VSD demonstrates outlet extension and appears to be doubly committed.

**Taussig-Bing Heart**

In the most representative cases, the Taussig-Bing heart is similar from heart to heart. The VSD is anterior and superior and subpulmonary. The left main coronary artery is anterior to the pulmonary trunk. The pulmonary trunk arises biventricularly over the VSD, and the aorta is to the right and slightly anterior to or alongside it (see Table 53-4). The first portions of aorta and pulmonary trunk are parallel rather than tending to spiral as do normally positioned great arteries. The infundibular septum is in the sagittal plane and is not part of the interventricular septum. Lev and colleagues were able to use specific morphologic features within the RV as the hallmark of Taussig-Bing heart, but this is rarely possible clinically or surgically.

Subaortic stenosis, from narrowing of the subaortic infundibulum, may develop in Taussig-Bing heart. Pulmonary stenosis is uncommon. The mitral valve may straddle across the subpulmonary VSD, and in such cases the LV may be hypoplastic. Associated coarctation of the aorta is
common (about 50% of cases). This contrasts with the 6% prevalence in transposition with VSD.

In borderline cases, this type of DORV merges with transposition of the great arteries and large VSD and, on the other hand, may merge with DORV and noncommitted VSD of the trabecular type.

### Double Outlet Right Ventricle with Doubly Committed Ventricular Septal Defect

In DORV with doubly committed VSD, an uncommon syndrome, the VSD is immediately beneath both aorta and pulmonary trunk and is juxta-arterial.

### Double Outlet Right Ventricle with Noncommitted Ventricular Septal Defect

When the VSD is in the trabecular septum and clearly far removed from the great arteries, the anomaly is easily categorized into this subset. When the VSD is in the inlet septum and up against the tricuspid valve, categorization as DORV with noncommitted VSD can be questioned, but at least the defect is further removed from the aorta than in most hearts with DORV and subaortic VSD.

### Double Outlet Right Ventricle with L-Malposition

DORV with L-malposition usually has a subaortic VSD (rarely extending back to the tricuspid anulus) and pulmonary stenosis and presents a rare but distinctive clinical and surgical syndrome. Rarely the VSD may be perimembranous and extend up toward the pulmonary valve, or it may be truly subpulmonary. The VSD may, contrariwise, extend into the inlet septum and be noncommitted. Mehrizi has reported DORV with L-malposition and doubly committed VSD.

### Double Outlet Right Ventricle with Complete Atrioventricular Septal Defect

In cases of DORV with complete AV septal defect, the interventricular communication is large and usually extends deeply beneath a bridging left superior leaflet (see “Atrioventricular Valves” under Morphology in Chapter 34) to be subaortic in position. Occasionally, however, the interventricular communication does not extend in this manner and is noncommitted.

### Double Outlet Right Ventricle with Superior-Inferior Ventricles

In most hearts with this ventricular position, there is a ventricular L-loop, atrial situs solitus, and AV discordant connection (see Chapter 55). Uncommonly, in DORV with atrial situs solitus, AV concordant connection, and D-ventricular loop, there is a positional anomaly termed superior-inferior ventricles (over-and-under ventricles, upstairs-downstairs ventricles) (see “Cardiac and Arterial Positions” under Terminology and Classification of Heart Disease in Chapter 1). The RV is superior (and sometimes a little posterior) and the LV inferior. There may be D- or L-malposition of the aorta. The VSD is usually perimembranous and in the inlet portion of the septum. The right AV valve is usually more superiorly placed than usual relative to the left AV valve, and either AV valve may straddle the VSD (see “Ventricular Septal Defect with Straddling or Overriding Tricuspid Valve” under Morphology in Chapter 35). Severe LV hypoplasia may be present, and pulmonary stenosis is common.

### CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

#### Pathophysiology

Clinical features of patients with this morphologically highly variable anomaly are necessarily also highly variable. In general, patients with a large VSD and no pulmonary stenosis or severe pulmonary vascular disease are not clinically cyanotic. This is because pulmonary blood flow (Qp) is high and the resultant mixture of blood in the RV has a high enough oxygen saturation to prevent clinically evident cyanosis; however, there is some arterial desaturation.

#### Streaming of Blood Flow

SaO₂ is also affected by streaming of blood within the RV, which is determined by the relationship of the semilunar valves to the VSD and the position and presence of the infundibular septum. Thus, in simple DORV, flow of highly oxygen-saturated LV blood through the VSD is directed preferentially beneath the infundibular septum into the adjacent aorta (particularly when the subaortic conus is short or absent), whereas systemic venous blood passes largely out of the pulmonary trunk. As a result, patients with this arrangement present in infancy with high Qp in heart failure without cyanosis and cannot be clinically distinguished from infants with a large VSD (see Clinical Features and Diagnostic Criteria in Section I of Chapter 35).

When the VSD is subpulmonary, as in Taussig-Bing heart, flow through it of highly saturated LV blood is directed into

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### Table 53-6 Associated Cardiac Anomalies in Patients with Varieties of Double Outlet Right Ventricle Other Than Those with Subaortic or Doubly Committed Ventricular Septal Defects

<table>
<thead>
<tr>
<th>Associated Cardiac Anomalies</th>
<th>n</th>
<th>Percentage of Total (n = 15)</th>
<th>Hospital Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoplasia of LV and MV</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Congenital mitral stenosis</td>
<td>7</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Two-storied heart</td>
<td>13</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Dextrocardia</td>
<td>13</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Juxtaposed atrial appendages</td>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>LSVC to CS</td>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Coarctation of aorta</td>
<td>1</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>MV override or straddling</td>
<td>1</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>TV override or straddling</td>
<td>1</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Hypoplastic RV and TV</td>
<td>1</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>AV discordant connection</td>
<td>20</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Multiple VSDs</td>
<td>2</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>ASD (moderate or large)</td>
<td>4</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>No associated anomalies (apart from P5 or small ASD)</td>
<td>5</td>
<td>33</td>
<td>1</td>
</tr>
</tbody>
</table>

aData from experience with surgical correction at GLH (1964-1984; n = 15). Because most patients had multiple anomalies, total is not cumulative, nor is list mutually exclusive.

Key: ASD, Atrial septal defect; AV, atrioventricular; CS, coronary sinus; LSVC, left superior vena cava; LV, left ventricle; MV, mitral valve; P5, pulmonary stenosis; RV, right ventricle; TV, tricuspid valve; VSD, ventricular septal defect.
the adjacent pulmonary trunk by the vertically positioned infundibular septum. SpaO₂ is then higher than Sao₂, with systemic venous blood from the RV tending to flow more into the aorta. This situation is aggravated when there is overriding of the pulmonary trunk onto the LV. Thus, these infants present in a fashion similar to patients with transposition of the great arteries with large VSD in heart failure with mild cyanosis (see “Large Ventricular Septal Defect, Large Patent Ductus Arteriosus, or Both [Good Mixing]” under Morphology in Chapter 52).

**Pulmonary Vascular Disease**

Pulmonary vascular disease may be more rapid in onset in patients with DORV without pulmonary stenosis than in patients with simple large VSD, particularly in Taussig-Bing heart (see “Pulmonary Vascular Disease” under Natural History in Section I of Chapter 35). The resultant reduction in Qp has a more marked influence on Sao₂ than in simple VSD, because it reduces the amount of highly saturated blood in a common mixing chamber.

**Pulmonary Stenosis**

When important pulmonary stenosis is present, cyanosis becomes severe, and the clinical features and presentation are similar to those of patients with tetralogy of Fallot (see Chapter 38).

**Examination**

On physical examination, no clinical signs distinguish patients with DORV with and without pulmonary stenosis from the conditions that they mimic. The electrocardiogram (ECG) is not diagnostic, nor is the chest radiograph. However, in those uncommon instances in which there is L-malposition of the aorta, the aorta may be evident on the posteroanterior chest radiograph as it ascends vertically from the cardiac silhouette in the left upper mediastinum; this finding is not specific, however (see Clinical Features and Diagnostic Criteria in Chapter 57).

**Echocardiography**

Two-dimensional echocardiography provides a considerable amount of information regarding size of the VSD, relationship of the VSD to the semilunar valves, presence of subvalvar conus, and AV valve abnormalities. Position of the great arteries and conus are usually apparent (Fig. 53-9). The coronary arterial anatomy can also generally be defined accurately in neonates and infants by echocardiography alone.

**Cardiac Catheterization and Cineangiography**

Because echocardiographic assessment of morphology is reliable, cardiac catheterization before surgical intervention is not routinely required in neonates and young infants. In older infants and children, it may be needed to assess hemodynamics such as pulmonary vascular resistance and ventricular end-diastolic pressure, and to define extracardiac morphology such as the peripheral pulmonary vasculature and presence of aortopulmonary collateral vessels. Cineangiography can be used when necessary to define intracardiac morphology (Fig. 53-10). The whole of the ventricular septum must be profiled so that its upper part can be projected cranially. In this way, great vessel positions can be assessed relative to the two ventricles, and location of the VSDs determined. VSD size can be judged and subsets such as Taussig-Bing heart identified (Fig. 53-12). Cineangiography is of particular value in assessing the complex interrelationships present in DORV with superior-inferior ventricles and criss-cross hearts.

**NATURAL HISTORY**

The natural history of patients with DORV and AV concordant connection is highly variable, but some general trends can be identified.

The natural history of simple DORV is similar to that of simple large VSD (see Natural History in Section I of Chapter 35); this is probably also true for patients with DORV whose VSD is doubly committed or noncommitted. The exception is that spontaneous VSD closure, which is fatal rather than curative, is rare in DORV.

When the VSD is subpulmonary, as in Taussig-Bing heart, the natural history is similar to that for transposition and large VSD, but it is even more unfavorable (see “Ventricular Septal Defects” under Natural History in Chapter 52). This is in part because severe pulmonary vascular disease occurs early in life. Poor prognosis for these patients may also be related to frequent occurrence of left-sided cardiac and extracardiac malformations such as coarctation of the aorta and LV and mitral valve hypoplasia (see “Coarctation as Part of Hypoplastic Left Heart Physiology” under Morphology in Section I of Chapter 48).

When pulmonary stenosis or atresia is present in DORV with subaortic VSD, and probably in those with doubly committed or noncommitted VSD as well, the natural history is indistinguishable from that of patients with tetralogy of Fallot and pulmonary stenosis or atresia (see Chapter 38).
Figure 53-10  Cineangiograms of simple double outlet right ventricle (DORV) with conoventricular ventricular septal defect (VSD). A, Left ventriculogram in elongated right anterior oblique view. Infundibular septum is well shown. B, Four-chambered view. VSD is also perimembranous and abuts tricuspid valve (TV). C, Left ventriculogram in four-chamber view of another patient in whom VSD is separated from the tricuspid valve (arrowheads) by a bar of muscle. D, This is from the same cineangiogram a few frames later.

Continued
PART VII  Congenital Heart Disease

Blood flow in doubly committed VSDs is usually baffled using a more complex patch from LV to aorta. Noncommitted VSD may be treated by baffling of blood through the VSD to the aorta, accompanied by myocardial flap reinsertion of the straddling tricuspid valve or by a Fontan type of procedure.

The natural history in some patients is dominated by an associated cardiac anomaly, such as a complete AV septal defect (see Natural History in Chapter 34).

TECHNIQUE OF OPERATION

The type of operation selected depends in part on position of the VSD, relationship of the great arteries, size of the patient, and adequacy of the resulting ventricles and their respective outflows after closing or baffling the VSD. In general:

- Subaortic VSD with an adequate tricuspid to pulmonary valve distance is treated by simple intraventricular baffling that directs LV blood through the VSD to the aorta (intraventricular tunnel repair).
- Subpulmonary VSD, as in Taussig-Bing heart, without pulmonary stenosis is treated with an arterial switch procedure with simple VSD closure that directs blood from the LV to the neo-aortic valve.
- Blood flow in doubly committed VSDs is usually baffled using a more complex patch from LV to aorta.
- Noncommitted VSD may be treated by baffling of blood through the VSD to the aorta, accompanied by myocardial flap reinsertion of the straddling tricuspid valve or by a Fontan type of procedure.

Various surgical procedures are described, but description does not imply recommendations. Indications are described later in this chapter under Indications for Operation. Only the general methods are described here, and each patient may be sufficiently unique to require an individual approach.

Intraventricular Tunnel Repair of Simple Double Outlet Right Ventricle

Preparation for operation, draping, arrangement for cardiopulmonary bypass (CPB), median sternotomy, and placing stay sutures and sutures for cannulation are as usual (see Section III in Chapter 2). The pericardium is cleared in case...
**Figure 53-11** Cineangiogram of simple double outlet right ventricle with restrictive subaortic ventricular septal defect (VSD). Early phase (A) and late phase (B) of cineangiogram made in long axial projection after injection of contrast into left ventricle. Key: Ao, Aorta; LA, left atrium; LV, left ventricle; MV, mitral valve; PT, pulmonary trunk; RV, right ventricle.

**Figure 53-12** Cineangiogram made in an elongated right anterior oblique view (A) and in a long axial view (B) of a Taussig-Bing heart. The prominent infundibular septum is seen between aorta (Ao) and pulmonary trunk (PT), but it is clearly (B) not interventricular in position. The ventricular septal defect is between the arrows, and the pulmonary trunk somewhat overrides it. Key: IS, Infundibular (conal) septum; LV, left ventricle; MV, mitral valve; RV, right ventricle; TV, tricuspid valve.
it is needed, and a double velour woven polyester tube (see “Decision and Technique for Transanular Patching” under Technique of Operation in Section I of Chapter 38) whose diameter is about 20% larger than that of the aorta is precotted, or a collagen-impregnated polyester tube is selected (see “Grafts for Use in Aortic Surgery” in Chapter 24). The intrapericardial anatomy is carefully evaluated.

Support technique and myocardial management are chosen from the usually available alternatives (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). If two venous cannulae are used, after placing the aortic clamp, the right atrium is opened through a small incision, and a pump-oxygenator sump sucker is placed across the natural or surgically created foramen ovale. A single venous cannula can be used if the operation is to be performed through the RV. Operation is performed at 25°C with continuous CPB at a flow of 1.6 L·min⁻¹·m⁻², or at 18°C with low CPB flow rate and circulatory arrest when needed for improved exposure. If the desire is to perform the operation entirely during hypothermic circulatory arrest, that technique may be chosen (see Section IV of Chapter 2).

A thorough examination of the intraventricular anatomy can usually be made through the tricuspid valve, and based on this examination, the repair is planned. Repair of simple DORV can be accomplished through the right atrium, although the most superior part of the repair must sometimes be made through a radial incision along the base of the tricuspid anterior and septal leaflets (see Fig. 35-26 in Chapter 35). Through the atrial approach, it is more difficult to be certain that the geometry of the intraventricular tunnel is exactly correct; lacking firm evidence for increased safety of the atrial approach to repair of isolated VSD (see Chapter 35) or tetralogy of Fallot (see Chapter 38), the RV approach may be equally satisfactory.

An intraventricular tunnel is created within the RV that conducts LV blood through the VSD to the aorta. For the transatrial approach, the right atrium is opened in a cephalad-caudal direction near the AV groove. Stay sutures are placed as for the approach for closure of an isolated VSD or as for transatrial repair of tetralogy of Fallot (see Technique of Operation in Section I of Chapters 35 and 38). The anterior tricuspid valve leaflet is elevated by fine stay sutures. For the RV approach, a transverse ventriculotomy is made low in the RV outflow tract, unless the distance between the left anterior descending coronary artery (LAD) on the left and the right coronary artery (RCA) on the right is inadequate, in which case a vertical infundibular incision is used. Special care is required if there is an anomalous origin of the LAD from the RCA. For exposure, stay sutures are placed on the ventriculotomy. The anatomy is carefully assessed, verifying anatomic details of the diagnosis. Location and size of the VSD are noted, and particularly whether it abuts the tricuspid valve or has a rim of muscle along its posterior border (Fig. 53-13). This latter determines the relationship of the bundle of His to the posterior margin of the VSD.

Small size of the VSD does not alone negate the possibility of an adequate intraventricular tunnel between LV and aorta. The possibility of enlarging it and creating a tunnel of adequate size and configuration depends primarily on the distance between the tricuspid and pulmonary valves. Sakata, Lecompte, and colleagues estimate that when this distance is less than the diameter of the aorta, a tunnel placed posterior to the pulmonary trunk will be stenotic; they recommend that in such a case, the tunnel be placed anterior to the orifice of the pulmonary trunk. However, in simple DORV, this distance is usually long (see Figs. 53-2 and 53-4), making this malformation suited for intraventricular tunnel repair, with the tunnel posterior to the orifice of the pulmonary trunk.

As a first step, the VSD is enlarged anteriorly if it is clearly restrictive to flow into a tunnel from the LV. Before this is done, the area of the proposed enlargement is carefully examined to be certain that it is interventricular septum and not hypertrophied and trabeculated anterior ventricular wall. Cutting into the latter imposes the risks of damaging the LAD and developing an LV false aneurysm. Generally, a simple incision into the interventricular septum from the VSD gapes open widely and suffices, but occasionally some muscle must be excised. In doing this, the mitral valve must be kept out of harm’s way.

The VSD patch is then cut from a polyester tube (see Fig. 53-13). Geometry of the patch is crucial in preventing subaortic stenosis after the repair. The patch will form the anterior half of the tunnel connecting the VSD to the aortic orifice; the posterior half of the tunnel will be heart tissue, and experience indicates that this provides adequately for growth of the tunnel. Thus, initial trimming is made to retain about half to two thirds of the circumference of the tube graft that was selected, so as to have a diameter about 20% greater than that of the ascending aorta. The patch is trimmed so that its length is the distance from the anterior angle of the VSD to the anterior edge of the subaortic conus or, if this is hypoplastic, LV-aortic junction (aortic valve “anulus”).

The technique for inserting the patch is analogous to that for inserting the patch in isolated VSD (see Fig. 35-24 in Chapter 35) or tetralogy of Fallot (see Chapter 38). Because correct orientation of the patch is essential to creating a geometrically correct tunnel, a marking stitch is placed at the most anterior part of the repair, and another is placed through the patch at a corresponding point. A similar marking stitch is placed over the midportion of the aorta anteriorly and in the patch. The first pledged mattress stitch is passed from the atrial to ventricular side through the base of the tricuspid commissural tissue between the anterior and septal leaflets (see Fig. 53-13). If the approach is through the right atrium and tricuspid valve, the suture is usually begun anteriorly at the most caudal aspect of the VSD. (If a bar of muscle separates the VSD from the tricuspid valve “anulus,” the sutures may be placed just on the right side of the subaortic infundibulum and then trimmed so that its length is the distance from the anterior angle of the VSD to the anterior edge of the subaortic conus.) Suturing is carried leftward for a short distance between the patch and tricuspid leaflet tissue and after a few stitches between the patch and ventriculoinfundibular fold and up along the right side of the subaortic infundibulum. When the marking stitch is reached, the suture is held. With the other arm of the suture, the patch is sewn to the RV side of the septum, 5 to 7 mm back from the edge of the VSD, proceeding rightward, anteriorly, and then superiorly (see Fig. 53-13). When the repair is completed, the contoured polyester patch forms the anterior portion of an unobstructed intraventricular tunnel between the VSD and aorta.

Rewarming the patient by the perfusate is commenced, and the interatrial communication is closed with a few sutures, but not tied until there is effective ventricular contraction (to
Figure 53-13  Intraventricular tunnel repair for simple double outlet right ventricle with subaortic ventricular septal defect (VSD). A, Pulmonary and aortic valves are at nearly the same level. The perimembranous VSD has been exposed through a right ventriculotomy. There is moderate hypertrophy of the parietal band, which is mobilized and partially resected. B, A polyester tube of diameter about 20% larger than that of the aortic root has been cut to a length that is the same as the distance from the anterior border of the VSD to the aortic valve. About three-fifths circumference of the tube is used and is contoured as shown. Corrugations in the polyester patch assist the surgeon in maintaining proper orientation of the patch as it is being sewn in place. A pledgeted mattress suture is placed through the base of the commissure between septal and anterior tricuspid leaflets to begin the tunnel repair. C, Suturing has been carried to the left along the ventriculoinfundibular fold and up over the subaortic conus. With the other arm of the suture, inferior and superior portions of the repair are completed. The contoured tunnel offers no obstruction to flow from left ventricle to aorta. Key: RBB, Right bundle branch; TV, tricuspid valve.
Repair of Double Outlet Right Ventricle with Subaortic Ventricular Septal Defect and Pulmonary Stenosis

Repair is essentially that for tetralogy of Fallot, as described in “Technique of Operation” in Section I of Chapter 38. The only difference is the intraventricular tunnel repair, as just described, rather than simple VSD closure.

Repair of Taussig-Bing Heart by Arterial Switch Repair

The usual Taussig-Bing type of DORV with subpulmonary VSD is best treated by closure of the VSD in such a manner that the LV ejects into the neo-aorta, and by an arterial switch (see “Arterial Switch Operation” under Technique of Operation in Chapter 52).

Approach to repair of the VSD is varied, and the decision is best made before operation, based on the following considerations (Quaegebeur JM; personal communication, 1991):

- When the VSD is perimembranous or juxta-tricuspid, and particularly when it extends toward the inlet septum, repair is probably most effectively accomplished from the right atrium.
- When the VSD extends toward the RV outlet and the pulmonary trunk does not override the VSD, repair is most easily accomplished through the proximal aortic (neopulmonary) segment after removing the aortic buttons containing coronary ostia. The landmarks and techniques are identical to those used when a VSD is repaired through a right ventriculotomy.
- When the pulmonary trunk is large and overrides the VSD, as is usually the case, an approach to the VSD through the proximal pulmonary (neoaortic) segment is convenient. However, the posteroinferior portion of the insertion of the patch to close the VSD (performed so that the LV ejects into the pulmonary trunk [neoaorta]) is approached from the RV aspect as a protection against damaging the conducting tissue.

The arterial switch is then performed (see “Arterial Switch Operation” under Technique of Operation in Chapter 52). Because the great arteries are often side by side, suitable adjustments are made in the operation (see Chapter 52, Fig. 52-28). If arch hypoplasia is present, it is addressed surgically with one of several possible approaches. Either a standard interrupted arch repair technique is used (see Technique of Operation in Section II of Chapter 48) or the relatively hypoplastic ascending aorta can be reoriented from its vertical position to a horizontal position and anastomosed end to end to the descending aorta, followed by anastomosis of the proximal pulmonary trunk (neoaorta) to the transversely positioned ascending aorta. When arch hypoplasia is present, there is a high likelihood of hypoplasia of the RV outflow tract, and clinically important postoperative infundibular obstruction is common. Therefore, the RV outflow tract should be addressed surgically when arch obstruction is present. In this setting, the VSD is best repaired through a vertical infundibular incision, with infundibular resection and patching.

Intraventricular Tunnel Repair of Taussig-Bing Heart

Although the place of the intraventricular tunnel repair of Taussig-Bing heart is not securely established, small series of successful operations have been reported.

Initial stages of operation are the same as in other operations for Taussig-Bing heart. After CPB and cold cardioplegia have been established and the right atrium opened, morphology within the RV is studied through the tricuspid valve. Distance from tricuspid to pulmonary valves is estimated; if this distance is too short, the LV-to–pulmonary trunk tunnel will probably need to pass anterior to the pulmonary valve (see “Intraventricular Tunnel Repair of Simple Double Outlet Right Ventricle” earlier in this chapter); alternatively, an arterial switch operation is used. Any attachment of tricuspid chordae to septal edges of the malaligned infundibular septum is noted because special measures are needed for these. Straddling or overriding of the mitral valve is of considerable importance because this may make the planned operation impossible. Usually, after completing the examination from the right atrium, a transverse right ventriculotomy is made for the repair, although sometimes repair may be accomplished from the right atrial approach.

Ideally, the surgically created intraventricular tunnel is fashioned to lie posterior to the pulmonary trunk (Kawashima method), but this depends on availability of space between the tricuspid and pulmonary valves, as noted earlier (Fig. 53-14). Adequate space is more likely to be available when the great arteries are side by side rather than in an anteroposterior position. Generally the VSD is enlarged anteriorly, and at least a portion of infundibular septum is excised. It may be helpful to open the pulmonary trunk and pass a Hegar dilator through the pulmonary valve to expose the infundibular septum and protect the mitral apparatus (see “Lecompte Intraventricular Repair” in text that follows). As this is being done, care is taken to avoid damaging the aortic valve cusps and chordae from the tricuspid valve. If these chordae attach alongside an area that requires enlargement, that portion is not excised but instead is turned up as a flap. After creation of the intraventricular tunnel, the flap of infundibular septum is sutured in place over the tunnel. The polyester patch is trimmed to an appropriate size and configuration (see Fig. 53-13) and sewn into place with the usual care to avoid damaging the conduction system (see Fig. 53-14).

When the aorta is directly anterior, there is usually insufficient space between the tricuspid and pulmonary valves for a posterior position of the intraventricular tunnel. If an intraventricular tunnel repair is performed, the VSD is enlarged appropriately and the tunnel created anterior to the
pulmonary orifice (Patrick-McGoon method)\textsuperscript{98,99,100} (Fig. 53-15). In some cases, if this technique is used, a prosthetic tube (rather than a patch) is needed for part of the pathway, and part of the tube is incorporated into the closure of the right ventriculotomy.\textsuperscript{101}

**Lecompte Intraventricular Repair**

Although the role of this operation, which Lecompte calls \textit{REV} (réparation à l’étage ventriculaire), is not yet certain, its concepts and results mandate consideration. In this operation, the LV is connected to the aorta and the RV to the pulmonary trunk by a technique that does not require an extracardiac conduit.\textsuperscript{98,99,100,101,102} It is designed for patients in whom a simple intraventricular tunnel repair is not possible, nor is an arterial switch operation combined with repair of the VSD in such a manner that the LV is connected to the proximal pulmonary trunk (neoaortic) segment. The reason for the latter is usually coexisting important pulmonary (LV outflow) stenosis. The diagnosis may be some form of DORV or transposition with VSD and LV outflow obstruction. The Lecompte operation has also been demonstrated to be applicable to double outlet LV in infancy, thus avoiding need for a valved extracardiac conduit (Bailey LL; personal communication, 1991).

Initial stages of operation are the same as for intraventricular repair. After CPB and cold cardioplegia have been established, and after the preliminary examination from the right atrium is accomplished, a vertical right ventriculotomy is made and extended as far cephalad as possible. After thorough assessment of intraventricular anatomy and great arteries, the aorta and pulmonary trunk are transected (Fig. 53-16, A). All interventricular and infundibular septal tissue between the VSD and great arteries is resected. A Hegar dilator introduced through the pulmonary trunk helps with exposure during resection (Fig. 53-16, B). Cusps of the aortic valve
must be visualized to protect them from damage in the course of resection. The excision is kept away from regions occupied by the bundle of His and its primary branches. When tricuspid chordae are attached to a portion of the infundibular or ventricular septum, this portion is raised as a flap with chordae attached. After completing the intraventricular repair, the flap is sutured to the roof of the tunnel, more or less in its original position.

The intraventricular tunnel repair is performed by suturing a polyester or polytetrafluoroethylene (PTFE) patch into place to form the roof of the LV-aortic pathway (Fig. 53-16, C).

The proximal segment of the pulmonary trunk is closed (for details, see “Bidirectional Superior Cavopulmonary Shunt” under Technique of Operation in Chapter 41). Because this repair is generally performed in patients in whom the aorta is anterior to the pulmonary trunk, the pulmonary trunk and its bifurcation are usually translocated anterior to the aorta. For this, the aortic clamp is repositioned, and the distal aortic segment is brought behind the bifurcation of the
Figure 53-16  Lecompte operation for double outlet right ventricle with pulmonary stenosis and for other abnormalities of ventriculoarterial connection and ventricular septal defect (VSD), including transposition of the great arteries with VSD and left ventricular outflow tract obstruction. A, Dashed lines indicate sites for transecting aorta and pulmonary trunk and for the right ventriculotomy. B, Right ventriculotomy has been made, great arteries have been transected, a Hegar dilator has been passed down through the proximal segment of the pulmonary trunk and into the left ventricle to improve exposure (and protect the mitral valve), VSD has been enlarged, and infundibular (conal) septum has been resected. C, Polyester patch has been sewn into place to form anterior portion of newly created left ventriculoaortic pathway, using the same general technique shown in Fig. 53-13. Proximal pulmonary trunk stump is oversewn. D, Aorta has been repositioned behind pulmonary trunk bifurcation and reconstructed. Pulmonary trunk has been enlarged by an incision anteriorly and its posterior wall anastomosed to the right ventriculotomy. E, Repair is completed with a polyester (or polytetrafluoroethylene or pericardial) patch placed as a roof over the right ventriculopulmonary trunk pathway, using the same principles as in placing a transanular patch in repair of tetralogy of Fallot (see Fig. 38-29 in Chapter 38).
pulmonary trunk (Fig. 53-16, D), as in the Lecompte maneuver for the arterial switch operation (see “Arterial Switch Operation” under Technique of Operation in Chapter 52). The aorta is reconstructed behind and to the right of the distal pulmonary trunk segment.

The posterior lip of the distal segment of the pulmonary trunk is anastomosed to the cephalad margin of the right ventriculotomy. The right ventricular–pulmonary trunk pathway is completed by suturing a roof of pericardium, polyester, or PTFE into place (Fig. 53-16, E). Lecompte incorporates a monocusp valve beneath the patch.

Nikaidoh Aortic Translocation and Right Ventricular Outflow Reconstruction

The first step in this procedure is to core out the intact aortic root from the RV, including aortic valve and coronary arteries, as described earlier by Bex and colleagues (Fig. 53-17). The pulmonary trunk is transected, and an incision in the interventricular septum between the VSD and lumen of the proximal stump of the pulmonary trunk opens this area widely. This allows the VSD (and through it the LV) to be joined to the aorta by a roofing patch, which is similar to that

Figure 53-17  Nikaidoh aortic translocation and right ventricular outflow tract reconstruction. A1, Anteriorly located aortic root is fully mobilized beneath the valve and both coronaries skeletonized. A2, Division of pulmonary trunk and infundibular (conal) septum (when present). Pulmonary-mitral continuity is demonstrated. B1, Anastomosis of aorta to open pulmonary “anulus” after posterior translocation. Ventricular septal defect (VSD) patch will be anastomosed to apical rim of VSD. B2, Anastomosis of superior portion of VSD patch to anterior rim of mobilized aortic root. C, Right ventricular outflow tract (RVOT) is reconstructed by anchoring right lateral wall of pulmonary trunk to aortic root and overlaying a patch of pericardium to cover aortic root, right ventriculotomy, and pulmonary trunk. D, Large pericardial patch is used to reconstruct RVOT. Care must be taken to avoid RVOT obstruction. A flat patch is required to curve longitudinally (along axis of aorta) and from anterior to posterior (to reach distal pulmonary trunk). (From Yeh 2006.)
placed in the other intraventricular tunnel repairs. The pulmonary trunk is then joined to the RV outflow tract as described for the Lecompte intraventricular repair.

**Repair of Taussig-Bing Heart by Atrial Switch Procedure**

Operation is begun through the atrial incision mandated by the venous switch procedure to be used (see “Atrial Switch Operation” under Technique of Operation in Chapter 52). Working through the tricuspid valve, the VSD is repaired so that the LV ejects into the pulmonary trunk. An atrial switch procedure is done. When important LV outflow obstruction is present, an allograft valved extracardiac conduit is also placed between the LV and pulmonary trunk.

**Intraventricular Tunnel Repair of Double Outlet Right Ventricle with Doubly Committed Ventricular Septal Defect**

After CPB and cold cardioplegia are established, a transverse right ventriculotomy is made. A slightly modified tunnel repair is done, very much as described under “Intraventricular Tunnel Repair of Simple Double Outlet Right Ventricle” earlier in this chapter. However, when the two semilunar valves lie side by side and the pulmonary “anulus” is the larger, contouring the patch to achieve this may be difficult without obstructing flow into the pulmonary trunk. This problem can be minimized by enlarging the VSD anteriorly as much as possible before placing the patch.

**Intraventricular Tunnel Repair of Double Outlet Right Ventricle with Noncommitted Ventricular Septal Defect**

When the noncommitted VSD is of the inlet septal type (see Morphology in Section I of Chapter 35), it extends beneath the tricuspid septal leaflet rather than anteriorly or superiorly. It may be possible to enlarge this defect anteriorly and superiorly so that a tunnel repair can be performed that connects the LV to the aorta (Fig. 53-18). The precautions used against damaging the conduction system are those used for repair of inlet septal VSD (see Fig. 34-20 in Chapter 34). If the tunnel obstructs access to the pulmonary valve, an allograft (or other biological) valved conduit is placed from the RV to the pulmonary trunk.

**Other Operations for Double Outlet Right Ventricle with Noncommitted Ventricular Septal Defect**

In some patients with an inlet septal type of noncommitted VSD, tricuspid valve chordae may overhang the defect; in these cases, its enlargement as described is not possible, and a tunnel repair cannot be carried out. The same situation may exist when there is a large single or multiple muscular VSDs in the trabecular septum.

When pulmonary stenosis coexists, a Fontan operation is performed. The technique of total cavopulmonary connection (see discussion under Technique of Operation in Chapter 41) is particularly suited to this situation because nothing has to be done to the AV valves or within the ventricle except to enlarge the VSD if it is restrictive.

When the tunnel repair cannot be made and pulmonary stenosis is not present, the situation should be identified very early in life, and a pulmonary trunk band should be placed (see “Pulmonary Trunk Banding” under Technique of Operation in Chapter 35). Subsequently a Fontan operation should be performed.

**Repair of Double Outlet Right Ventricle with Complete Atrioventricular Septal Defect**

Technique of repair is similar to that for repair of complete AV septal defect and tetralogy of Fallot as described under Technique of Operation in Chapter 34. However, the situation becomes considerably more complex in the setting of heterotaxy syndromes, in which anomalous pulmonary venous connection is common and the VSD of the AV septal defect may be remote from the aortic valve in the presence of a muscular subaortic infundibulum (conus) (see Chapter 58).

**Repair of Double Outlet Right Ventricle with L-Malposition of the Aorta**

In nearly all surgical patients in this subset, the VSD is subaortic and pulmonary stenosis coexists. The heart is opened by a vertical incision in the RV. Usually, the VSD is easily visualized anterosuperiorly in the ventricular septum and well away from the tricuspid anulus. An intraventricular tunnel repair with a contoured patch may not be necessary, and a simple polyester or PTFE patch may be used to close the VSD in such a way that the LV ejects into the aorta. Stitches may be placed along the edge of the VSD posteriorly unless the defect abuts the tricuspid valve. An allograft valved extracardiac conduit is usually placed between the RV and pulmonary trunk, because of associated severe valvar and subvalvar pulmonary stenosis (see Figs. 38-68 and 38-70 in Chapter 38).

**Repair of Double Outlet Right Ventricle with Discordant Atrioventricular Connections**

A complete discussion of discordant AV connections is found in Chapter 55. In DORV with discordant AV connections, three major options are available:

- Traditional or physiologic repair in which the morphologic RV is retained as the systemic ventricle
- Anatomically corrective operations that leave the morphologic LV as the systemic ventricle
- Single-ventricle strategies ending in the Fontan operation

**Traditional repairs** that use the RV as the systemic ventricle include VSD closure and the Rastelli procedure, or VSD closure with baffling of LV to pulmonary trunk, with or without relief of LV outflow tract obstruction to the pulmonary trunk. **Anatomic repairs** include the “double switch” procedure (atrial switch procedure and arterial switch combined with VSD closure to direct blood from LV to neoaortic valve) and atrial switch procedure with rerouting of blood from LV through VSD to aortic valve, with or without a Rastelli procedure.
Palliative Operations

Shunting operations are described in Chapter 38 (see “Technique of Shunting Operations” under Technique of Operation in Section I) and pulmonary trunk banding in Chapter 35 (see “Pulmonary Trunk Banding” under Technique of Operation in Section I).

SPECIAL FEATURES OF POSTOPERATIVE CARE

Care after corrective or palliative operations for DORV is described in Chapter 5.

RESULTS

Survival

Early (Hospital) Death

Even intraventricular tunnel repair of simple DORV in heterogeneous patient populations has had a hospital mortality through the years of about 20%.

Currently, patients undergoing repair of simple DORV during the first 6 months of life have about a 99% chance of 1-month survival and a 95% chance of long-term survival and surgical cure.

Among patients with Taussig-Bing heart, age greater than about 6 months is a risk factor for mortality, likely related to pulmonary vascular disease. However, Feng and colleagues found similar survival among a small group of patients with transposition and VSD and those with Taussig-Bing heart who underwent an arterial switch operation and VSD closure before or after age 6 months.

Type of Double Outlet Right Ventricle

Simple DORV and DORV with doubly committed VSD and no pulmonary stenosis are particularly favorable types of DORV with regard to survival after repair and are not risk factors for death.

In the past, DORV with subpulmonary VSD was a strong risk factor for death early or late after repair, largely related to combining repair of the VSD with an atrial switch procedure. Early and long-term survival after repair of the VSD combined with an arterial switch procedure are similar to those after the arterial switch repair of transposition of the great arteries and VSD (see Chapter 52, Fig. 52-37).

In the past, survival after repair of DORV with noncommitted VSD has been less than that of any other group, but assignment of patients to this group is almost by exclusion.

This makes it the least homogeneous group morphologically; also, a number of different kinds of repairs are used. The anatomic subset is sufficiently uncommon, the categorization of patients into it sufficiently arguable, and operations for difficulty is true of DORV with noncommitted VSD, exacerbated by the variety of operations used and the uncertainty of categorization of many patients in this group. Early mortality has probably been about 50%. The Fontan operation should be expected to yield the same mortality as in patients with univentricular AV connection, which is less than 5% in appropriately selected patients (see Chapter 41).

Time-Related Survival

Long-term survival after repair of simple DORV exceeds 95% at 15 years (see Fig. 53-19).

Incremental Risk Factors for Premature Death

An analysis based on the UAB experience between 1967 and July 1984 probably still serves reasonably well for simple DORV and DORV with doubly committed VSD, but not for varieties of DORV in which the arterial switch operation is now performed.

Age at Repair

Currently, and in contrast to an era before about 1980, young age at operation is not a risk factor for death early or late after repair of simple DORV and probably of DORV with doubly committed VSD. In fact, older age at operation is now the risk factor, and it is a particularly strong risk factor in the constant hazard phase (see Fig. 53-19). These relationships, and indeed survival in general, are similar to those obtained after repair of primary isolated VSD, and they probably are explained largely by absence or presence and severity of pulmonary vascular disease. Currently, patients undergoing repair of simple DORV during the first 6 months of life have about a 99% chance of 1-month survival and a 95% chance of long-term survival and surgical cure.

Factors for Premature Death

Factors for premature death include age at operation (< 6 months), male sex, the presence of additional cardiac anomalies (other than VSD), and the presence of pulmonary stenosis (PS). Long-term survival is now best for patients with simple DORV and DORV with doubly committed VSD, but not for other varieties of DORV in which the arterial switch operation is now performed.

Given the frequency of concomitant coarctation and the possible application of preliminary pulmonary trunk banding for Taussig-Bing hearts, controversy exists regarding the advisability of initial repair of coarctation only vs. one-stage correction using the arterial switch operation. In the current era, low mortality (< 5%) has been reported both with initial repair of coarctation through a left thoracotomy followed by subsequent arterial switch and with single-stage repair via sternotomy.

Kawashima and colleagues used an interventricular rerouting repair with extensive resection of the infundibular septum in 10 of 41 patients with Taussig-Bing heart (average age 2 years), with no deaths (0%; CL 0%-17%).

Estimating overall early mortality after repair of DORV with doubly committed VSD is difficult because of the small number of reported cases, but in general it has been about the same as after repair of simple DORV. The same mortality has probably been about 50%. The Fontan operation should be expected to yield the same mortality as in patients with univentricular AV connection, which is less than 5% in appropriately selected patients (see Chapter 41).
correcting it sufficiently variable that some time may elapse before early and intermediate-term survival are known with a reasonable degree of certainty. When known, it may indicate more frequent use of the Fontan group of operations in this subset of patients.

**Major Associated Cardiac Anomalies**

*Pulmonary stenosis* coexists with DORV in many patients, and its presence often requires creating a nonvalved or valved connection to the pulmonary trunk. Related to this, the presence of pulmonary stenosis is probably an incremental risk factor for death, because both procedures increase mortality.\(^{513}\)

*Complete AV septal defects, straddling AV valves, hypoplasia of a ventricular chamber, mitral valve abnormalities, and other coexisting anomalies increase risk.*\(^{84}\) This has usually been related to persisting in an attempt to perform an optimal operation rather than accepting the need for a more appropriate and often simpler procedure such as the Fontan group of operations.

---

**Figure 53-18** Repair of double outlet right ventricle with noncommitted inlet septal ventricular septal defect (VSD). A, VSD is noncommitted, but typically is not far from being either subaortic or subpulmonary. It is enlarged anteriorly (dashed line) after visualizing the mitral apparatus, being certain not to damage the anterior free wall or anterior descending coronary artery with the enlargement. B, An intraventricular tunnel repair is made. In the case illustration, the pulmonary trunk is left on the right ventricular side, but the tunnel partially obstructs approach to it. In some patients, an appropriate tunnel cannot be made except by leaving the pulmonary trunk on the left ventricular side of the tunnel; entry into the pulmonary trunk is closed off before making the tunnel repair, or the pulmonary trunk is divided when the conduit is placed. Right ventriculopulmonary artery continuity is established with a xenograft (C) or allograft valved extracardiac conduit (D).
Relationship between age at operation and early and long-term survival after repair of simple double outlet right ventricle. Depiction is a nomogram of a specific solution of a multivariable risk factor equation. Solid lines represent continuous point estimates, and dashed lines enclose 70% confidence intervals. A, Percent survival. B, Hazard function for death. Key: VSD, Ventricular septal defect. (From Kirklin and colleagues.)

Surgical Era

Earlier date of operation has been clearly identified as a risk factor for death by several studies. This indicates that outcomes after repair of all types of DORV are currently better than at any time in the past, and this difference is quantifiable.

Type of Operation

Atrial Switch Operation Use of an atrial switch operation in conjunction with an intraventricular tunnel repair has given poor results in general, including hospital mortalities of 30% to 40%. In this setting, the atrial switch repair is at least as strong a risk factor as it is in transposition of the great arteries and VSD (see Chapter 52). For this reason, it is no longer used.

Complex Intraventricular Tunnel Repair A simple intraventricular tunnel repair, such as that performed for DORV with subaortic VSD, has no more demonstrable risk than repair of a large primary isolated VSD with a patch (see Chapter 35). This is the reason for excellent outcome after repair of simple DORV in early life.

A somewhat more complex intraventricular tunnel repair, such as that used to redirect LV outflow in the Rastelli operation (see “Rastelli Operation” under Technique of Operation in Chapter 52) but with minimal excision of septal tissue and a resultant straight and relatively short pathway leading to the aorta, has little demonstrable incremental risk. This is supported by the current low early mortality after the Rastelli operation and by the low prevalence of complications from the tunnel itself late postoperatively. When used under proper circumstances for Taussig-Bing malformation, early and intermediate-term survival has been good and comparable to that obtained with the arterial switch repair.

More complex intraventricular tunnel repairs appear to be incremental risk factors, although this idea has not been properly tested by analysis. Hospital mortality has been 10% to 15% after such procedures but may currently be less than 5%. However, late mortality may be affected by baffle obstruction and patch dehiscence with complex tunnels.

Transanular Patches and Extracardiac Conduits Use of transanular patches and extracardiac conduits has increased the risk of operations for DORV, but at times their use is inescapable. As in other situations, controversy exists as to whether absence of a valve in the RV–pulmonary trunk connection adds to risk. Whether the risk of these procedures is any different from that imposed by the type of RV–pulmonary artery connection used in the Lecompte operation (REV) remains to be determined.

Operations for Double Outlet Right Ventricle with Atroventricular Discordant Connections A variety of operations have been successfully applied to this subset of DORV. No single strategy has proved superior in terms of long-term survival and freedom from reoperation. Shin’oka and colleagues found no significant difference in late survival 15 to 20 years after operation according to procedure performed, whether traditional repair, anatomic repair, or Fontan procedure was employed.

Complications of Intraventricular Tunnel Repair

Need for reoperation for complications of the tunnel repair (leakage or obstruction primarily) is directly related to complexity of the tunnel. Thus, in simple intraventricular tunnel repair for DORV and subaortic VSD, only 1% of patients have had catheterization evidence of tunnel leakage or obstruction, or reoperation for it. By contrast, 18% or more of patients with complex intraventricular tunnel repairs have required reoperation for important obstruction or leakage, or have had evidence of these problems (P = .005). An analysis by Fujii and colleagues indicated that length of the intraventricular tunnel is predictive of mortality. Among patients in whom the length between the top of the interventricular septum and aortic valve was less than 80% of normal LV end-diameter, event-free survival at 7 years was 89%, vs. 26% when it was greater than 80%. Late tunnel obstruction of complex intraventricular tunnel repairs may be more likely to develop when performed in young infants.

The likelihood of reoperation for LV outflow tract (LVOT) obstruction also relates to presence of potentially obstructing infundibular muscle in the new LVOT under the patch. Dearani and colleagues have emphasized the importance of VSD enlargement and infundibular septal resection when performing the Rastelli operation. Similarly, Rubay and colleagues emphasized the importance of conal resection in the REV procedure. Yeh and colleagues have reported the advantages of the Nikaidoh procedure in preventing late LVOT obstruction. In the setting of Taussig-Bing heart with valvar or subvalvar pulmonary stenosis of sufficient severity to
Complications after Taussig-Bing Repair

Complications of complex intraventricular tunnel repair have been detailed in the preceding discussion. Reoperations following the arterial switch operation have also been common, most notably RV outflow tract (RVOT) obstruction, both supravalvar—likely related to insufficient mobilization of the pulmonary arteries in preparation for the Lecompte maneuver, pericardial patch shrinkage, or inadequate patch size (see Chapter 52)—and subvalvar. Alsoufi and colleagues reported a 10-year freedom from RVOT obstruction of 55%.\(^1\) They indicate that alterations in constructing the patch for pulmonary trunk reconstruction have reduced supravalvar obstruction. More complete resection of the subaortic RV outlet has reduced occurrence of RVOT obstruction requiring reoperation.\(^2,3,4\) Further studies are needed to clarify the importance of these problems with current techniques.

INDICATIONS FOR OPERATION

Much of the previous information on outcomes after surgical repair of DORV is not applicable to patient care decisions in the current era, except that it permits developing equations that take into account the change in outcomes related to more recent dates of operation. Greater safety of intracardiac operations done early in life and good results of the arterial switch operation are two important factors in the improvement of current results. Improvements in myocardial management, support techniques, and intensive care unit management of neonates and infants undoubtedly play a role as well.

Recommendations for specific operations can only be general, and some cases may require special consideration. Representative strategies based on location of the VSD are presented in Table 53-7.

Simple Double Outlet Right Ventricle with Subaortic Ventricular Septal Defect

Simple DORV can be diagnosed very early in life, often by echocardiography alone. Repair should be electively planned by age 3 to 6 months, or sooner if signs of heart failure or failure to thrive persist. The operation should be intraventricular tunnel repair performed via a right atrial or, more frequently, RV approach.

When important pulmonary stenosis coexists, indications for operation and the operation are the same as for tetralogy of Fallot (see Indications for Operation in Section I of Chapter 38). Essentially, repair is advisable whenever important symptoms develop or electively, according to the same principles that apply to tetralogy of Fallot.

Double Outlet Right Ventricle with Subpulmonary Ventricular Septal Defect (Taussig-Bing Heart)

Taussig-Bing heart should be repaired by closure of the VSD so that the LV ejects into the pulmonary trunk (neoaorta), combined with an arterial switch repair. Operation should be performed during the first month of life or as soon as possible thereafter. Some surgeons continue to prefer the Kawashima procedure when the great arteries are side by side.\(^2,3,4\) but many currently apply the arterial switch operation irrespective of great artery position.\(^2,3,4\)

There is possibly no longer an indication for one of the intraventricular repairs for this anomaly unless there is coexisting subpulmonary obstruction of such a type and severity as to contraindicate arterial switch repair. Under these circumstances, an intraventricular tunnel repair (Kawashima) is indicated, supplemented by RV–pulmonary trunk valved conduit or a reconstruction of the type described under “Lecompte Intraventricular Repair.” Nikaidoh aortic translocation and RV outflow reconstruction can also be considered in this setting. The atrial switch type of operation no longer has a place in managing this group of patients.

Operations other than those including the arterial switch repair but including an extracardiac conduit should ideally be deferred until about 3 to 6 years of age. However, if more than a single systemic-pulmonary shunt appears to be necessary in the interim, it is preferable to proceed prematurely with complete repair (see Indications for Operation in Section II of Chapter 38).

Double Outlet Right Ventricle with Doubly Committed Ventricular Septal Defect

Generally this malformation is uncomplicated by coexisting cardiac anomalies, and the rationale and timing of repair are the same as for simple DORV.

Double Outlet Right Ventricle with Noncommitted Ventricular Septal Defect

Placing a patient in the subset of DORV with noncommitted VSD is often controversial, complicating the discussion of indications. When the malformation truly seems to be of this type, repair should consist of appropriately enlarging the VSD if possible so that an intraventricular tunnel can be created to direct LV blood to the aorta. When the pulmonary trunk is obstructed by the tunnel, a RV–pulmonary trunk valved extracardiac conduit or the Lecompte procedure is added. Hu and colleagues have reported using the translocation technique for this anomaly, with a double root translocation procedure.\(^5\) When the anatomy dictates that the tunnel be directed to the pulmonary trunk, and if pulmonary stenosis

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Table 53-7  Type of Operation for Double Outlet Right Ventricle by Ventricular Septal Defect Relation

<table>
<thead>
<tr>
<th>Relationship of VSD</th>
<th>IVR</th>
<th>ASW</th>
<th>Senning</th>
<th>Fontan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subaortic</td>
<td>80</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Subpulmonary</td>
<td>2</td>
<td>27</td>
<td>10(^\text{a})</td>
<td>6</td>
</tr>
<tr>
<td>Noncommitted</td>
<td>14</td>
<td>4</td>
<td>0</td>
<td>11</td>
</tr>
<tr>
<td>AV septal defect</td>
<td>6</td>
<td>0</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Doubly committed</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>107</td>
<td>35</td>
<td>6</td>
<td>31</td>
</tr>
</tbody>
</table>

From Kleinert and colleagues.\(^1\)\(^2\)

\(^{a}\)Four of these patients later converted to arterial switch.

Key: ASW, Arterial switch operation; AV, atrioventricular; IVR, intraventricular tunnel repair; VSD, ventricular septal defect.
is not present, the tunnel is made and an arterial switch operation added. Alternatively, pulmonary trunk banding early in life and a subsequent Fontan operation may be considered.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Single-Ventilcle Strategy versus Biventricular Repair for Complex Double Outlet Right Ventricle**

There is controversy regarding the optimal treatment strategy for certain forms of complex DORV related to the most reliable approach to achieve long-term survival, maintain good functional outcome, and minimize reoperation. Evidence-based recommendations are confounded by the large variety of anatomic variants within specific morphologic subsets (and potential importance of such variants for the conduct of and outcome after specific operations), the small number of specific operations for these anatomic variants at any given institution, the duration of follow-up needed to fully evaluate newer surgical procedures, and “philosophical” differences among institutions regarding single versus biventricular approaches. The controversial aspects relate primarily to two areas: hypoplasia of mitral valve or LV and nonsubaortic VSDs that are not reparable with the arterial switch operation and simple baffling of the LV to the neoaoaric valve. Bradley and colleagues have drawn attention to this controversy with an elegant analysis of nearly 400 patients in which they conclude that extending biventricular repair in “borderline anatomic candidates” may be of questionable long-term benefit compared with the Fontan pathway. Similar observations have been made by others. In favor of the Fontan approach is its current low operative risk, low risk of reoperation, and excellent functional outcomes in most patients. This may be especially relevant given the improved results with the Fontan approach in the presence of two functioning ventricles. The major limitations of the Fontan operation relate to the increasing hazard of ventricular dysfunction and heart failure after 15 to 18 years. Whether this risk will be decreased or neutralized by more current energy-efficient methods of Fontan construction remains to be determined. It is also important to consider the reality that certain components of these “borderline anatomic variants” (eg, modest elevation of pulmonary vascular resistance, ventricular hypertrophy, AV valve regurgitation) may represent risk factors for the Fontan operation.

The increasing late risk for reoperation and mortality after Rastelli-type operations for DORV have been well documented. Late morbidity and mortality relate not only to RVOT and extracardiac conduit obstruction but also to progressive LVOT obstruction in the setting of complex intraventricular baffles (see preceding text under Results). However, encouraging early and midterm results are emerging from newer procedures such as the REV procedure, and single and double root translocation operations (see also previous discussions under Technique of Operation and Results), as well as modifications of baffling techniques that provide some optimism for improved late survival and freedom from reoperation. For example, Devaney and colleagues reported biventricular repairs in 12 patients with AV septal defect with an interventricular communication remote from the aortic valve in the presence of a muscular subaortic infundibulum. There were 11 early and 10 late survivors. Infundibular resection and a complex extended intraventricular baffle contributed to absence of late LV outflow obstruction.

Until appropriate short- and longer-term outcome analyses are available, coupled with experiential insights, selection of one- or two-ventricle strategies for many of these complex variants will remain a function of institutional bias and surgeon preference.

**REFERENCES**


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Chapter 53 Double Outlet Right Ventricle


## Definition 1962

### Historical Note 1962

### Morphology and Morphogenesis 1962

ATRIAL SITUS SOLITUS AND VENTRICULAR RIGHT-HANDEDNESS (D-LOOP) (ATRIOVENTRICULAR CONCORDANT CONNECTION) 1963  
Ventricular Septal Defect 1963  
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ATRIAL SITUS INVERSUS AND VENTRICULAR LEFT-HANDEDNESS (L-LOOP) (ATRIOVENTRICULAR CONCORDANT CONNECTION) 1964

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### MAGNETIC RESONANCE AND COMPUTED TOMOGRAPHY IMAGING 1965

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### REPAIR OF DOUBLE OUTLET LEFT VENTRICLE AND ATRIOVENTRICULAR CONCORDANT CONNECTION 1966

### WITH PULMONARY STENOSIS 1968

### DOUBLE OUTLET LEFT VENTRICLE WITH ATRIOVENTRICULAR CONCORDANT CONNECTION AND IMPORTANT HYPOPLASIA OF RIGHT VENTRICLE AND TRICUSPID VALVE 1969

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### Double Outlet Left Ventricle

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**DEFINITION**

Double outlet left ventricle (DOLV) is a cardiac anomaly in which both great arteries arise from the left ventricle (LV). The great arteries are assigned to one or the other ventricle by the rules described under Definition in Chapter 53. DOLV may occur with atrioventricular (AV) concordant or discordant connection, as does double outlet right ventricle (DORV; see Chapter 53). DOLV with AV discordant connection is discussed in Chapter 55. DOLV, like DORV, may also occur in patients with univentricular AV connections (see Chapter 56) and in those with atrial isomerism (see Chapter 58).

**HISTORICAL NOTE**

Marechal is credited with describing the first case of DOLV in 1819, but this was in a heart with double inlet LV with an infundibular outlet chamber. The first reported case in a heart with two ventricles and without pulmonary stenosis was that of Sakakibara and colleagues in 1967, for which they performed a successful intraventricular repair. Marechal is therefore another congenital cardiac anomaly that remained, for all practical purposes, undescribed until the advent of intracardiac surgery. It is also of interest that the first case reported by Potts and colleagues as tetralogy of Fallot and receiving a side-to-side aortopulmonary artery anastomosis underwent subsequent repair for well-documented DOLV with pulmonary stenosis (John Kirklin: personal communication; 1983). A unique case of DOLV with an intact ventricular septum was reported by Paul and colleagues in 1970, establishing with certainty the existence of the entity. Subsequent reports expanded the surgical possibilities by reporting reconstruction of the pulmonary pathway in cases in which a completely intraventricular repair was not possible, usually by a valved extracardiac conduit from the right ventricle to pulmonary trunk. Anderson and colleagues reported the sixth case of DOLV in 1974. Sharratt and colleagues in 1976 reported use of a Fontan-type procedure in hearts with DOLV and severe right ventricular hypoplasia. Five cases were added to the literature in 1976. Additional cases have been reported by Urban and colleagues and Stegmann and colleagues.

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**MORPHOLOGY AND MORPHOGENESIS**

As with DORV, there is great variability among hearts with DOLV and AV concordant connection. Because of its rarity, generalizations are even more difficult than for DORV.

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1. The adjectives left and right used to modify atrium or ventricle mean morphologically left and morphologically right. Position of the chamber is referred to as right-sided or left-sided.
Diagnosis can be ambiguous, because some override of one of the great arteries is commonly present. Defining a DOLV based on 50% or more of great arterial override may result in a substantially higher number of cases being reported. Many patients with complete transposition of the great arteries with subaortic ventricular septal defect (VSD), pulmonary stenosis, and a variable degree of aortic override have been misclassified as having DOLV. An exclusive or near-exclusive origin of both great arteries from the left ventricle (<20% override) will identify the classic form of DOLV and prevent misdiagnosis. Although it was initially thought bilateral absent conus was a prerequisite for the diagnosis of DOLV, all possible conal configurations have been described: subpulmonary, subaortic, bilaterally present, and bilaterally absent. When present, the length of conus under either great artery is typically relatively short and is an important factor in causing the great artery to embryologically align with the left ventricle.

A segmental approach is necessary for complete understanding of this malformation (see “Terminology and Classification of Heart Disease” in Chapter 1). DOLV occurs in each of the four basic hearts (Fig. 54-1) but is most common in hearts with atrial situs solitus and ventricular right-handedness or D-loop (S,D,D). Morphologic characteristics of the VSD and its relationship to the great arteries at the level of the semilunar valves are similar to those in DORV and described by terms defined in “Ventricular Septal Defect” under Morphology in Chapter 53. Subaortic VSD is the most common, followed by subpulmonic, and then by doubly committed. VSD remote from the great arteries is rare (Table 54-1). Absence of a VSD (intact ventricular septum) is also rare but has been described.

Atrial Situs Solitus and Ventricular Right-Handedness (D-Loop) (Atrioventricular Concordant Connection)

In this subset, the aorta is usually in D-malposition (S,D,D), but examples occur with it in L-malposition (S,D,L) (see “Symbolic Convention of Van Praagh” in Chapter 1). In the former, the great arteries may appear in relatively normal position (aorta to the right and somewhat posterior to pulmonary trunk), side to side, or with aorta somewhat anterior to the pulmonary trunk.

**Table 54-1 Double Outlet Left Ventricle with Situs Solitus and Atrioventricular Concordance in 71 Patients**

<table>
<thead>
<tr>
<th>Type</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subaortic VSD:</td>
<td>73</td>
</tr>
<tr>
<td>Right anterior aorta with pulmonary stenosis</td>
<td>49</td>
</tr>
<tr>
<td>Left anterior aorta with pulmonary stenosis</td>
<td>24</td>
</tr>
<tr>
<td>Subpulmonary VSD with right anterior aorta</td>
<td>15</td>
</tr>
<tr>
<td>Doubly committed VSD with right anterior aorta</td>
<td>10</td>
</tr>
<tr>
<td>Remote VSD with left anterior aorta</td>
<td>1</td>
</tr>
</tbody>
</table>

Data from Menon and Hagler. Key: VSD, Ventricular septal defect.

**Ventricular Septal Defect**

The ventricular septum is rarely intact. Usually, a large VSD is present and lies between the limbs of the trabecula septomarginalis (septal band).

Most commonly, the VSD is *subaortic* in position (Fig. 54-2; see Table 54-1). It may extend back to the tricuspid anulus, or it may be separated from the anulus by a muscular bridge. When the aorta overrides the VSD and arises in part from the right ventricle, the VSD is *juxtaaortic*, and this entity begins to merge with transposition of the great arteries.

When the VSD is subpulmonary, it is usually more anterior and well separated from the tricuspid valve by a rather wide band of muscle. In some cases, the pulmonary trunk origin overrides the VSD and lies in part over the right ventricle. Malalignment of conal septum may be present and can cause aortic outflow obstruction and be associated with aortic arch hypoplasia.

Occasionally the VSD is juxtaarterial and lies immediately below both great arteries (*doubly committed*; see Chapter 53, Fig. 53-6). The VSD is typically very large, and there is absence or near absence of conus bilaterally, resulting in aortic-mitrall and pulmonary-mitrall fibrous continuity and side-by-side great arteries. It is frequently difficult to decide whether DOLV or DORV is present, in which case the term *double outlet both ventricles* is appropriate.

**Conal Pattern**

Most often there is absence of a subaortic conus and presence of aortic-mitrall fibrous continuity and a subpulmonary conus displaced into the LV (Fig. 54-3). Rarely, bilaterally absent conus permits aortic-mitrall-tricuspid and pulmonary-tricuspid fibrous continuity (see Fig. 54-2). In this event, both semilunar valves arise at the same level. Very rarely, only a subaortic conus is present. There may be a conus bilaterally.

**Pulmonary Stenosis**

Pulmonary stenosis is present in most cases and is either valvar (sometimes with anular stenosis) or subvalvar when it is due to a restrictive subpulmonary conus with secondary fibrosis of the ostium. When the VSD is subaortic and there is infundibular pulmonary stenosis, the great arteries are usually relatively normally interrelated.

**Right Ventricular and Tricuspid Valve Hypoplasia**

There is a tendency for the right ventricular sinus and tricuspid valve to be at least somewhat hypoplastic. The
PART VII  Congenital Heart Disease

Figure 54-2  Specimen of double outlet left ventricle and atrioventricular concordant connection. A, Viewed from opened left ventricle (LV) and aorta (Ao). Aortic valve (AoV) is bicuspid but otherwise normal. Ventricular septal defect (VSD) is subaortic, with its upper margin separated from AoV by 4 mm. Tricuspid valve (TV) is visible through VSD (Ebstein anomaly of tricuspid valve is present). B, Close-up of LV outflow tract before aorta was opened. Pulmonary valve (PV) is not stenotic, and AoV and PV are in continuity, separated only by a thin fibrous ridge called the truncal septum (TS). There is both PV and aortic–mitral valve (MV) fibrous continuity (i.e., conus is absent bilaterally). (From Brandt and colleagues.13)

extreme example is coexistence of tricuspid atresia, with the two reported cases having ventricular right-handedness (S,D,D).22,23 Rarely, the tricuspid valve may show an Ebstein anomaly.23

Left Ventricle
The LV is usually well formed. One case of mitral atresia with large LV and infundibular outlet chamber (S,D,D segmental arrangement) has been reported.22

Conduction System
Position of AV node and bundle of His is normal. Thus, the bundle penetrates from a normally positioned posterior AV node through the right trigone in the region of the commissure between tricuspid septal and anterior leaflets and at the base of the noncoronary aortic cusp, and its two branches distribute in normal fashion. Whether it is at risk during repair depends on the relationship of the lower VSD margin to the tricuspid anulus (see “Location in Septum and Relationship to Conduction System” under Morphology in Section 1 of Chapter 35).

Atrial Situs Inversus and Ventricular Left-Handedness (L-Loop) (Atrioventricular Concordant Connection)
Both I,L,L and I,L,D arrangements have been reported (i.e., aorta to the left or right), although both are rare. Usually the VSD is subaortic, and pulmonary stenosis coexists.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Pathophysiology
In hearts with DOLV and AV concordant connection, the LV is a common mixing chamber, receiving pulmonary venous blood through the mitral valve and caval blood through the right ventricle and VSD. Clinical presentation, however, is dominated by varying degrees of cyanosis due to a combination of the frequent occurrence of pulmonary stenosis and streaming caused by the variable malposition of the great arteries and their relationship to the VSD. Thus, streaming of desaturated right ventricular blood into the aorta may occur when the VSD is subaortic, leading to unexpectedly severe cyanosis. In the absence of pulmonary stenosis, heart failure often develops early in life because of large pulmonary blood flow.

In hearts with DOLV and AV discordant connection, the LV receives caval blood through the mitral valve, and pulmonary venous blood through the right ventricle and VSD. The tendency to develop severe cyanosis is more likely than in AV concordant connection.

Examination
Physical findings, chest radiograph, and electrocardiogram are not diagnostic, but reflect cardiopulmonary physiology in each case.

Echocardiography
Echocardiography with color flow imaging may be diagnostic, and associated morphologic lesions are readily detected.22,23 The main challenge is to distinguish DOLV from other, more common conotruncal anomalies such as transposition of the great arteries and DORV (Fig. 54-4). The focus is on defining the VSD and the relationship of the VSD to the two great arteries, presence or absence of conus under each great artery, presence or absence of pulmonary stenosis, and positioning of the two great arteries in relation to each other. Coronary artery pattern is also important because some surgical repair techniques used for DOLV require specific knowledge of coronary artery course. Other imaging studies are not usually performed unless clinical presentation indicates that specific and quantitative knowledge of physiologic of the pulmonary vasculature is important in formulating the management plan. Even with increased recognition of DOLV by echocardiography, diagnosis may be elusive. In a recent experience with six patients with both echocardiography and cardiac catheterization available, diagnosis was made preoperatively in four patients and intraoperatively in two.23
Cardiac Catheterization and Cineangiography

Biplane cineangiography, selecting injection sites and projections suited to the individual problem, is diagnostic but provides little additional morphologic information beyond that obtained by echocardiography. Because DOLV is rare, cineangiography was once performed to support a diagnosis made by echocardiography, but this role has now been overtaken by magnetic resonance imaging (MRI). Cardiac catheterization, however, remains the only way to obtain specific hemodynamic and oxymetric data if it is necessary to define the physiology of the pulmonary vasculature.

When catheterization is performed, both left and right ventricular injections are desirable. With appropriate projections, angiography can confirm the diagnosis of DOLV and rule out other conotruncal anomalies, but it is rarely necessary in current practice. Angiography can also define the position and number of VSDs, presence and site of pulmonary and aortic stenosis, and size of the right ventricle and tricuspid valve relative to the LV and mitral valve (see Fig. 54-3).

Magnetic Resonance and Computed Tomography Imaging

Computed tomography provides no specific advantages over MRI in diagnosing DOLV and thus is not routinely used. MRI may be used to supplement the intracardiac
entities the degree of hypoxia and clinical course are directly related to severity of pulmonary stenosis.

**TECHNIQUE OF OPERATION**

**Identification of Morphology**

There are no clues to the specific diagnosis of DOLV from external examination of the heart when it is exposed at operation. Generally, only AV connection—concordant or discordant—can be confirmed by external observation. For this reason, detailed and complete preoperative imaging must be performed to identify all aspects of the anomaly. Even when this has been done, relation of the great arteries to VSD, and VSD to AV valves, may be different from that anticipated from preoperative imaging. Thus, when the heart is opened, accurate evaluation must be made of all aspects of morphology.

When the AV connection is **concordant**, finding a large VSD located far downstream (distally) and anterosuperiorly in the ventricular septum mandates thorough consideration of all diagnostic possibilities associated with a VSD in this position, including not only DOLV but also ordinary subpulmonary VSD with ventriculocardiac discordant connection, tetralogy of Fallot with subpulmonary VSD (if pulmonary stenosis coexists), anterosuperior VSD with complete transposition of the great arteries, DORV with doubly committed VSD, and Taussig-Bing-type DORV (which has its VSD in this same position, but an aorta far removed from the VSD and clearly originating from the right ventricle alone).

When the AV connection is **discordant**, the same detailed observations must be made. These generally reveal findings similar to those of congenitally corrected transposition of the great arteries (see Chapter 55), but in DOLV, the aorta as well as the pulmonary trunk arise entirely or in large part from the right-sided (in atrial situs solitus) LV.

**Repair of Double Outlet Left Ventricle and Atrioventricular Concordant Connection**

Preparations for operation, sternotomy, and placement of purse-string sutures are those generally used (see “Preparation for Cardiopulmonary Bypass” in Section 3 of Chapter 2). Cardiopulmonary bypass (CPB) is established, perfusate temperature lowered to 25°C, the aorta clamped, and usual techniques of myocardial management instituted (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). The usual oblique right atriotomy is made (see Chapter 30, Fig. 30-14, A), and the interior of the right ventricle is inspected through the tricuspid valve. It can usually be confirmed from the right atrium that neither great artery arises wholly or in large part from the right ventricle, and that the VSD is in the outlet portion of the ventricular septum.

Usually, repair is made through a vertical incision in the distal portion of the right ventricle. After placing stay sutures, position of VSD, origin of aorta and pulmonary trunk from LV and their relationships to the VSD, and the nature of any pulmonary stenosis are verified.

**With Pulmonary Stenosis**

When pulmonary stenosis is present in a DOLV, it is usually not possible to relieve it directly and do a completely

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**NATURAL HISTORY**

Natural history of patients with DOLV without pulmonary stenosis appears to be similar to that of patients with isolated large VSD (see Natural History in Section 1 of Chapter 35), except that progressive VSD narrowing and closure has not been documented in DOLV. Cyanosis may be present because of the common mixing chamber beneath the great arteries, but considerable streaming of flow is often present and accounts for significant variability in arterial oxygen levels.

Natural history of patients with DOLV and pulmonary stenosis is similar to that of patients with tetralogy of Fallot (see Natural History in Section 1 of Chapter 38), and in both morphologic information obtained by echocardiography (Fig. 54-5).
patch, because the left anterior descending coronary artery is immediately in front of the pulmonary anulus, and a valved extracardiac conduit or a variant of the Lecompte operation (réparation à l’étage ventriculaire [REV]) is necessary. In the former, the pulmonary trunk is transected at the sinutubular junction, and the proximal pulmonary trunk stump is oversewn by placing two rows of continuous polypropylene sutures at the level of the valve. Then the VSD is closed by suturing into place a patch, taking the usual precautions to avoid damaging the bundle of His (Fig. 54-6, A). An intraventricular repair, as is described for patients with no coexisting pulmonary stenosis. However, if examination of the pulmonary valve through a vertical anterior incision in the pulmonary trunk or through the ventricle shows it to be widely patent and the subvalvar fibromuscular obstructing ring localized, the ring may be excised satisfactorily, permitting a completely intraventricular repair.

Usually the pulmonary anulus is small and the subvalvar stenosis too long and narrow for a simple intraventricular repair to be effective. It is not possible to place a transanular patch.
allograft-valved extracardiac conduit is prepared (see Figs. 38-77 and 38-78 in Chapter 38) and sutured distally to the pulmonary trunk and proximally to the right ventriculotomy (Fig. 54-6, B). Returning to the right atrium, the foramen ovale is closed, and the remainder of the operation is completed in the usual manner.

Alternatively, a Lecompte operation (REV) can be performed (see “Lecompte Intraventricular Repair” under Technique of Operation in Chapter 53). This has the great advantage of not requiring an extracardiac conduit. Transfer of the pulmonary trunk to the right ventricle can be accomplished without the need to transect and reconstruct the aorta.\(^{3,1,31}\)

Patch augmentation of the right ventricular outflow tract may be possible in selected cases of DOLV with pulmonary stenosis. For this to be possible, the pulmonary trunk must be either anterior or side by side relative to the aorta, and the coronary arteries must course behind the pulmonary root\(^{13}\) (Fig. 54-7).

**Without Pulmonary Stenosis**

When pulmonary stenosis is not present, the morphologic arrangements may allow intraventricular tunnel repair. A contoured patch is placed into the VSD so that the right ventricle ejects into the pulmonary trunk while the LV continues to ejet into the aorta. The VSD may have to be enlarged anteriorly and superiorly before this is done. When an intraventricular tunnel repair is not possible, the pulmonary orifice is closed off from within the ventricle or from within the pulmonary trunk, or the pulmonary trunk is divided; the VSD is closed, leaving the aorta coming off the LV; and an allograft-valved extracardiac conduit is placed between the right ventricle and pulmonary trunk. Alternatively, the pulmonary trunk can be connected to the right ventricle by the Lecompte operation (REV). If the pulmonary valve is relatively normal in size (with or without subpulmonic stenosis), the pulmonary root, including the valve, can be translocated to the right ventricle in the same fashion. This has been described in patients with DOLV who have a subpulmonic conus.\(^{1,3,31}\) Additionally, the intact pulmonary valve and root can be translocated to the right ventricle even when a subpulmonic conus is absent, as described by Hanley and colleagues\(^{33}\) (Fig. 54-8). Pulmonary root translocation in the presence of severe pulmonary stenosis, using a monocusp valve and patch augmentation of the small pulmonary anulus, has also been described.\(^{11}\)

Rarely, in the absence of pulmonary stenosis, are these types of repair not possible. It may then be possible to close the VSD with a contoured patch so the right ventricle ejects into the aorta and the LV into the pulmonary trunk, and to

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**Figure 54-7**  Patch augmentation of right ventricular (RV) outflow tract in double outlet left ventricle with pulmonary stenosis. **A**, Great arteries are side by side, with aorta (Ao) to right of pulmonary trunk (PT). Right coronary artery arises anteriorly from aorta, and left anterior descending coronary artery (LAD) is shown, with left main coronary artery arising posteriorly and passing behind PT. Right ventriculotomy is performed overlying subaortic ventricular septal defect (VSD). Pulmonary arteriotomy is also performed to expose stenotic pulmonary valve orifice (PO). **B**, Bridge of muscle between right ventriculotomy and pulmonary arteriotomy has been incised to create continuity between these two openings. VSD has been closed with a Dacron patch (DP). Various options for RV outflow reconstruction can be used, but stenotic native pulmonary valve opening is always closed from within pulmonary artery. In this illustration, a monocusp valve is used. Triangular-shaped patch is sutured to edges of ventriculotomy, serving as a monocusp valve. Woven Dacron vascular graft patch (VG) is placed to construct a roof for RV outflow tract. Alternatively (not shown), vascular graft roof can be used without monocusp prosthesis, or a full prosthetic valve can be positioned within RV outflow tract underneath the roof. Key: AV, aortic valve; MP, monocusp patch. (Redrawn from Sohn and colleagues.\(^{31}\))
**Figure 54-8** Repair of double outlet left ventricle (DOLV) without pulmonary stenosis: pulmonary root translocation. A, Pulmonary root (including intact pulmonary valve) (PT), positioned to left and slightly posterior to aorta (Ao), being excised. Care is taken to separate pulmonary valve from any attachments to central fibrous body or mitral valve anulus. Through a right ventriculotomy and ventricular septal defect (VSD), aortic (AV) and mitral (MV) valves can be visualized in LV. B, Two separate polytetrafluoroethylene patches (PP) have been used to close VSD and defect in LV created from excision of pulmonary root. If pulmonary-mitral fibrous continuity is present, patch on LV will be partially sewn to anterior mitral leaflet hinge point. Posterior rim of mobilized pulmonary root (PT) is sutured to superior aspect of right ventriculotomy. C, Procedure is completed by creating a hood (PH) across anterior aspect of anastomosis. (Redrawn from Menon and Hagler.546)

**Complete the operation by performing an arterial switch procedure** (see “Arterial Switch Operation” under Technique of Operation in Chapter 52).

**Double Outlet Left Ventricle with Atroventricular Concordant Connection and Important Hypoplasia of Right Ventricle and Tricuspid Valve**

An important degree of hypoplasia of the right ventricle and tricuspid valve (see later text on Indications for Operation) makes the types of repair described in the preceding text inadvisable. A Fontan operation may be performed (see Technique of Operation and Indications for Operation in Chapter 41), or one combining an intracardiac septation with a bidirectional cavopulmonary anastomosis (“one-and-a-half” ventricle repair; see Chapter 40).

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Postoperative care follows the usual protocols (see Chapter 5).

**RESULTS**

Survival

**Early (Hospital) Death**

In the current era, hospital mortality is expected to be about 5%, based on recent reports of patients doing well after surgical correction.51,104 Total number of surgically managed cases reported, however, is only several dozen. The experience of McElhinney and colleagues has been updated to include six patients undergoing intracardiac repair, with no early or midterm deaths (FL Hanley: personal communication; 2002).513

**Time-Related Survival**

The number of cases is so small, and variability of the anomaly and repairs so great, little useful information is available about time-related survival and risk factors for death. However, these are probably similar to those for DORV (see Fig. 53-19 in Chapter 53) and transposition, VSD, and LV outflow obstruction (see Figs. 52-53 and Figs. 52-54 in Chapter 52).

**Other Outcome Events**

The small number of patients and variability in the morphology and surgical procedures mitigate against obtaining sufficient information in this area to draw reasonable inferences.

When an allograft-valved extracardiac conduit is used, reoperation will probably be necessary at some time (see “Reoperation” under Results in Section II of Chapter 38).

**INDICATIONS FOR OPERATION**

Diagnosis of DOLV is an indication for operation. When pulmonary stenosis coexists, Lecompte intraventricular repair (REV; see Chapter 53) may be considered optimal, and in this case, young age is not a contraindication. Conduit repair may be performed in infancy, accepting the need for early reoperation and conduit replacement. Classic shunting operations (see Chapter 38) remain an alternative. Arguments for and against this approach are similar to those outlined for tetralogy of Fallot (see Chapter 38).

In the absence of pulmonary stenosis, corrective operation should usually be performed in the first 6 months of life if preoperative imaging studies support the likely success of a completely intraventricular repair. Alternatively, but less desirably, pulmonary trunk banding may be performed if the patient has heart failure or if pulmonary vascular resistance is
ranging, and repair delayed until later in life. Ideal timing of the subsequent repair may be influenced by morphology. If preoperative imaging studies suggest that a completely intraventricular repair will be straightforward, repair can be pursued at age 1 to 2 years. If morphology is more challenging for a completely intraventricular repair, some believe it may be of benefit to delay repair beyond age 2 years to maximize the likelihood of success. The logic underlying this approach is not proven, but the argument is that a complex intracardiac baffle is more likely to remain unobstructed over time if operation is performed in a more fully grown patient.

When there is right ventricular and tricuspid valvar hypoplasia, with z value for diameter of the tricuspid valve less than −2, a Fontan operation (see Chapter 41) or, alternatively, the “one-and-a-half” ventricle repair (see Chapter 40) should be considered. Usual indications, timing, and techniques of the Fontan operation are used (see Chapter 41).

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Section I  Congenitally Corrected Transposition of the Great Arteries

DEFINITION

Congenitally corrected transposition of the great arteries is a congenital cardiac anomaly with ventriculoarterial discordant connection (transposition of the great arteries) and atrioventricular (AV) discordant connection, the right atrium connecting to left ventricle and left atrium connecting to right ventricle. Circulatory pathways are therefore in series. The condition occurs in atrial situs solitus and atrial situs inversus. Ventricles may lie in any position.

HISTORICAL NOTE

Rokitansky probably was first to describe a case of congenitally corrected transposition of the great arteries (CCTGA) in 1875. After that, pathologists recognized the condition easily but considered it rare. With advent of cardiac surgery, interest and knowledge expanded rapidly, and papers by Anderson and colleagues from the University of Minnesota in 1957 and by Schiebler and colleagues from the Mayo Clinic in 1961 established the clinical syndromes associated with it.

Monckenberg (1913) and later Uher (1936) described the anterior position of the AV node, its usual location in CCTGA. In 1931, Walmsley recognized fundamental differences in cardiac structure in such hearts, including a different coronary arterial pattern and altered morphology in the central fibrous body and conduction system. In 1963, Lev and colleagues again described the anomalous position of the AV node and His bundle. Clinicians, however, remained unaware of these observations until Anderson and colleagues confirmed the unusual position of the AV node and extended knowledge of the pathway of the bundle of His.

First repairs of a cardiac malformation associated with CCTGA were reported in 1957 by Anderson, Lillehei, and Lester from the University of Minnesota. This repair and others reported from the Mayo Clinic resulted in the morphologic right ventricle serving the systemic circulation. In 1990, Ilbawi and colleagues introduced the double switch concept in which the morphologic left ventricle serves the systemic circulation.

MORPHOLOGY

In atrial situs solitus, the most common arrangement of CCTGA is ventricular L-loop and L-malposition of the aorta (S,L,L; see “Symbolic Convention of Van Praagh” under Terminology and Classification of Heart Disease in Chapter 1) (Fig. 55-1). The left ventricle (LV) usually lies to the right side and right ventricle (RV) to the left side. The mitral valve then lies to the right side and tricuspid valve to the left side. The LV is usually slightly posterior and inferior to the RV.

Fig. 55-1  Diagrammatic models of the four basic hearts (see Appendix 1H in Chapter 1) as they occur in transposition of the great arteries (ventriculoarterial discordant connection), with most common great arterial positions indicated. Degree of elevation of great arteries above their respective ventricles corresponds to usual type of conal development. Models 1 and 4 are complete transposition of the great arteries, and models 2 and 3 are congenitally corrected transposition of the great arteries. Key: LA, Left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.
along its long axis occurs, resulting in atypical topology (criss-cross heart). For example, in atrial situs solitus, there may be a discordant AV connection, but the ventricles are D-loop; similarly, discordant AV connection in atrial situs inversus will have L-loop ventricles.\textsuperscript{12}

Ventricles

Usually there is fibrous continuity in the right-sided LV between the right-sided mitral and pulmonary valves and a well-developed left-sided RV infundibulum separating left-sided tricuspid and aortic valves. However, rare cases have been described with bilateral conus or bilaterally deficient conus.\textsuperscript{3}

The LV outflow tract beneath the pulmonary valve lies between the septal (pulmonary) leaflet of the mitral valve on the right and muscular ventricular septum on the left (Fig. 55-2). In its anterior part, there is often a prominent recess.\textsuperscript{13} Ventricular outflow tracts do not cross, and ascending aorta and pulmonary trunk are parallel.

In atrial situs solitus, the apex of the heart is usually to the left and is formed by the RV. Dextrocardia exists in about 25% of cases, and occasionally mesocardia.\textsuperscript{2} In atrial situs inversus, there is nearly always dextrocardia.

Other bizarre rotational anomalies occasionally occur in this and other hearts with AV discordant connections (see Morphology in Section II later in this chapter).

Pulmonary Outflow Tract

The pulmonary valve lies in a transverse plane and arises from the right-sided LV in a wedged position between the mitral and tricuspid valves. Wedging of the pulmonary valve is said to be more marked in corrected than in complete transposition (see Morphology in Chapter 52) and more marked than that of the aorta in the normal heart\textsuperscript{7} (see Chapter 1). The pulmonary valve lies to the right and posterior to the aortic valve. Axis of the AV valves is partway between transverse and sagittal planes as in the normal heart.

The long axis of pulmonary outflow from the right-sided LV is obliquely oriented\textsuperscript{5,14} and potentially restrictive, particularly when there is LV hypertrophy. Obstruction is organic in about half the hearts,\textsuperscript{5,14} and in at least 25% it is hemodynamically important.\textsuperscript{17}

Pulmonary valve cusps may be thickened and fused or occasionally bicuspid or unicuspid. When valve stenosis is present, the pulmonary trunk may be narrowed by valve tethering, as in tetralogy of Fallot (see “Pulmonary Valve” under Morphology in Section I of Chapter 38). There may be pulmonary atresia with or without confluence between right and left pulmonary arteries. There may be subvalvar narrowing due either to a membrane that is adherent on its right (laterally) with the right-sided anterior mitral leaflet (see Fig. 55-2) or to an aneurysmal bulging of the membranous septum into the posterior part of the outflow tract with or without a ventricular septal defect (VSD)\textsuperscript{5,12} (Fig. 55-3). Less severe obstruction is usually due to fibrous tags (valvar...
excrences) attached to the LV–pulmonary trunk junction, membranous septum, or right-sided mitral valve or due to valvar excrescences projecting through a VSD from the left-sided tricuspid valve leaflet. In about 1% of cases, pulmonary atresia is associated with arborization abnormalities of the branch pulmonary arteries and presence of major aortopulmonary collateral arteries.

### Atrial Septum

Atrial and ventricular septa are malaligned except where pulmonary, mitral, and tricuspid valves lie in close proximity and are joined by the right fibrous trigone. Elsewhere, atrial septal attachment to the fibrous skeleton of the heart is moved to the right of ventricular septal attachment. These alignment differences are usually severe enough in hearts with atrial situs solitus to prevent the normally positioned (regular) AV node (known as posterior, inferior, or lateral node) from reaching the underlying ventricular septum.

### Mitral Valve

The right-sided mitral valve lies at the entrance to the right-sided LV. Because of the wedged position of the pulmonary valve, the mitral anulus extends anterior to the pulmonary anulus so that the pulmonary valve is tucked beneath (to the left of) the septal mitral valve leaflet (see Fig. 55-2). The mitral valve is rotated so that its usual septal leaflet, which is in fibrous continuity with the pulmonary valve and can therefore be called the pulmonary leaflet, is posterior and its mural leaflet anterior (see Fig. 55-3). The smaller papillary muscle arises from the anterolateral free wall of the ventricle, where it can be damaged by left ventriculotomy. Its position is frequently marked by direct coronary artery branches crossing the front of the LV from the anterior descending coronary artery. The larger papillary muscle arises from the posterolateral free wall of the ventricle, having been found in 55% of an autopsy series (Fig. 55-4). Mitral valve abnormalities are common, having been found in 55% of an autopsy series (Fig. 55-4).

### Aortic Valve

The aortic valve, usually normal, is over the RV infundibulum, and it and the aorta are usually in a leftward and anterior position (S,L,L). Occasionally the aorta lies to the right and anterior to the pulmonary artery (S,L,D), associated with infundibular rotation in this direction. In atrial situs inversus, the aorta is virtually always to the right (I,D,D).

Subaortic obstruction rarely occurs in the left-sided RV outflow tract.

### Tricuspid Valve

The left-sided tricuspid valve lies at the entrance to the left-sided RV, which has usual coarse trabeculations, a trabecula septomarginalis (septal band), and an infundibular septum. The valve is positioned almost in a sagittal plane and has the usual three leaflets but with the septal leaflet more medial and anterior than normal. According to some, it is nearly always structurally abnormal (90% of cases according to Allwork et al.). Others report fewer structural abnormalities, ranging from 23% to 43%. In most instances, there is leaflet dysplasia with abnormal thickened chordal attachments of the septal and posterior leaflets, and in a minority there is a true Ebstein anomaly with downward displacement of origins of septal and posterior leaflets. Ebstein anomaly often differs from that in a heart with normal connections in three respects:

- The anterior leaflet is normal in size rather than large and sail-like.
- The anulus is not dilated.
- The RV sinus is not enlarged.

In about 30% of hearts, morphologic changes make the tricuspid valve regurgitant or, rarely, stenotic. There may be a thinned, dilated atrialized portion of the RV with a variable degree of hypoplasia.

### Atrioventricular Node and Bundle of His

The AV node and bundle of His in CCTGA (and in most, if not all, hearts with atrial situs solitus and AV discordant connection) differ from normal. Although a regular (posterior) AV node is present in front of the coronary sinus ostium in the apex of the triangle of Koch, the penetrating bundle of His usually does not extend from it because of septal malalignment. In exceptions in which the regular (posterior) AV node gives rise to the penetrating bundle, septal malalignment is mild. Degree of septal malalignment is influenced by size of the pulmonary trunk. Thus, presence of either pulmonary atresia or severe pulmonary stenosis results in less septal malalignment and an increased chance that the posterior AV node will align with the penetrating bundle.

In contrast, in atrial situs inversus, the penetrating bundle of His most commonly extends from the regular (posterior)
Ventricular Septal Defect

VSD is the most common coexisting anomaly and is present in about 80% of hearts. Usually it is large, subpulmonary, and associated with virtual absence of the membranous septum (infundibulum). The pulmonary valve commonly overrides the VSD to arise from the left-sided RV. As viewed from the right (LV) side (Fig. 55-5), the VSD is bounded superiorly by the pulmonary anulus or pulmonary valve itself, depending on degree of overriding. There may be membranous septal remnants along this margin (see Fig. 55-3). Posteriorly, it is bounded by that part of the right-sided mitral anulus from which the septal leaflet arises, and anteriorly and inferiorly by infundibular and muscular interventricular septa, respectively. Its postero-inferior margin may extend to the mitral anulus with a zone of mitral-pulmonary-tricuspid fibrous continuity. It is frequently narrowed or nearly closed by an aneurysm of the membranous septum (see Fig. 55-3) or valvar excrescences from the left-sided tricuspid valve (see Section IV in Chapter 38).

Viewed from the RV (left) side, this perimembranous VSD lies, as usual, within the Y of the trabeculae septomarginalis and beneath the infundibular septum; the VSD, in other words, is infundibular in type and is often accompanied by some malalignment of the infundibular septum that

Figure 55-5  Specimen of a heart with congenitally corrected transposition of the great arteries in which a large conoventricular ventricular septal defect had been closed with a polyester patch 4 years before death. Right-sided left ventricle and pulmonary trunk have been opened. Limits of patch are easily discerned. Defect is bounded superiorly by the pulmonary anulus, posteriorly by the mitral ring, anteriorly by the infundibular (conal) septum, and inferiorly by the muscular ventricular septum. Key: Cs, Infundibular (conal) septum; D, ventricular septal defect closed by a patch; LV, left ventricle; MV, septal mitral valve leaflet; PT, pulmonary trunk; PV, normal pulmonary valve; VS, ventricular septum.
Coronary Arteries

Coronary arteries demonstrate anatomy appropriate to their ventricles. Thus, the right-sided left coronary artery (coronary artery to right-sided LV) with its left anterior descending and circumflex branches supplies the LV, and the right coronary artery and its conal and posterior descending branches supplies the RV. Aortic origins are, however, peculiar to the malformation. The anterior sinus is the noncoronary one; the right-sided left coronary artery arises from the right posterior sinus and passes directly in front of the pulmonary valve to divide into left anterior descending and circumflex branches, the latter passing in front of the right atrial appendage in the AV groove; the left-sided right coronary artery arises from the left posterior sinus and runs in the AV groove and in front of the left atrial appendage, terminating posteriorly as the posterior descending artery. Lev and Rowlatt used the terms “right sided” and “left sided” to describe these vessels.\(^1,3\) The most common major variation from this arrangement is for a single coronary artery to arise from the right sinus and divide into right and left main branches; this occurs in less than 10% of cases. Other minor variations occur.\(^1,3,4\)

Other Associated Anomalies

Only 1% to 2% of hearts with CCTGA have no coexisting anomalies.\(^4,6,16,17\) Coexisting anomalies other than those described in the preceding text include a supravalvar left atrial ring, which may be a cause of left-sided (tricuspid) valve stenosis,\(^16\) and coarctation of the aorta in association with a VSD.\(^18,54\) Coarctation may be particularly common when severe forms of Ebstein anomaly are present.\(^4\) A patent ductus arteriosus is sometimes present, as is a true atrial septal defect in about 20% of cases.

Overriding or straddling of AV valves is more common when there are positional anomalies, as is hypoplasia of one or other ventricle.\(^31\) The left-sided tricuspid valve may over-ride or straddle a VSD,\(^35\) which is at times associated with hypoplasia of the left-sided RV and at times with superior-inferior ventricles (see “Positional Anomalies” under Ventricular Position and Rotation in Section II of this chapter and “Cardiac and Arterial Positions” under Terminology and Classification of Heart Disease in Chapter 1). The left-sided tricuspid valve straddles the posterior part of the ventricular septum, which is then prevented from reaching the crux, and the conduction tissue passes anterior to the pulmonary anulus.\(^51,11\) More rarely, the right-sided mitral valve may behave similarly (as it does at times in AV discordant connection with double outlet right ventricle [see Section II]); invariably this is associated with LV hypoplasia and superior-inferior ventricles.\(^8,69\) The mitral valve straddles the anterior part of the septum so that it does not extend to the crux, and a regular posterior node only may be present, with the bundle passing posterior to the pulmonary anulus.\(^86\)

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**

Clinical features depend solely on the presence and combination of associated cardiovascular lesions. The rare patient with no associated lesions will be asymptomatic for years or decades and may present with left-sided RV failure after several decades or more. More commonly, clinical features are dominated by a large VSD associated with some restriction of features:

**Contribution to Subpulmonary Stenosis**

The bundle of His courses along its anterior margin on the LV (right) side in a subendocardial position and bifurcates at its anteroinferior angle with the right bundle branch crossing this angle of the defect to reach the RV.

In about 10% of cases (more often in Japanese patients),\(^12\) the VSD lies within the infundibular septum; when it completely replaces it, it is immediately below both great arteries (doubly committed, juxta-arterial) (Fig. 55-6). Uncommonly, it is muscular, lying in the sinus (trabecular) septum. A large, typical inlet septal VSD may uncommonly occur. Also, there may be multiple VSDs.

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**Figure 55-6** Specimen of a heart with congenitally corrected transposition of the great arteries and doubly committed subarterial ventricular septal defect (VSD). A. Viewed from right-sided left ventricle (LV). There is a partially obstructing subpulmonary fibrous membrane present (arrows). B. Viewed from left-sided right ventricle (RV). Infundibular septum is absent, but there is a relatively short subaortic conus and tricuspid-mitral-pulmonary fibrous continuity through VSD. Key: C, Subaortic conus; LC, left coronary (right-sided) aortic cusp; MV, mitral valve; NC, non-coronary (anterior) aortic cusp; PVC, pulmonary valve; RC, right coronary (left-sided) aortic cusp; TV, tricuspid valve.
pulmonary blood flow attributable to morphology of the subpulmonary LV outflow tract. Therefore, symptoms from sequelae of large pulmonary blood flow occur in only about 30% of cases, but finding a loud second heart sound at the second left intercostal space is suggestive because it may represent closure of the leftward and anterior aortic valve.

Although chest radiography may suggest that a congenital cardiac malformation has AV discordant connection by an ascending aortic shadow appearing along the left upper cardiac silhouette, this is not diagnostic because there are many other anomalies with the aorta in L-malposition (see Clinical Features and Diagnostic Criteria in Chapter 57). Echocardiography (ECG) may suggest a correct diagnosis when there is reversal of precordial Q-wave pattern with deep Q waves in leads V_2 and aVR, and QS complexes in leads V_3 and aVF in right precordial leads. Congenital or developing complete heart block is also suggestive of CCTGA. Additional findings of transposed great arteries with aorta anterior and to the left, and a left-sided ventricle containing a coarsely trabeculated endocardial surface and moderator band, help confirm the diagnosis (Fig. 55-8). Presence of VSDs, valve function, and venous connections can all be defined.

Computed tomography (CT) and magnetic resonance imaging (MRI) provide excellent delineation of the morphology of CCTGA, but in neonates and infants, these imaging modalities add little to echocardiography with respect to making the diagnosis and identifying associated cardiac anomalies. These additional studies can be extremely helpful, however, in providing additional information that may be important in complex management decisions that eventually must be made for many of these patients. MRI can be particularly helpful in quantitating ventricular volumes and valve regurgitant fraction (Fig. 55-10). It can also be helpful in quantitating LV mass and determining the ventricular septal position in cases being evaluated for a double switch procedure (Fig. 55-11). Volume-rendered CT imaging is capable of showing excellent spatial resolution of the coronary arteries and is particularly helpful in demonstrating the interrelationships between the coronary arteries and adjacent structures (Fig. 55-12).

Cardiac catheterization and biplane cineangiography provide confirmatory diagnostic data (Fig. 55-13). Pressure and flows are measured to quantify severity of pulmonary stenosis and any intracardiac shunt. Angiographic views must profile the ventricular septum and establish morphology of various chambers and sites of systemic and pulmonary venous connection and, thus, cardiac connections present. They can define location and number of VSDs, nature of the pulmonary stenosis and of tricuspid valve function, and other associated anomalies. Catheterization is rarely used in modern practice to define morphology, because echocardiography, CT, and MRI adequately provide these details in essentially all cases. Catheterization is indispensable if pulmonary vascular resistance, shunt fractions, or ventricular end-diastolic pressure is required for decision making.
potentials are not recordable, and morphologic evidence of a connection between an AV node and more distal parts of the His bundle cannot be found. At least 40% to 50% of patients with AV discordant connection are born with first- or second-degree AV block. As time passes, prolongation of the PR interval often develops, even in those with originally normal intervals. Thus, Gillette and colleagues found normal AV conduction at age 6 to 7 years in only 38% (CL 29%-47%) of 40 patients with CCTGA. Progressive prolonging of the PR interval may eventuate in

NATURAL HISTORY

Heart Block

About 5% to 10% of infants with CCTGA or other types of AV discordant connection (see Section II) have complete heart block at birth. This proportion slowly increases at about 2% per year to reach a prevalence of about 10% to 15% by adolescence and 30% by adulthood. Block may be in the AV node or in single or multiple sites more distally. In some infants born with complete heart block, bundle of His potentials are not recordable, and morphologic evidence of a connection between an AV node and more distal parts of the His bundle cannot be found.

At least 40% to 50% of patients with AV discordant connection are born with first- or second-degree AV block. As time passes, prolongation of the PR interval often develops, even in those with originally normal intervals. Thus, Gillette and colleagues found normal AV conduction at age 6 to 7 years in only 38% (CL 29%-47%) of 40 patients with CCTGA. Progressive prolonging of the PR interval may eventuate in
**Figure 55-9** Computed tomography (CT) image of corrected transposition of the great arteries. Axial maximum intensity projection CT image shows the right atrium (RA) connects to the morphologic left ventricle (MLV), and the left-sided ventricle shows prominent trabeculation (stars) with a thickened moderator band (arrow), which are characteristic of a morphologic right ventricle (MRV). Key: Ao, Aorta; LA, left atrium. (From Kantarci and colleagues [Fig. 1].)

**Figure 55-10** Four-chamber view from magnetic resonance imaging (MRI) cine sequence of a 33-year-old man with congenitally corrected transposition of the great arteries. The patient has symptoms of heart failure. The right ventricle (RV) is enlarged, with reduced ejection fraction. Tricuspid anulus enlargement caused multiple tricuspid regurgitant jets (arrow), which worsen the volume loading of the right ventricle.

**Figure 55-11** Mid-short-axis view from a cardiac gated computed tomography angiogram (CTA) of a 4-year-old girl with congenitally corrected transposition of the great arteries without ventricular septal defect or pulmonary stenosis. Note the thin left ventricular (LV) wall and bulging of the septum (arrowhead) from right ventricle (RV) to the LV because the RV is pumping at systemic pressure. RV is hypertrophied and dilated. LV wall and septum are thin. Patient underwent this study as a baseline evaluation in preparation for placing a pulmonary artery band for LV retraining in anticipation of performing a double switch procedure.

**Figure 55-12** Three-dimensional volume-rendered computed tomography image shows spatial relationship of great arteries, with ascending aorta anterior and to left of pulmonary trunk. Anterior descending artery (short arrow) and circumflex artery (arrowhead) arise from common left anterior descending coronary artery off anterior aortic sinus. Right coronary artery (long arrow) arises from posterior aortic sinus. (From Chang and colleagues [Fig. 1F].)
Figure 55-13  Cineangiograms in congenitally corrected transposition of the great arteries. A, Left ventricular injection in four-chamber position, anteroposterior (AP) projection. Pulmonary trunk arises from right-sided left ventricle (RV). Note concavity into low-pressure left ventricle (LV) produced by the nonopacified high-pressure left-sided RV. B, RV injection in four-chamber position, AP projection. Aorta arises from left-sided RV. C, In another patient, RV injection in four-chamber position, AP projection. In this patient, in contrast to the first one, a ventricular septal defect allows dye to pass into right-sided LV and out pulmonary trunk. Pulmonary trunk and ascending aorta are superimposed. D, In a patient with coexisting subvalvar pulmonary stenosis, LV injection in four-chamber position, AP projection. Severe subvalvar narrowing is evident as well as poststenotic dilatation of the pulmonary trunk. E, LV injection, lateral projection. The long severe subvalvar narrowing is evident.

episodic or permanent complete heart block. However, about 40% of patients with AV discordant connection retain normal PR intervals and QRS durations throughout their lives.

Ventricular Function

General outlines of the truth about systemic (morphologic right) and pulmonary (morphologic left) ventricular function are gradually becoming apparent, although many of the details are missing (see Special Situations and Controversies later in this section). Ventricular function is not normal but is sufficiently good that a large proportion of patients maintain essentially normal functional status well into adult life. In 12 adults with CCTGA, many with associated anomalies, followed longitudinally for 10 years, ventricular ejection fraction did not change. However, systemic ventricular function (function of the RV) tends to gradually deteriorate during and after the second decade of life; isolated reports of survival into the seventh, eighth, and ninth decades do exist.

In the unusual circumstance of CCTGA without other cardiac anomalies, an adequate cardiac index is usually sustained during exercise, but increase in heart rate accounts for this, and stroke volume is not increased. Response of the systemic (right) ventricular ejection fraction to exercise is variable, the ejection fraction increasing in some patients but not in others. Systemic (right) ventricular end-systolic and end-diastolic volumes also behave variably during exercise, but on the average do not change, whereas in normal individuals, systemic (left) ventricular end-systolic volume decreases with exercise.

Pulmonary (left) ventricular ejection fraction usually increases with exercise in patients with CCTGA without other cardiac anomalies. Other indices do not change systematically with exercise, as is also the case in normal individuals.
Etiology of ventricular dysfunction is poorly understood. Myocardial perfusion plays a role. Perfusion defects at rest are common in the morphologic RV in CCTGA, and their extent correlates inversely with ejection fraction.\textsuperscript{134,164,147}

Women of childbearing age seem to tolerate pregnancy and delivery moderately well, with some increased risk of maternal complications and fetal loss.\textsuperscript{137,144}

**Effect of Coexisting Cardiac Anomalies**

Because of the high prevalence of coexisting cardiac anomalies, survival free from cardiac intervention is less than 30% at 36 months after birth.\textsuperscript{132} Even without coexisting anomalies, the likelihood of developing heart block and reduced systemic (right) ventricular function probably adversely affects natural history; coexisting cardiac anomalies further affect it. A multicenter study involving 182 patients confirms these points: By age 45 years, 25% of patients without coexisting anomalies developed heart failure, and 67% of those with associated anomalies did.\textsuperscript{139} Other studies link heart failure in this setting to increased risk of death.\textsuperscript{144}

The natural history of CCTGA patients whose only coexisting lesion is a large VSD tends to be slightly better than that of patients with isolated large VSDs (see Fig. 55-7); this may be because their VSDs are smaller than in patients presenting with isolated VSDs. (This difference was not apparent in the report of Friedberg and Nadas,\textsuperscript{135} possibly related to their inclusion of patients with univentricular AV connection [single ventricle] in their study.) Chronic symptoms of effort intolerance and growth failure are common in patients with CCTGA in the first 2 decades of life, but death is infrequent. Although estimates of survival are unavailable, presumably death from chronic heart failure occurs with increasing frequency during the third, fourth, and fifth decades of life.

When important pulmonary stenosis coexists with VSD, cyanosis appears in early life, and the natural history may be similar to that of tetralogy of Fallot (see Natural History under Section I of Chapter 38). However, compared with tetralogy of Fallot, lack of a subpulmonic infundibulum in CCTGA may substantially alter the likelihood of a dynamic muscular component of pulmonary obstruction.

The natural history of the left AV valve in patients with CCTGA and other types of AV discordant connection is unclear. Occasionally the valve may be importantly regurgitant from early in life, but more commonly there is little or no regurgitation initially, and then its prevalence and magnitude increase progressively during the second through fifth decades. The exception is Ebstein anomaly of the left-sided tricuspid valve, when regurgitation is commonly present from birth.

In atrial situs inversus, VSD and pulmonary stenosis are more likely to be present than in atrial situs solitus. However, there is less likelihood of developing spontaneous complete heart block, because of the considerably higher prevalence of the penetrating bundle connecting to a normally positioned AV node.\textsuperscript{138}

**TECHNIQUE OF OPERATION**

**Repair of Coexisting Ventricular Septal Defect**

Preparations for operation, median sternotomy, and placing pericardial stay sutures are as usual (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). Placing purse-string sutures for aortic cannulation and cannulation itself are more difficult than usual because of aortic L-malposition. These procedures are facilitated by grasping aortic adventitia with one or two small curved hemostats and retracting them inferiorly and rightward. Usual purse-string sutures are placed for aortic cannulation and the cardioplegic catheter; caval tapes and purse-string sutures are also placed. In atrial situs solitus and dextrocardia, right atrium and vein cavae are hidden behind the ventricle, making cannulation difficult, although difficulty of direct caval cannulation is not increased.

**Through Right-Sided Mitral Valve**

Cardiopulmonary bypass (CPB) is established in the usual manner, as are cardioplegia and controlled reperfusion (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” in Chapter 3). The right atrium is opened through an oblique incision (Fig. 55-14). A pump-oxygenator sump sucker is introduced through the right superior pulmonary vein across the left-sided AV valve into the left-sided ventricular chamber.

The VSD is examined through the right-sided mitral valve (Fig. 55-15, A). Although it does not permit quite as free access to the interior of the ventricle as the normal right-sided tricuspid valve, in most cases the VSD can be repaired through the intact mitral valve. When exposure is suboptimal, an incision is made in the base of the mitral valve septal leaflet near the superior commissure and through the base of the
Figure 55-15  Repair of ventricular septal defect (VSD) in patient with situs solitus, congenitally corrected transposition of the great arteries, and VSD. A, Close-up view of VSD through intact mitral valve. Intracardiac exposure is gained through a right atrial incision as shown in Fig. 55-14. Exposure of a typical conoventricular VSD is more difficult working through the mitral valve orifice compared with a similar defect in a patient with atrioventricular concordant connection working through tricuspid valve. However, VSD can be exposed and closed in most circumstances without incising the posterior leaflet. The retractor is used to move aside anterior aspect of mitral valve anulus and anterior valve leaflet. In this case, the VSD patch is sewn into place with a running monofilament nonabsorbable suture, beginning at the most anterior aspect of the rim of the VSD. To avoid injury to the conduction system, sutures must be placed on morphologic right ventricular side of VSD rim along its anterior and superior aspects. Here, a single felt pledget is positioned on morphologic right ventricular side of septum to initiate the suture line. Two dashed lines to left and right of pledget represent partial thickness suture placement on morphologic right ventricular side of defect along its anterior aspect. Branching bundle of His is shown coursing along anterior aspect of VSD. B, If VSD cannot be adequately exposed through the mitral valve orifice, it may be beneficial to incise the posterior mitral valve leaflet 1 to 2 mm from its anular attachment as shown by dashed lines. C, Incised posterior leaflet of mitral valve has been retracted anteriorly, allowing direct exposure of conoventricular VSD. VSD patch is then sewn into place exactly as described in A.

The technique is similar to that used occasionally for inlet septal VSD. Working through the aperture created, VSD repair can be accomplished nicely (Fig. 55-15, D-E). However, the alternative of repairing the VSD through the aorta should be considered when approach through the right atrium is not optimal (see text that follows).

Margins of the VSD are studied (see Fig. 55-15, A and C). Location of the anterior AV node and bundle of His arching over the subpulmonary outflow tract and passing anterior to the VSD are conceptualized (in fact, the bundle often can be seen as a thin, pale line as shown in Fig. 55-14). Electrophysiologic mapping is unnecessary. The left-sided tricuspid valve can usually be seen through the
VSD, and some of its chordae often attach to the inferior VSD border.

VSD repair is made by sewing into place a properly sized patch of either glutaraldehyde-treated autologous pericardium or double-velour knitted polyester, keeping sutures on the left (RV) side of the defect anterosuperiorly, anteriorly, and as much as possible inferiorly (see Fig. 55-15, A and D). Chordae from the left-sided tricuspid valve, often attached to the inferior edge of the VSD, limit this possibility inferiorly. Continuous polypropylene suture, ranging from 6-0 to 4-0 depending on the size of the patient, is used, or interrupted pledgeted mattress sutures when exposure is difficult because of overlying chordal structures. After VSD repair is complete, if a circumferential incision has been made in the mitral leaflets, this incision is closed with continuous polypropylene suture using previously placed fine stay sutures to keep the closure properly oriented so valve distortion is avoided (Fig. 55-15, E). If a patent foramen ovale or atrial septal defect is present, it is closed.

The subpulmonary (LV outflow) tract is examined. Unless the pulmonary valve itself is stenotic or valvar excrescences obstruct the subvalvar area, little can be done to improve the variable degree of narrowing usually present (see Results). Only placing an LV–pulmonary trunk valved extracardiac conduit provides good relief. However, if pulmonary blood flow has been large (>2.0 preoperatively), even a 50-mmHg gradient does not necessarily indicate need for a conduit. With elimination of left-to-right shunt by closing the large VSD, right-sided LV pressure usually decreases appreciably.

The usual de-airing procedures are accomplished (see “De-airing the Heart” in Section III of Chapter 2). The aortic clamp is removed, and the right atrial incision is closed with a continuous polypropylene suture. The remainder of the procedure, including placing temporary atrial and ventricular pacing wires, is carried out in the usual manner (see “Placing Epicardial Pacemaker Leads” later in this section and “Completing Cardiopulmonary Bypass” in Section III of Chapter 2).

Through Aorta
An attractive alternative approach is closing the VSD through the aorta, which allows the patch to be sutured into place from the RV (left-sided) aspect of the septum. Experience of Russo and colleagues suggests this may reduce the prevalence of perioperative complete heart block. This approach is more attractive than that through the pulmonary trunk, which some advocate.

Through Left-Sided Tricuspid Valve
When isolated dextrocardia complicates CCTGA and VSD, the VSD can be repaired through a left-sided incision in the usually large left-sided left atrium. Exposure through the left-sided tricuspid valve usually allows good exposure, and surgically induced heart block should be avoidable because suturing is all on the RV (left) side of the septum.

Repair of Coexisting Ventricular Septal Defect and Pulmonary Stenosis
The main decision-making challenge is determining whether satisfactory repair can be accomplished without a valved extracardiac conduit. When the pulmonary valve is stenotic, it is approached through a pulmonary arteriotomy during moderately hypothermic CPB and cold cardioplegia,
and valvotomy is performed as for isolated pulmonary valve stenosis (see Fig. 39-10 in Chapter 39). The pulmonary arteriotomy is best closed with a patch and continuous suture. Obstructing fibrous subvalvar tags are excised, bearing in mind the His bundle position (see Fig. 55-14). A subvalvar fibrous membrane can be excised with utmost care if it is at the anteroinferior angle. Aneurysm of the membranous ventricular septum is excised and the deficiency closed as part of VSD repair. If other excrescences are present, they are first examined to ensure they are not functioning parts of the AV valves or subvalvar mechanisms; then they are sharply resected.

Muscle must never be removed from the rightward (medial) aspect of the right-sided LV outflow tract or from the anterior part adjacent to the pulmonary anulus, because the His bundle lies there. Then Hegar dilators are used to measure the resulting orifice and the z value estimated (see “General Plan and Details of Repair Common to All Approaches” under Technique of Operation in Section I of Chapter 38). Valvotomy may be inadequate because of a bicuspid valve, supravalvar pulmonary trunk narrowing (tethering) at the level of commissural attachment, or (most commonly) a narrow subpulmonary LV outflow tract. However, if the z value is greater than ~1, the pulmonary trunk is repaired, usual de-airing and other procedures carried out, and CPB discontinued.

Pressures are measured before removing the cannulae. Relationship between the postvalvotomy left-to-right ventricular pressure (P_{LV/RV}) in the operating room and that the next morning and late postoperatively is not known. However, it has seemed reasonable not to revert to CPB and place a valved extracardiac conduit if P_{LV/RV} in the operating room is less than about 0.85, considering that the right-sided ventricle and valve are a morphologic LV and mitral valve. On the other hand, pulmonary stenosis usually represents a fixed resistance, and the LV-to-pulmonary trunk gradient will increase with exercise.

A polyvinyl catheter is placed in the right-sided LV and, if possible, threaded into the pulmonary trunk. LV pressure is remeasured the next morning in the intensive care unit with this catheter, and if calculated P_{LV/RV} is less than about 0.7, the patient is not returned to the operating room for placing a valved extracardiac conduit.

**Placing Valved Extracardiac Conduit**

When pulmonary stenosis is so severe that the patient is cyanotic preoperatively, or when simple procedures to relieve the stenosis are unsatisfactory (see earlier) or postrepair P_{LV/RV} is too high, a valved extracardiac conduit is used. After VSD repair, working through the right atrium, a site is chosen for attaching the conduit to the right-sided LV by examining the LV interior through the mitral valve. A site is chosen on the anterior wall, but rather inferior and away from any papillary muscles and major coronary artery branches. Left ventriculotomy is then made. If there is reasonable flow across the native LV–pulmonary trunk outflow tract, it can be left intact, creating an end-to-side anastomosis of conduit to pulmonary trunk. This results in LV ejection via two routes: native tract and conduit. More commonly when a conduit is required, obstruction is severe; therefore the pulmonary trunk is transected at the valve level, the proximal stump oversewn, and the conduit connected end to end to the distal pulmonary trunk (Fig. 55-16).

Reconstruction can be accomplished in a number of ways. An allograft-valved conduit has previously been prepared by extending it proximally with a woven polyester tube (see Fig. 55-16). Alternatively, proximal extension may be with an aortic allograft, or the allograft aortic valve and ascending aorta may be left long distally, and proximal anastomosis augmented with a pericardial hood (see “Placement of Valved Conduit” in Section II of Chapter 38). These extensions are particularly necessary in this situation because the conduit must be of sufficient length to prevent kinking, and the valve must lie away from the LV so that it is not distorted. Estimating length and lie of the conduit is important to avoid its compression by the sternum.

The conduit is trimmed to size, cutting the distal end square but leaving more of the ascending aorta beyond the aortic valve than in the case of tetralogy, because this facilitates a smooth conduit contour and limits length of the polyester extension. The proximal polyester end of the conduit is trimmed to make a cobra head, the distal allograft end anastomosed end to end to the distal pulmonary trunk, and the proximal polyester end anastomosed to the
ventriculotomy. The conduit most commonly is placed to the right around the right atrium and atrial appendage (see Fig. 55-16), although extreme deviations in cardiac position may influence conduit position, occasionally making a left-sided placement appropriate. Aeba and colleagues describe placing the conduit from the apex of the LV to the pulmonary trunk to avoid the well-known problem of sternal compression.\textsuperscript{A2}

**Transanular Patch**

Doty and colleagues\textsuperscript{D10} proposed using a posteriorly placed transanular patch across the pulmonary valve anulus in this situation. However, average gradient across the repair was 40 mmHg.

**Correction for Regurgitant Left-Sided Tricuspid Valve**

When important left-sided tricuspid valve regurgitation coexists, repair and anuloplasty are only occasionally successful but should be attempted if it seems feasible.\textsuperscript{D9} If replacement is required, the same considerations apply to the replacement device as in ordinary left-sided mitral valve replacement (see “Choice of Device for Valve Replacement” in Section I of Chapter 11). Valve replacement is the same as for a left-sided mitral valve, including choice of venous cannulae and approach through the right side of the left atrium (see “Mitral Valve Replacement” in Section I of Chapter 11 and Fig. 11-19). The replacement device is either sewn in with interrupted pledgeted mattress sutures or simple interrupted sutures. A continuous suture technique is not desirable when there is absence of a well-defined anulus in some areas, as may occur when there is downward displacement into the ventricle of some of the left-sided tricuspid valve leaflets, as in Ebstein anomaly.

**Double Switch Procedures**

Because of concern over long-term fate of the morphologic LV and mitral valve in the systemic circulation, some suggest placing the morphologic LV and mitral valve into the systemic circulation. This requires switching both venous return and arterial outflow (double switch) by one of several procedures, all of which are technically substantially more complex than those already described. The double switch concept was originally suggested by Ilbawi and colleagues for patients with CCTGA, VSD, and pulmonary stenosis.\textsuperscript{D11} In this setting, the morphologic LV is connected to the aorta by creating an intraventricular baffle (which also closes the VSD); an extracardiac conduit is placed from morphologic RV to pulmonary trunk, and a Mustard or Senning intraatrial transposition of venous return is performed. The concept was subsequently applied to CCTGA without pulmonary stenosis, with or without VSD. In this setting, an arterial switch is performed to correct the ventriculoarterial discordant connection. (All of these reconstructive procedures used in combination in the double switch procedures are individually described in detail in Chapter 52.) Aortic translocation has also been used for selected cases of CCTGA with VSD and pulmonary stenosis.\textsuperscript{D9,D10,K14}

If these procedures are being considered for patients without VSD in whom the morphologic LV is working at low pressure, the same considerations must be addressed as in simple transposition of the great arteries (TGA) with unprepared LV (see “Simple Transposition of the Great Arteries Presenting after Age 30 Days” under Indications for Operation in Chapter 52).

Both major double switch procedures are performed using a standard median sternotomy incision, CPB with moderate hypothermia using bicaval venous cannulation through purse-string sutures placed directly on the vena cavae, aortic cannulation at the base of the brachiocephalic artery, and venting of the systemic ventricle by way of a cannula introduced through the right upper pulmonary vein. Multiple doses of cold cardioplegic solution are used for these extensive procedures (see “Methods of Myocardial Management” under Neonates and Infants in Chapter 3). Individual components of the two major double switch procedures are as follows:

1. The *atrial baffle procedure*, which is performed exactly as for simple TGA (see “Mustard Technique” and “Senning Technique” under Technique of Operation in Chapter 52). It is not uncommon in CCTGA of both the S,L,L and the I,D,D types for cardiac positioning abnormalities such as mesocardia or apicocaval juxtaposition to be present. In these cases, the free wall of the systemic venous atrium is likely to be deficient, making the Mustard technique preferable to the Senning. Atrial baffle placement may be more difficult than in simple TGA, because the left-sided tricuspid valve is positioned much more posteriorly across the atrial septum in relation to the vena cavae.

2. For patients with VSD and pulmonary stenosis, the *morphologic LV-to-aortic intracardiac baffle procedure*, which is accomplished through a subaortic incision in the infundibulum of the morphologic RV as described under “Intraventricular Repair” in Chapter 52, for S,D,D transposition with VSD and pulmonary stenosis or atresia. The morphologic RV-to-pulmonary trunk conduit is placed as described under “Rastelli Operation” in Chapter 52. This procedure is shown in Fig. 55-17, A to E.

3. For patients without pulmonary stenosis, the *arterial switch procedure* is performed using the same techniques described under “Arterial Switch Operation” in Chapter 52 for simple TGA. If a VSD is present, it is closed as described earlier under “Repair of Coexisting Ventricular Septal Defect.” This procedure is shown in Fig. 55-18, A to D.

**Double Switch Procedures Combined with Bidirectional Superior Cavopulmonary Anastomosis**

Bidirectional superior cavopulmonary anastomosis may provide substantial advantages in the setting of both double switch procedures. It reduces complexity of the intratrial procedure, because only the inferior vena cava is baffled to the tricuspid valve. This reduces myocardial ischemia time because (1) the cavopulmonary anastomosis can be performed during rewarming after the aortic clamp is removed and myocardial reperfusion is established, and (2) the simplified inferior vena cava baffling can be accomplished much more quickly than a full Mustard or Senning procedure. An additional advantage is that recognized complications of the full Mustard or Senning procedure (e.g., superior caval obstruction, pulmonary venous obstruction, sinus node dysfunction) are eliminated.
Figure 55-17 Double switch concept using a Rastelli morphologic left ventricle-aortic intraventricular tunnel and an intraatrial Mustard baffle. A, Dashed lines on inset show the two incisions used for this procedure; one is along right atrial free wall, the other along subaortic infundibulum of left-sided morphologic right ventricle (MRV). Routine cardiopulmonary bypass techniques and myocardial protection are used. After cardiac arrest, right atrium is opened and Mustard intraatrial baffle constructed. As illustrated, baffle suture line is almost completed. Details of Mustard procedure are provided in Chapter 52. The only important difference when the Mustard procedure is performed in congenially corrected transposition is that the surgeon must be aware of superior displacement of the atrioventricular node. B, After completing Mustard intraatrial baffle, the right atriotomy is closed with a running monofilament suture. The left-sided MRV infundibular incision is made, and exposure to intraventricular morphology is aided by a combination of stay sutures and retractors. In this case, the stenotic pulmonary valve and subpulmonic morphologic left ventricular (MLV) outflow tract are identified and closed internally with doubly pledgeted interrupted mattress sutures. Pulmonary anulus and subpulmonic region are exposed by gently retracting superior anterior aspect of rim of the ventricular septal defect (VSD) with a vein retractor, as illustrated.
Vein retractor on rim of VSD has been removed. Dotted line shows suture line used to create intraventricular baffle that will establish a pathway from the right-sided posterior MLV through VSD to left-sided anterior aorta. Note that exposure through this incision in MRV allows the surgeon to directly view MRV aspect of the ventricular septum, making it easy to place all sutures on right ventricular aspect of the rim of VSD, thereby avoiding direct injury to conduction system. It is important to realize that from this perspective on the MRV side, the vulnerable area for conduction injury is now at posterior and inferior aspect of VSD. A polyester tube graft of diameter approximately equal to that of the aorta is used to create MLV-to-aortic baffle. Natural curvature of resulting baffle patch is placed such that it is seen as convex when viewed through infundibular incision in MRV. Typically a running monofilament suture technique is used to place baffle. Routine care must be taken with respect to the conduction system along posterior inferior rim of VSD (see Chapter 35). Aortic end of baffle is sewn into place along the immediate subaortic musculature (see text for further details). As can be seen from C, there is potential for an hourglass deformity in the pathway from MLV to aorta at its midportion as the baffle passes the tricuspid valve anulus. Obstruction at this level can be avoided by attending to several factors. The baffle itself should be made particularly wide at its midportion. Additionally, the suture line should be placed into anulus of tricuspid valve at this level in order to maximize width of the pathway. Finally, judicious resection of muscle along floor of pathway in subpulmonic region at the upper rim of VSD may be helpful. It is critical to perform this resection with absolute knowledge of the position of conduction system.
**Figure 55-17, cont’d** E, Procedure is completed by placing an external valved conduit from left-sided anterior MRV to pulmonary trunk. In this instance, the subpulmonic area was closed previously during the intracardiac portion of the operation (B). Conduit is placed from infundibular incision in the MRV, coursing either to left or right side of aortic valve and ascending aorta. Positioning of conduit in this operation is somewhat more problematic than placing conduit from right-sided MLV to pulmonary trunk, as described in the “standard repair” in Fig. 55-16. Ventricular incision in MRV is more anterior and much more likely to be immediately substernal, increasing risk of compression. Whether to place the conduit to left or right of aortic valve and ascending aorta is an individual decision based on particular details of cardiac position within chest cavity. The principle is to place conduit in such a way that minimizes sternal compression. In this case, a composite graft of polyester and a bioprosthetic valve is used. Again, length of conduit is typically much longer than in cases of tetralogy of Fallot with pulmonary atresia. Similar to the situation described in Fig. 55-16, the valve is placed distally within the conduit, close to conduit to pulmonary trunk anastomosis.

**Figure 55-18** Double switch concept for situs solitus congenitally corrected transposition of the great arteries (CCTGA), with or without ventricular septal defect, and without pulmonary stenosis. A, Dashed line on right atrium shows proposed incision for performing Mustard intraatrial baffle. Dashed lines on aorta and pulmonary trunk show proposed incisions for transecting the great arteries and mobilizing coronary arteries. Cardiopulmonary bypass and myocardial protection are standard. B, Mustard intraatrial baffle is performed as described in Fig. 55-17 and as detailed in Chapter 52.
Other advantages exist specifically in CCTGA with VSD and pulmonary stenosis. If an extracardiac conduit is necessary owing to severe pulmonary stenosis, its longevity will be extended because of reduced volume of flow it carries. This may be particularly pertinent in a small growing child. Additionally, if the morphologic RV size is reduced, either because of intrinsic reasons or as a result of a large morphologic LV–aortic baffle occupying part of its cavity, the bidirectional superior cavopulmonary anastomosis may provide superior hemodynamics. Finally, in patients with positional abnormalities such as situs solitus with mesocardia or dextrocardia, or with situs inversus, simplicity of the “hemi-Mustard” procedure makes it preferable to the full Mustard or Senning procedure.

For these reasons, bidirectional superior cavopulmonary anastomosis with hemi-Mustard procedure has become the preferred technique for performing the atrial component of the operation in both forms of the double switch for at least one of the authors. The procedure is performed as described in Chapter 41 under “Bidirectional Superior Cavopulmonary Shunt.” The double switch procedure, inferior vena cava–to–tricuspid valve atrial baffle (hemi-Mustard), and bidirectional superior cavopulmonary anastomosis are shown in Fig. 55-19.

Placing Epicardial Pacemaker Leads
When complete heart block has been present intermittently or permanently preoperatively, or when it has developed intraoperatively, permanent epicardial atrial and ventricular pacemaking leads are placed, and a permanent pacemaker pulse generator is placed subcutaneously (see “Technique of Intervention” in Section I of Chapter 16).

SPECIAL FEATURES OF POSTOPERATIVE CARE
Patients are managed with protocols generally used after cardiac surgery (see Chapter 5). In patients with AV discordant connection such as these, particular attention is paid to the cardiac rhythm. When complete heart block is present, AV sequential pacing augments cardiac output and is therefore used routinely.
PART VII  Congenital Heart Disease

Figure 55-19  Bidirectional superior cavopulmonary anastomosis and “hemi-Mustard” modification for double switch procedure for congenitally corrected transposition of the great arteries. As in all double switch variations, atrial and arterial components can be performed in any order desired. In certain circumstances (see text), modifying the atrial component by performing a hemi-Mustard connection of the inferior vena cava to the tricuspid valve in combination with a bidirectional superior cavopulmonary anastomosis, rather than the full Mustard procedure, is beneficial. When this procedure is elected, the simplified intraatrial baffle can be performed either before or after the great artery component, whether that be a formal arterial switch or a Rastelli morphologic left ventricle–aortic intraventricular baffle. It is advantageous, however, to perform the bidirectional superior cavopulmonary anastomosis as the last component of the operation after removing the aortic clamp and establishing myocardial reperfusion. The intraatrial component of this procedure proceeds by performing a formal atrial septectomy (see “Mustard Technique” under Technique of Operation in Chapter 52). It may be advantageous in some cases to further enlarge the intraatrial opening by incising superiorly into the limbus of the atrial septum. The intraatrial baffle is much simplified, in essence constructing only inferior vena caval limb of Mustard baffle. Shape of baffle patch used is circular. Diameter of patch is equal to the straight-line distance measured from most superior limit of tricuspid valve anulus to orifice of inferior vena cava. Suture line follows exact details of the standard Mustard patch around inferior vena cava orifice. Superior aspect of baffle is sewn around tricuspid valve orifice. Bidirectional superior cavopulmonary anastomosis is performed exactly as described in Chapter 41.

RESULTS

Survival

Morphologic Right Ventricle Supporting Systemic Circulation

Early (Hospital) Death  When operation is performed for CCTGA and VSD, hospital mortality has been 5% to 10%. When performed for CCTGA with coexisting VSD and important pulmonary stenosis, it has been 10% to 20%. When performed for coexisting left-sided tricuspid valvar regurgitation requiring valve replacement, it has been 15% to 25%.11,B13,D3,I8,M6,M8,S1,T3,W4,W6,Y4 Reducing hospital mortality is surely possible and has been documented in studies showing a reduction from 21% (17/82; CL 16%–26%) for operations performed prior to 1987 to 3.4% (1/29; CL 0.6%–11%) for those performed between 1987 and 1996.11

Time-Related Survival  The 1-month and 1-, 5-, 10-, and 20-year survivors after repair of important coexisting cardiac anomalies in heterogeneous groups of patients with CCTGA repaired over the past 35 years have been about 88%, 80%, 76%, and 46%, respectively, including hospital deaths.11,12,Y8 In more recent experience, close to 90% 10-year survival has been demonstrated in a risk-unadjusted population of patients undergoing surgery for CCTGA.58,Y8 When a later-rising phase of hazard will become evident in patients operated on in the current era is not yet known.

Hrasko and colleagues suggest that time-related survival is best when a Fontan procedure is performed (100% at 5 years), with lower survival in septated patients undergoing VSD closure (75% at 5 years) and even lower survival in septated patients undergoing tricuspid valve surgery (55% at 5 years).311 It should be emphasized that their patients underwent surgery between 1963 and 1996. Hörer and colleagues found similar long-term outcomes in patients undergoing septation and those undergoing a Fontan procedure.315

Morphologic Left Ventricle Supporting Systemic Circulation

Early (Hospital) Death  Early outcomes appear to be as good or better with more complicated double switch procedures (“anatomic repair”) that assign the morphologic LV to the systemic circulation than with the “physiologic” procedures just described. Jahangiri and colleagues reported no mortality in the anatomic repair group (0 of 19 patients; 0%; CL 0%–10%), and 7% mortality in the physiologic repair group (5 of 70 patients; CL 4%–12%), P = .31

In a group of patients with structurally abnormal tricuspid valves, mortality was 11% (1 of 9 patients; CL 1%–33%) following anatomic repair and 33% (5 of 15 patients; CL 19%–50%) following physiologic repair (P for difference = .2).11
Results reported from 10 single institutional experiences between 1993 and 2002 reveal that early mortality for procedures placing the morphologic LV in the systemic circulation compares favorably with that of simpler, more classic repairs. In these 10 studies, early mortality ranged from 0% to 14%. Each experience was small, with a combined total of 150 patients with 11 early deaths (7.3%; CL 5.1%-10%).12,13,15,K2,R2,S5,S11,S12

Reports between 2002 and 2010 have larger numbers of patients and confirm that early mortality can be low. In three recent large single-institution studies, early mortality was 0% (46 patients; CL 0%-4.0%),14,15 2.1% (1 of 48 patients; CL 0.3%-6.8%),14 and 6.8% (3 of 44 patients; CL 3.0%-13%).15 These studies included both the arterial switch type and the Rastelli type of double switch. In another study focusing on 20 patients with the arterial switch type of double switch only, there was no early mortality.19 Other large series report early mortality of about 15%.57 Most studies show similar early mortality of the two major double switch operations, but Gaies et al. found a difference, with 94% early survival (33 of 35 patients; CL 87%-98%) in the arterial switch type and 77% survival (23 of 30 patients; CL 66%-85%) in the Rastelli type.41

**Time-Related Survival** Recent data suggest midterm survival is excellent. Two studies with follow-up extending to 15 years (mean 5 years) show no intermediate mortality.13,41 Another shows 15-year survival of 75% in patients with the arterial switch type of double switch and 80% in patients with the Rastelli type.58 Still another study of 45 patients (38 underwent the Rastelli type and 7 the arterial switch type) showed survival of 84% at 5 years and 78% at 10 years.60 As with early mortality, most studies show similar time-related survival of the two major double switch operations, but the Gaies group reported a substantial difference, with 10-year survival of 91% in the arterial switch type and 55% in the Rastelli type.41

**Modes of Death**

Some patients die suddenly.58,60 This has even been noted when operation places the morphologic LV as the systemic ventricle,51; however, one large study suggests that it is more common following anatomic repair than physiologic repair.58 Whether this is due to sudden appearance of complete heart block with ventricular asystole or fibrillation or to pacemaker failure or change in conductance of leads is unknown. Well-documented progression of morphologic RV dysfunction and tricuspid valve regurgitation when these structures are in the systemic circulation no doubt play a role, particularly in those dying from low-output state and heart failure.51 Table 55-1 shows cause of death in one series of 151 patients.58

### Incremental Risk Factors for Death

Systemic tricuspid valve regurgitation is a risk factor for death.12,38,58 Studies identifying Ebstein anomaly and tricuspid valve replacement as risk factors are probably identifying the same underlying problem of systemic tricuspid valve regurgitation.12,51 Risk factors for death following anatomic repair have been identified and include left ventricular training using a pulmonary artery band and severe preoperative RV failure.52,58 Inclusion of a bidirectional cavopulmonary anastomosis as part of the repair has a survival benefit.58 Reasons for lower survival in patients with CCTGA than that observed after repair of VSD, AV septal defect, tetralogy of Fallot, or transposition with AV concordant connection are not evident, even after risk adjustment. Speculatively, the major reasons may be abnormalities of the conduction system, imperfection of methods used to prevent and manage heart block, and abnormalities of systemic (right) ventricular function. It follows that patients receiving anatomic repair, although subject to the same conduction risks, would not have the additional risk of the systemic RV. In an analysis of 40 patients with a mean follow-up of 20 years, important regurgitation of the systemic tricuspid valve was found to be the major risk factor for death.50 In another study,31 presence of an abnormal systemic tricuspid valve resulted in early mortality of 33% (5 of 15 patients; CL 19%-50%) when the morphologic RV was assigned to the systemic circulation. Another study examining both anatomic and physiologic repair identified tricuspid regurgitation as a risk factor for physiologic but not anatomic repair patients.58 Subsequent studies show both early and late survival after anatomic repair to be similar to survival following repair of the other index lesions mentioned.15,41,19,51 This improvement is probably due to multiple factors including presence of a systemic LV,

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**Table 55-1 Causes of Early and Late Death in 151 Patients**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Physiologic Repair (n = 67)</th>
<th>Anatomic Repair (n = 84)</th>
<th>Fontan (n = 38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>CL (%)</td>
<td>No.</td>
</tr>
<tr>
<td>Low-output syndrome</td>
<td>4</td>
<td>6.0</td>
<td>3</td>
</tr>
<tr>
<td>Heart failure</td>
<td>8</td>
<td>12.0</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Infection</td>
<td>2</td>
<td>3.0</td>
<td>3</td>
</tr>
<tr>
<td>Arrhythmia/sudden death</td>
<td>1</td>
<td>1.5</td>
<td>5</td>
</tr>
<tr>
<td>Noncardiac</td>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Cerebral damage</td>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>1.5</td>
<td>1</td>
</tr>
</tbody>
</table>

Adapted from Shin’oka and colleagues (Table E1).58
Multivariable analysis indicates that chordal straddling or insertion on the septal crest (usually from the left-sided tricuspid valve) increases the probability of producing complete heart block at the time of VSD repair (Table 55-3). This arrangement may prevent surgeons from placing sutures precisely where they prefer them. Presumably, placing the LV in the systemic circulation should have little effect on these rhythm complications. Malhotra and colleagues noted that 21% of patients developed complete heart block following surgery in a series of 48 double switches. In patients with complete heart block and systemic RV failure, improved ventricular function has been demonstrated in selected individuals by upgrading the pacing system to a biventricular system to achieve cardiac resynchronization.

Development of Tricuspid Valve Regurgitation

Immediately after simple classic repair of CCTGA with VSD, left-sided tricuspid valve regurgitation sometimes appears. Fox and colleagues reported this to have occurred immediately after repair in 6 of 14 patients (43%; CL 27%-60%) in whom it was not present before operation. Westerman and colleagues observed the same phenomenon. Its mechanism is not completely understood, but as best as can be determined, regurgitation does not result from direct damage to valvar tissue or chordae. Rather, its mechanism when the tricuspid valve is abnormal is primarily related to decreased morphologic LV pressure after VSD closure, resulting in shifting of the ventricular septum toward the morphologic LV side. It seems likely a similar mechanism is involved when the tricuspid valve is normal.

Operations assigning the morphologic LV to the systemic circulation result in improved tricuspid valve function, increased experience with the complex procedures involved in anatomic repair, and improved management of conduction problems. In the meta-analysis performed by Alghamdi and colleagues, anatomic repair—in particular anatomic repair of the Rastelli type—had a beneficial effect on early survival compared with physiologic repair.

Reoperation

Reoperation is common after all types of surgery for CCTGA except for the Fontan operation. The morphology of associated cardiac defects and the type of operation both influence the prevalence of reoperation (Fig. 55-20). Common causes for reoperation are those to be expected: heart block, ventricular-to-pulmonary trunk conduit obstruction or regurgitation, and systemic tricuspid valve regurgitation.

Postrepair Complete Heart Block

It was anticipated that a repair (see Technique of Operation earlier) based on secure knowledge of location of the cardiac conduction system would eliminate complete heart block as a complication of VSD repair in patients with CCTGA. Such has not been the case. In all reported series, prevalence has been 15% to 30% (Table 55-2). This is very different from the near-zero prevalence after repair of VSD in hearts with AV concordant connection. Westerman and colleagues observed the same phenomenon. Its mechanism is not completely understood, but as best as can be determined, regurgitation does not result from direct damage to valvar tissue or chordae. Rather, its mechanism when the tricuspid valve is abnormal is primarily related to decreased morphologic LV pressure after VSD closure, resulting in shifting of the ventricular septum toward the morphologic LV side. It seems likely a similar mechanism is involved when the tricuspid valve is normal.

Operations assigning the morphologic LV to the systemic circulation result in improved tricuspid valve function,
Table 55-2 Heart Block after Operation in Patients with Congenitally Corrected Transposition of the Great Arteries

<table>
<thead>
<tr>
<th>Operation</th>
<th>n</th>
<th>Preoperative Complete Heart Block</th>
<th>Postoperative Permanent Complete Heart Block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repair VSD</td>
<td>16</td>
<td>2</td>
<td>5-31</td>
</tr>
<tr>
<td>Repair VSD + PS</td>
<td>15</td>
<td>1</td>
<td>10-38</td>
</tr>
<tr>
<td>Repair VSD + valved extracardiac conduit to PT</td>
<td>26</td>
<td>3</td>
<td>16-39</td>
</tr>
<tr>
<td>Tricuspid valve repair</td>
<td>1</td>
<td>0</td>
<td>0-85</td>
</tr>
<tr>
<td>Tricuspid valve replacement</td>
<td>5</td>
<td>1</td>
<td>0-38</td>
</tr>
<tr>
<td>With VSD repair</td>
<td>8</td>
<td>2</td>
<td>2-46</td>
</tr>
<tr>
<td>With VSD + PS repair</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>With VSD repair + CABG</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Repair ASD</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Fontan-type operation</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>75</td>
<td>10</td>
<td>13 (CL 9-9)</td>
</tr>
</tbody>
</table>

Data from McGrath and colleagues.\textsuperscript{1,6}

\textsuperscript{1}Heart block developed in 0 (0%; CL 0%-24%) of 7 patients whose repair did not include closure of a VSD and in 12 (21%; CL 15%-28%) of 58 who had a VSD closed as part of the procedure \((P\text{Fisher}) = .22\).

\textsuperscript{2}In one, complete heart block preoperatively was episodic and was permanent after repair.

Key: ASD, Atrial septal defect; CABG, coronary artery bypass grafting; CL, 70% confidence limits; PS, pulmonary stenosis; PT, pulmonary trunk; VSD, ventricular septal defect.

Table 55-3 Incremental Risk Factors for Development of Complete Heart Block in Patients with Atrioventricular Discordant Connection Undergoing Closure of a Ventricular Septal Defect

<table>
<thead>
<tr>
<th>Incremental Risk Factors</th>
<th>Logistic Coefficient ± SD</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Older)</td>
<td>1.0 ± 0.38</td>
<td>.009</td>
</tr>
<tr>
<td>Morphology other than CCTGA</td>
<td>1.0 ± 0.62</td>
<td>.10</td>
</tr>
<tr>
<td>Chordae straddling or attaching to edge of VSD</td>
<td>1.6 ± 0.66</td>
<td>.01</td>
</tr>
</tbody>
</table>

Data from McGrath and colleagues.\textsuperscript{1,6}

\textsuperscript{1}Patients with complete heart block before repair were excluded. Excluded also were patients \((n = 9)\) in whom repair did not include either closure of the VSD or an intraventricular tunnel repair, because developed heart block was limited to these two groups.

Key: CCTGA, Congenitally corrected transposition of the great arteries; VSD, ventricular septal defect.

probably for two reasons: the pressure in the morphologic RV is markedly reduced, and the ventricular septum is shifted toward the morphologic RV.\textsuperscript{1,3,12,41} This hypothesis is further supported by the work of Kollars and colleagues, who showed not only that systemic tricuspid valve regurgitation improved by increasing LV pressure with pulmonary artery banding but also that tricuspid regurgitation became worse in patients in whom LV pressure was reduced to less than half of systemic levels with an LV-to–pulmonary trunk conduit.\textsuperscript{110} It also may be associated with development of complete heart block.\textsuperscript{64}

Tricuspid regurgitation may be sufficiently severe to require later valve replacement. Attempts at valve repair when the valve is in the systemic circulation are usually futile.\textsuperscript{1,63} In one series of 52 patients with up to 10 years of follow-up, tricuspid valve regurgitation was severe enough to require reoperation in 12 (24%).\textsuperscript{13} When the RV is placed in the pulmonary circulation, tricuspid valve function typically improves, often without specifically surgically addressing the valve.\textsuperscript{13,15,21,41}

Functional Status

In the study by Malhotra and colleagues in which all patients underwent anatomic repair, 91% were in New York Heart Association (NYHA) class I postoperatively.\textsuperscript{41} Similar functional outcome has been reported by others following anatomic repair.\textsuperscript{\textsuperscript{11}} In the multicenter study of Graham and colleagues of patients with physiologic or no repair, 60% of those with associated defects were in NYHA class I, and 70% of patients without associated defects were in NYHA class I.\textsuperscript{65} Despite these functional class findings, the same study showed that by age 45 years, clinical heart failure was present in 67% of those with associated lesions and 25% of those without associated lesions; moderate or severe systemic RV dysfunction was present in 56% and 32%, respectively.\textsuperscript{65} Hraska and colleagues showed that only 40% of physiologically repaired patients were free of RV failure at 15 years.\textsuperscript{41}

Ventricular Function

The preponderance of evidence suggests that the systemic RV functions abnormally in unoperated patients at rest, even if they are asymptomatic.\textsuperscript{65} If some form of physiologic repair has been performed, these preoperative abnormalities are more severe. Ischemia appears to play an underlying role in deterioration in most cases, along with other hemodynamic stresses such as volume overload from tricuspid regurgitation. Systemic RVs commonly show evidence of deterioration over time. Giardini and colleagues studied 34 patients at a mean age of 25 years with either CCTGA not undergoing anatomic repair or simple TGA following atrial baffles surgery.\textsuperscript{43} The groups were similar. Abnormal myocardial fibrosis, determined by late gadolinium enhancement at MRI, was found...
in 41%. These findings were associated with RV dysfunction, poor exercise tolerance, arrhythmias, and progressive clinical deterioration. However, normal systemic RV systolic function late postoperatively has been found in some patients. The rule is that after physiologic repair, even asymptomatic adult patients demonstrate abnormalities of the systemic RV, including reduced resting and stress ejection fraction, large ventricular volumes, and regional wall motion abnormalities. Asymptomatic patients also demonstrate a neurohormonal profile typical of heart failure. Additionally, systemic RV coronary flow reserve is reduced, even in unoperated patients and those with isolated CCTGA, with both ischemic and persistent perfusion defects.

When surgery involves placing the morphologic LV in the systemic circulation, early and midterm follow-up studies demonstrate both well-maintained LV and RV function. However, late systemic LV dysfunction has been observed, mostly in association with prior LV training and in patients with complete heart block requiring pacemakers.

**INDICATIONS FOR OPERATION**

CCTGA per se is not a definitive indication for a reparative operation. On the other hand, the natural history of the morphologic RV in the systemic circulation presents enough concern that the question of performing a double switch procedure should be left open. When VSD coexists, indications for operation are those for repair of VSD in otherwise normal hearts (see Indications for Operation in Section I of Chapter 35).

When VSD and important pulmonary stenosis coexist, repair may require an allograft-valved extracardiac conduit; surgical indications and staging are therefore the same as described for tetralogy of Fallot with pulmonary atresia (see Indications for Operation in Section II of Chapter 38). When important left-sided tricuspid regurgitation coexists, indications for operation are the same as those described for acquired mitral regurgitation (see Indications for Operation in Section I of Chapter 11). When complete heart block develops, indications and techniques for pacemaker intervention are those described in Technique of Intervention in Section I of Chapter 16.

Certain morphologic characteristics may increase difficulty of the various septation procedures described in this chapter: (1) presence of straddling tricuspid chordae—increasing complexity of the surgery and risk of postoperative complete heart block, (2) AV septal defect, and (3) non-committed VSD with pulmonary stenosis. These, among others, may be considered by some to be indications for a Fontan rather than a biventricular repair. Whatever the initial interventions, patients may ultimately develop a situation in which only cardiac transplantation can be effective.

**SPECIAL SITUATIONS AND CONTROVERSIES**

**Anatomic versus Physiologic Repair**

Definitive data are unavailable to determine whether long-term outcome is better in CCTGA with the morphologic RV or LV in the systemic circulation. A multicenter retrospective study of 167 patients undergoing repair did, however, show that long-term systemic AV valve function and systemic ventricular function were better in patients undergoing a double switch type operation compared with those undergoing physiologic repair (Fig. 55-21). Surgical procedures are simpler technically when the morphologic RV is assigned to the systemic circulation, in theory reducing both short- and long-term complications related to reconstruction. However, available data from the same study indicate that surgically induced arrhythmias and reoperation are not higher in the more complex anatomic repair group (Fig. 55-22). Operative, midterm, and late mortalities following procedures placing the LV in the systemic circulation have been well documented over the past decade and are excellent.

Even prior to 1998, superiority of the anatomic repair was evident. The meta-analysis of 11 different studies (in which all dates of operation were 1998 or earlier) performed by Alghamdi and colleagues showed that anatomic repair of the Rastelli type had superior outcomes to physiologic repair. In a limited study of nine patients who underwent a procedure assigning the morphologic LV to the systemic circulation and six who underwent a procedure assigning the morphologic RV to the systemic circulation, exercise capacity was equivalent, but this does not mean exercise capacity was normal. Other studies testing patients after both anatomic and physiologic repair reveal that oxygen uptake, exercise duration, heart rate responses, and other variables measured are subnormal.

**Left Ventricular Training**

An important variable that must be considered when assessing long-term outcome following the double switch is whether it is necessary to train the morphologic LV with a pulmonary artery band. This situation arises only when the double switch is being considered in patients in whom the LV myocardial mass has involuted because it has been functioning at low pressure—that is, when CCTGA is present without VSD or pulmonary stenosis.

Although definitive evidence is lacking that trained LVs are functionally different from normal, there is concern and some suggestion that when placed in the systemic circulation, involuted LVs trained with a band may not perform as well as those that never involuted. Comparing trained LVs and those not requiring training, Quinn and colleagues showed that the early outcome after the double switch was similar for mortality and LV function, but there was increased risk of LV deterioration and death or transplantation over time in the trained LV group. Lim and colleagues suggest that LV training is a risk factor for death after anatomic repair. However, Bautista-Hernandez and colleagues showed that after anatomic repair, there was no reduction in LV function and no deaths at midterm follow-up in the cohort of patients who had received LV training with a band.

An important factor that limits drawing definitive conclusions about the adequacy of the trained LV is that there are currently no standardized criteria for defining when an LV is trained. Thus, any reduction in function of trained LVs following anatomic repair may represent an intrinsic limitation of the trained LV itself, or the fact that an adequate training protocol was not in place. It is clear that some LVs do not respond to training, and these patients never become candidates for a double switch procedure.
Use of Bidirectional Superior Cavopulmonary Anastomosis

Use of the bidirectional superior cavopulmonary anastomosis with hemi-Mustard atrial baffle, either selectively or exclusively, as part of operations for CCTGA when the morphologic LV is placed in the systemic circulation has a number of specific advantages:

- It may benefit the small or poorly functioning RV.
- It importantly reduces complexity of the atrial baffle procedure.
- It eliminates complications related to the superior limb of the atrial baffle.
- It reduces flow across an RV–pulmonary trunk conduit.
- It likely increases conduit longevity.
The study by Malhotra and colleagues documents that RV–pulmonary artery conduits have increased longevity when a bidirectional superior cavopulmonary anastomosis is used. Lim and colleagues have described improved survival when it is used. In some cases with VSD and moderate pulmonary stenosis, a bidirectional superior cavopulmonary anastomosis may allow use of the small native pulmonary valve as an adequate structure for RV outflow, avoiding a prosthetic conduit. In this operation, the native pulmonary valve and anulus, in continuity with the pulmonary trunk, are removed from the LV outflow tract intact and transposed onto the RV infundibulum. The resulting opening in the LV outflow tract is closed with a patch, and the LV is baffled to the aorta with an intraventricular tunnel. The bidirectional cavopulmonary anastomosis and hemi-Mustard can also be helpful when constructing a full atrial baffle is difficult, such as in patients with juxtaposition of the ventricular apex and inferior vena cava, as found in mesocardia or dextrocardia with situs solitus. The bidirectional superior cavopulmonary anastomosis can also be used in specific cases when physiologic repair is performed.

Fontan versus Intracardiac Repair

After weighing the benefits and risks of performing the complex procedures described in this chapter versus those of a Fontan operation, one study concludes that the Fontan operation is advisable. Many surgeons disagree, and recent outcomes after any of the various procedures that use the double switch concept or physiologic repair concept support their position. Reoperation is almost certainly higher after operations (both anatomic and physiologic) that separte the heart in CCTGA than for the Fontan, at least up to midterm follow-up (see Fig. 55-20).

Neonatal Congenitally Corrected Transposition of the Great Arteries without Associated Cardiac Anomalies

The era of anatomic repair presents an interesting possibility for patients with CCTGA without associated lesions. Compared with normal control subjects, these patients are considered to have a reasonable prognosis without intervention, but a number of studies document that abnormal systemic RV function and even RV failure with systemic AV valve regurgitation are much more likely to occur over time, usually over decades. The question arises whether anatomic repair would benefit them. Although there is no evidence available to answer this question, it has been posed by many in the field.

If it is hypothesized that anatomic repair is beneficial, it can be argued that the neonatal period would be the optimal time for surgery to take advantage of the prepared LV. Allowing the LV to involute, followed by retraining with a pulmonary artery band, before anatomic repair is much less attractive because of concerns about the function of a retrained LV. To date, there are no reports of elective neonatal anatomic repair in asymptomatic patients with this anatomic profile. Bautista-Hernandez and colleagues report successful neonatal anatomic repair in two patients with Ebstein-like changes of the systemic AV valve and severe regurgitation with severe heart failure.

An alternative to neonatal anatomic repair in asymptomatic patients without associated cardiac anomalies is neonatal placement of a band, thereby preventing LV involution. Metton and colleagues have placed bands in 11 asymptomatic neonates and infants with isolated CCTGA. Some degree of systemic AV valve regurgitation was present preoperatively in eight patients and depressed systemic RV function in two. The band procedure was performed without mortality, but five patients required inotropic support. There was one late death. In the remainder, there was no progression of systemic AV valve regurgitation in seven and improvement in three. Only one patient has undergone anatomic repair, successfully. The others are candidates, having preserved LV mass and function.

Section II Other Forms of Atrioventricular Discordant Connection

DEFINITION

Atrioventricular discordant connection is a congenital cardiac anomaly in which the right atrium connects to the LV and the left atrium connects to the RV (see “Cardiac Chambers and Major Vessels” in Chapter 1). When AV discordant connection occurs in atrial situs solitus, there is ventricular L-loop (left handedness of the ventricular internal architecture), when it occurs in atrial situs inversus, there is ventricular D-loop (right handedness).

Conditions with AV discordant connection (other than CCTGA, covered earlier) are discussed together in this section. Were accumulated experience large enough, each of the other subsets would deserve separate chapters, just as in the setting of AV concordant connection.

HISTORICAL NOTE

History of development of knowledge and surgical treatment of CCTGA is discussed in Section I. The time of first recognition of AV discordant connection associated with double outlet right ventricle (DORV) is not clear, but as late as 1960 the entity was not distinguished from DORV with concordant AV connection. Ruttenberg and colleagues described DORV coexisting with AV discordant connection in 1964. In 1965, this type of DORV (with VSD and pulmonary stenosis) was recognized and repaired using an extracardiac conduit for rerouting pulmonary blood flow, perhaps for the first time. Double outlet left ventricle (DOLV) associated with AV discordant connection is rare; the first surgical case was reported in 1976 by Brandt and colleagues. Isolated ventricular inversion was named by Van Praagh in 1966 when he described one such case, but a similar malformation had been reported by Ratner, Abbott, and Beattle in 1921 and by Lev and Rowlett in 1961. In 1975, Quero-Jimenez and colleagues reviewed six reported cases, as noted in Section 1 of this chapter, the adjectives left and right used to modify atrium or ventricle always mean morphologically right or left. Position of the chamber is referred to as right-sided or left-sided.
including two of their own.\textsuperscript{Q1} Isolated atrial inversion was named when the first such case was reported in 1972.\textsuperscript{C6}

**MORPHOLOGY**

Among hearts with AV discordant connection, there is great variability in ventriculoarterial connections and in many other morphologic details.\textsuperscript{A4}

**Ventricular Architecture**

The ventricles are said to be inverted, but because many ventricular positional anomalies occur, the term ventricular inversion is not very useful; it is necessary to describe the internal architecture of each ventricle more specifically. A convenient way of doing this is with Van Praagh's terms ventricular D-loop and ventricular L-loop, defined in Chapter 1 (see “Situs of the Ventricles” under Terminology and Classification of Heart Disease in Chapter 1), or right handedness and left handedness,\textsuperscript{C9,Q1,V1,V6} also defined in Chapter 1.

**Ventricular Position and Rotation**

In patients with atrial situs solitus, the RV is generally left sided and the LV lies side by side and to the right of it. The entire length of the ventricular septum is usually visualized in profile in an anteroposterior view during diagnostic imaging. However, there are variations in anterosuperior orientation of the ventricles and variations in their rotation (see “Cardiac and Arterial Positions” under Terminology and Classification of Heart Disease in Chapter 1).

**Positional Anomalies**

An extreme variation of anterosuperior position occurs in so-called superior-inferior ventricles (“over-and-under” or “upstairs-downstairs” ventricles). The septum is not vertically oriented, as is usual in AV discordant connection, but horizontal, and the LV lies inferiorly and RV superiorly. This may have been described first by Kinsley and colleagues.\textsuperscript{E3} When ventricles are positioned in this manner, there is usually AV discordant connection, an inlet VSD, and DORV.\textsuperscript{L3,E4} One chamber may be hypoplastic, and there may be AV valve straddling. Rarely, superior-inferior ventricle position is associated with AV discordant connection and DORV (see “Double Outlet Right Ventricle with Superior-Inferior Ventricles” under Morphology in Chapter 53).

**Rotational Anomalies**

When rotational anomalies are present, even more bizarre situations occur. Although the LV inlet portion generally remains on the right side in patients with atrial situs solitus, trabecular and outlet portions may be left sided and present a confusing picture.\textsuperscript{A9,V3} Generally, however, the ventricular septum is in the coronal plane, the LV is posterior, and the RV anterior. In the domain of these extreme rotational anomalies, criss-cross pathways occur in which inflow pathways of the ventricles appear to cross rather than being parallel.\textsuperscript{A15,F3,F4,S14,T6} Then the question arises as to whether an AV discordant connection necessarily implies ventricular L-loop (or left handedness) in atrial situs solitus, and D-loop or (right handedness) in atrial situs inversus. In this text, the assumption is made that it does, although this may not always be the case.\textsuperscript{D12}

**Ventricular Size**

Varying degrees of hypoplasia of the left-sided RV may be present.\textsuperscript{E3} When the ventricles are in a superior-inferior position, the LV may be hypoplastic. Ventricular hypoplasia is frequently associated with straddling and overriding of the AV valve of the hypoplastic ventricle.

**Cardiac Position**

Dextrocardia occurs in about 25% of cases with atrial situs solitus, and rarely levocardia exists when the atrial situs is inverted.\textsuperscript{C2}

**Ventriculoarterial Connection**

**Discordant Connection**

The morphology of congenitally corrected transposition of the great arteries (AV discordant connection and ventriculoarterial discordant connection) is described in Section I.

**Double Outlet Right Ventricle**

Double outlet left-sided RV may coexist with situs solitus and AV discordant connection (L-loop), and in nearly all cases VSD and pulmonary stenosis coexist. Because the left-sided RV is the systemic ventricle, cyanosis is not a necessary result of the ventriculoarterial connection, but of associated pulmonary stenosis. The apex of the heart may point to the right (dextrocardia with atrial situs solitus and ventricular L-loop).\textsuperscript{E4} The aorta is usually in L-malposition but may be in any position. The VSD is usually very distal in the septum and beneath the adjacent great arteries (usually pulmonary) but can be anywhere.

The pulmonary trunk is not in a wedged position. Probably related to this, location of the conduction system tends to be different from that in corrected transposition (see “Atrioventricular Node and Bundle of His” later).\textsuperscript{L7} This entity is closely related to corrected transposition with VSD in which the pulmonary trunk partially overrides the VSD and partly arises over the left-sided RV. Corrected transposition is the appropriate diagnosis when there is fibrous continuity between the pulmonary and mitral valves. When there is lack of continuity between these valves, there is subpulmonic conus muscle, and the case is assigned the diagnosis of AV discordant connection with DORV. In most cases of DORV and AV discordant connection, the pulmonary trunk is nearly completely over the left-sided RV.

**Double Outlet Left Ventricle**

DOLV may coexist with AV discordant connection.\textsuperscript{B17,S12,V5} Because the right-sided LV is the pulmonary ventricle, cyanosis is the necessary result. The VSD is in a position similar to that in DORV with AV discordant connection, but the aorta overrides the VSD to such an extent that it emerges wholly or in large part from the right-sided LV. This may occur in patients with atrial situs inversus.\textsuperscript{A3}

**Concordant Connection**

Ventriculoarterial concordant connection is unusual in AV discordant connection and is of two types: isolated ventricular inversion\textsuperscript{Q1,V2} and isolated atrial inversion.\textsuperscript{C6} The systemic and pulmonary circulations are parallel, and the physiology is that of ordinary transposition of the great arteries (see “Essentially
Intact Ventricular Septum [Poor Mixing] under Clinical Features and Diagnostic Criteria in Chapter 52), and cyanosis results.

In isolated ventricular inversion with atrial situs solitus, as originally defined,\(^{22}\) the aortic origin lies to the right and posterior to the pulmonary trunk origin, and there is aortic-mitral fibrous continuity and a muscular subpulmonary infundibulum (conus), as in the normal heart. However, there is AV discordant connection, and the aorta arises from a right-sided LV; for this reason, both great arteries are parallel. Other variations exist and are due to positioning of the great arteries and presence or absence of a subaortic and subpulmonary conus.\(^{23}\) A VSD may be present; pulmonary stenosis is generally absent.\(^{24}\) When there is situs inversus, a mirror-image pattern occurs.\(^{21,23}\)

As in CCTGA, the inverted ventricles in patients with isolated atrial or ventricular inversion usually lie side by side with the ventricular septum in a sagittal plane and have a coronary artery distribution pattern similar to that in CCTGA (see Morphology in Section I). It is important surgically to note that in isolated ventricular inversion, the right-sided left coronary artery does not cross in front of the pulmonary outflow, so its enlargement anteriorly is feasible. Although Losekoot and colleagues have suggested that the conduction tissue will be as for CCTGA,\(^{25}\) position of cardiac conduction tissue in this condition is at present uncertain.

In isolated atrial inversion, there is atrial situs inversus with ventricular D-loop and dextrocardia with fibrous aortic-mitral continuity and a subpulmonary conus (Fig. 55-23, A, model 3). However, in a case reported by Clarkson\(^{16}\) (Fig. 55-24), the great arteries crossed in a virtually normal fashion, with the morphologic RV lying to the right and posterior to the morphologic LV. The unusual feature of this heart was viscerocorial discordance, with abdominal organs in situs solitus position and the atria (and their venous connections) inverted. This rare additional feature did not alter the circulatory pathways from those present in isolated ventricular inversion.

In addition to the heart just described, there are others with identical connections but conal development that is the reverse of that described in isolated ventricular inversion (see Fig. 55-23, B, models 2 and 3). That is, the aorta arises from the morphologic LV and lies, in a situs solitus heart, to the right of the pulmonary trunk, but it is separated from the mitral valve by a muscular subaortic conus. Under these circumstances, there is usually pulmonary-tricuspid fibrous continuity, but a subpulmonary conus may also (rarely) be present. These hearts can be considered to have anatomically corrected malposition of the great arteries,\(^{22}\) or contrariwise (as in this text) a variant within the general category of AV discordant connection and ventriculocardiacal concordant connection.

Atrioventricular Node and Bundle of His

The AV conduction tissue is abnormal in most patients with AV discordant connection and typically so in the subset of CCTGA with atrial situs solitus, where an anterior AV node gives rise to the bundle of His (see “Atrioventricular Node and Bundle of His” under Morphology in Section I).

When DORV coexists and left-sided RV wedging of the pulmonary trunk is not present, both anterior and posterior AV nodes usually persist, connected by a sling of conduction tissue around the VSD, which continues on as the branching bundle.\(^{17}\) However, only the anterior AV node or the regular
posterior one gives rise to the penetrating bundle. This variability may predispose patients to surgically induced complete heart block.

When there is DOLV, the AV node connecting to the penetrating bundle is usually the anterior one. Duplicated, or twin, AV nodes may exist, especially in the presence of malaligned AV septal defect. Reciprocating tachycardia may then be present. Position of conduction tissue is uncertain in patients with isolated ventricular or atrial inversion.

Accessory Conduction Pathways

Kent bundles may occur, particularly in those with CCTGA, and may give rise to preexcitation and the Wolf-Parkinson-White syndrome (see “Wolf-Parkinson-White Syndrome” in Section III of Chapter 16). Kent bundles may be in the posterior wall of the left-sided RV or posterolateral wall of the right-sided LV. It is presumed by Harrati and colleagues that the relative frequency of these findings is associated with the high prevalence of Ebstein anomaly of the left-sided tricuspid valve in these cases.

Coronary Arteries

Coronary arteries are abnormal, but appropriate terminology for describing them is controversial. The simple terms right-sided and left-sided seem best. The right-sided coronary artery, arising from the right posterior coronary sinus and analogous to the normal left coronary artery, gives rise to the anterior descending coronary artery, coursing from right to left, and circumflex artery. The left-sided coronary artery arises from the left posterior aortic sinus and passes around the left-sided tricuspid orifice, usually to become the posterior descending artery on the back of the heart.

Atroventricular Valves

The right-sided mitral valve typically has two leaflets and usually is in fibrous continuity with the pulmonary valve. As in the normal heart, it has no septal attachments but rather has typically paired papillary muscles.

The left-sided tricuspid valve consists of three leaflets. The septal leaflet, and often the posterior (inferior) leaflet, is displaced more than normally into the ventricle, but the deformity is not typically an Ebstein anomaly of the left-sided tricuspid valve in these cases.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

The clinical features of patients with AV discordant connection vary widely, depending on ventriculoarterial connection and associated cardiac anomalies, most commonly VSD or pulmonary stenosis. Thus, there is no typical clinical picture.

Double Outlet Right Ventricle and Double Outlet Left Ventricle

There is no characteristic presentation of either DORV or DOLV coexisting with AV discordant connection. However, because with DORV there is usually coexisting pulmonary stenosis, cyanosis is usually evident; and because in this setting with DOLV the aorta arises from the ventricle receiving systemic venous blood (see Morphology earlier in this section), cyanosis is evident. Diagnosis is made by the same methods as described for CCTGA (see Section I). Echocardiography can usually define the morphology definitively, even in very complex cases.

Isolated Ventricular or Atrial Inversion

Patients present similarly to those with complete transposition of the great arteries (see Clinical Features and Diagnostic Criteria in Chapter 41). When the ventricular septum is intact, there is severe cyanosis in infancy; when there is a large VSD, moderate cyanosis is accompanied by heart failure and cardiomegaly. Pulmonary stenosis adds to degree of cyanosis. Diagnosis is made by the same methods as described for corrected transposition (see Section I). Cineangiography has been important in the past for definitive diagnosis (Fig. 55-25), but now two-dimensional echocardiography is extremely reliable, even in this complex setting.

NATURAL HISTORY

Most of the information concerning natural history drawn from patients with CCTGA is discussed in Section I. Other morphologic findings may affect natural history. For example, patients with situs inversus are more likely to have DORV and tetralogy of Fallot physiology, but less likely to have systemic AV valve regurgitation and heart block than patients with situs solitus.

TECHNIQUE OF OPERATION

Except for CCTGA, most malformations associated with AV discordant connection require complex and often unique operations, and only their general nature can be described.
is less complete. Further, there is controversy as to whether a completely intraventricular repair is adequate or whether a valved extracardiac conduit between LV and the pulmonary trunk is usually necessary.\textsuperscript{34,47} In part because of the data presented by Tabry and colleagues\textsuperscript{71,75} and in part because important subpulmonary stenosis is usually present, use of a valved extracardiac conduit has been preferred. However, the concepts underlying the Lecompte, or REV (réparation à l’étage ventriculaire), operation (see “Lecompte Intraventricular Repair” under Technique of Operation in Chapter 53) may well be applicable in this and other subsets of AV discordant connection and would avoid use of an extracardiac conduit. Also, various double switch operations may be applicable (see Technique of Operation in Section I).

**Double Outlet Left Ventricle**

The preferred surgical option consists of leaving the aorta with the right-sided LV, connecting pulmonary trunk to RV with a conduit, and performing an atrial switch operation\textsuperscript{812} utilizing the double switch concept described under Technique of Operation in Section I.

The alternative physiologic repair, an intraventricular tunnel repair, may be used (see “Intraventricular Tunnel Repair of Simple Double Outlet Right Ventricle” in Chapter 53) and constructed so as to conduct blood from the left-sided RV (in atrial situs solitus) through the VSD and then to the aorta. Sutures between the polyester patch for the tunnel and the ventricular septum are placed with due regard for location of the conducting tissue (see “Double Outlet Right Ventricle and Pulmonary Stenosis” earlier in this section). On occasion, it may be possible to do this repair without obstructing LV access to the pulmonary trunk. However, if access is compromised or if pulmonary stenosis is present, an allograft-valved extracardiac conduit is placed between the LV and the pulmonary trunk (see Technique of Operation in Section I) or a Lecompte procedure (REV) performed (see “Lecompte Intraventricular Repair” under Technique of Operation in Chapter 53).

**Isolated Ventricular or Atrial Inversion**

When the ventricular septum is intact, balloon septotomy is required in infancy, followed by an atrial switch operation (see Technique of Operation in Chapter 52). This returns the circulation functionally and anatomically to normal, because the LV is the systemic ventricle.\textsuperscript{59}

When there is a large VSD, it is closed through the left-sided RV in a fashion similar to that for primary VSD (presuming the bundle lies on the LV side) or from the right atrium.\textsuperscript{82} An atrial switch operation is then performed.\textsuperscript{117}

**Placing Epicardial Pacemaker Leads**

When complete heart block is present preoperatively or develops intraoperatively, and when in sinus rhythm the PR interval is long, permanent epicardial atrial and ventricular pacemaking leads are placed and connected to a permanent pacemaker pulse generator placed subcutaneously (see Technique of Intervention in Section I of Chapter 16 for the details of the technique).
**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Patients are managed with protocols generally used after cardiac surgery (see Chapter 5). Particular attention is paid to cardiac rhythm. When complete heart block is present, AV sequential pacing is advantageous to cardiac output and therefore is used routinely.

**RESULTS**

**Survival**

**Early (Hospital) Death**

Hospital mortality after intracardiac repair of coexisting cardiac anomalies in patients with CCTGA was discussed in detail in Section I. In series reported prior to 1985, mortality was generally higher in patients with AV discordant connection and other types of ventriculoarterial connections such as DORV, DOLV, and isolated ventricular inversion.\textsuperscript{13,31} This is probably related to complexity of the operations required for these conditions, often involving intraventricular rerouting and extracardiac conduits. However, increased knowledge about congenital heart disease, improved surgical techniques, and improved techniques for cardiopulmonary bypass and myocardial management currently allow lower mortalities.\textsuperscript{13,14,39,56,58,59,12,14} This has been verified by recent studies indicating that when either classical repair techniques or the double switch concept are used, outcomes are comparable whether the associated morphology is transposition (CCTGA) or one of the other ventriculoarterial connections.\textsuperscript{81,13,38}

**Time-Related Survival**

Among all patients with AV discordant connection undergoing intraventricular repair prior to 1985, long-term survival has been compromised by a slowly rising late phase of hazard.\textsuperscript{36} The long-term outcome concerns are supported by data from Yeh and colleagues, who show survival of 48% at 20 years.\textsuperscript{34} It is not yet certain that deaths occurring late postoperatively can be prevented as effectively as those occurring early after operation, nor has it yet been demonstrated that the double switch concept benefits long-term outcome.

**Modes of Death**

In the past, most patients dying after early operation had acute or subacute cardiac failure.\textsuperscript{36} Although abnormal ventricular architecture probably contributed to this, current methods, including improved methods of myocardial management, should considerably reduce the prevalence of this mode of death.

Some deaths late postoperatively have been sudden.\textsuperscript{36,48,56} Whether this is due to sudden appearance of unidentified complete heart block with ventricular asystole, ventricular fibrillation related to myocardial dysfunction, or pacemaker failure is unknown.

**Incremental Risk Factors for Death**

Probably AV discordant connection itself is a risk factor for death after intracardiac repair (see “Incremental Risk Factors of Death” in Section I). This is the result of abnormal ventricular architecture (see “Ventricular Function” under Natural History in Section I), abnormalities in the conduction system, problems associated with the tricuspid valve being a part of the systemic circulation, and relative unfamiliarity of even experienced congenital heart surgeons with approach and exposure to the surgical procedures required for this type of congenital heart disease.

Although early-era experience suggested that ventriculoarterial connections other than discordant ones (CCTGA) were risk factors for premature death,\textsuperscript{36} more recent experience does not support the position that ventriculoarterial connections other than discordant ones are risk factors.\textsuperscript{13,14,39,52}

**Postrepair Complete Heart Block**

It is disappointing that reasonably secure knowledge of the location of the bundle of His has not allowed complete heart block to disappear as a postoperative complication of repairing a VSD or constructing an intraventricular tunnel. There is about a 20% risk of developing complete heart block after repair of a VSD (Table 55-4; see also “Postrepair Complete Heart Block” under Results in Section I).

**Table 55-4 Development of Postoperative Complete Heart Block after Intracardiac Repair in Patients with Discordant Atroventricular Connection**

<table>
<thead>
<tr>
<th>Ventriculoarterial Connection</th>
<th>Preoperative Complete Heart Block</th>
<th>Developed Postoperative Complete Heart Block</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>No.</td>
</tr>
<tr>
<td>Discordant\textsuperscript{a}</td>
<td>75</td>
<td>10</td>
</tr>
<tr>
<td>DORV</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>DOLV</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Concordant\textsuperscript{c}</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>SORV</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>99</td>
<td>11</td>
</tr>
<tr>
<td>(P(\chi^2))</td>
<td>45</td>
<td></td>
</tr>
</tbody>
</table>

Data from McGrath and colleagues.\textsuperscript{36}

\(\textsuperscript{a}\)Congenitally corrected transposition of the great arteries.

\(\textsuperscript{b}\)Isolated ventricular inversion.

\(\textsuperscript{c}\)Heart transplant patient not considered at risk.

Key: CL, 70% confidence limits; DOLV, double outlet left ventricle; DORV, double outlet right ventricle; SORV, single outlet right ventricle.
Abandoning ECG monitoring of each stitch\textsuperscript{52} in favor of a repair\textsuperscript{29} based on knowledge of morphology during cold cardioplegic cardiac arrest has not increased the risk of heart block.\textsuperscript{36} Prevalence of surgically induced heart block was not demonstrated to have been reduced by electrophysiologic mapping at surgery.\textsuperscript{28,29}

Risk factors for developing complete heart block are discussed in Section I of this chapter.

Other Outcome Events

The discussions of developing left-sided tricuspid valve regurgitation, functional status, and ventricular function after repair of CCTGA (see Results in Section I) apply to all subsets of patients with AV discordant connection undergoing repair. When indications for cardiac transplantation are present, the procedure should be carried out.\textsuperscript{19,23}

Outcome of valved extracardiac conduits frequently used in repairs for this group of anomalies appears to be the same as for their use in general (see “Reoperations” under Results in Section II of Chapter 38).

INDICATIONS FOR OPERATION

The diagnoses of DORV, DOLV, and isolated ventricular or atrial inversion in patients with AV discordant connection are indications for operation, but each has special considerations.

Isolated ventricular and atrial inversion have un repaired pathophysiology and prognosis similar to that of patients with complete transposition of the great arteries (see “Essentially Intact Ventricular Septum [Poor Mixing]” in Chapter 52). Therefore, repair is indicated, and it should be performed as early in life as possible.

DORV and DOLV in the setting of AV discordant connection usually require a valved extracardiac conduit (or the Lecompte operation [REV]) for repair. Thus, there are advantages to deferring repair until age 3 to 4 years when an adult-sized conduit can be inserted, even though a palliative shunt or pulmonary trunk banding may be required in the interim. Alternatively, primary repair may be done in early life, accepting the likelihood of early conduit replacement.

Knowledge of the concepts and techniques of Lecompte and others (see “Lecompte Intraventricular Repair” under Technique of Operation in Chapter 53) may, in some cases, allow repair without an extracardiac conduit, and this permits repair earlier in life.

When one ventricle is importantly hypoplastic, a Fontan operation can provide the same result as in other single-ventricle patients (see Chapter 41).\textsuperscript{55}

When myocardial function has deteriorated severely, cardiac transplantation can provide the same result as in patients with AV concordant connection. Abnormal positions of the great arteries are not contraindications.

SPECIAL SITUATIONS AND CONTROVERSIES

Many of the controversies surrounding management of CCTGA apply to all subsets of AV discordant connection (see Special Situations and Controversies in Section I).

Intraoperative Electrophysiologic Mapping

The bundle of His can often be identified during cardiac operations by electrophysiologic mapping techniques\textsuperscript{1,13,22} that usually (but not always) allow localization of the bundle and, by implication, locus of the AV node. However, the procedure is cumbersome surgically because the heart must be open but perfused and beating during mapping, which means the patient must be on CPB at a normal or near-normal temperature with the aorta not clamped for more than a few minutes (unless controlled aortic root perfusion is used during mapping). Risk of air embolization exists, and the CPB time is prolonged by 5 to 20 minutes. In the Mayo Clinic\textsuperscript{25} and UAB experiences,\textsuperscript{28} mapping did not reduce prevalence of complete heart block during VSD repair in patients with CCTGA, so intraoperative mapping is not routinely used at present.

Routine Placement of Permanent Epicardial Pacemaker Leads

A selective approach to placing permanent epicardial pacemaker leads is followed, but some prefer to routinely place such leads. Should heart block develop, the transvenous route of placement (usually through the subclavian vein\textsuperscript{113}) is simple. Difficulty with stability of the intraventricular endocardial pacemaker lead has not been encountered, despite the relatively smooth interior of the right-sided morphologic LV.\textsuperscript{22} Placing prophylactic epicardial myocardial leads at operation without connecting them to a pacemaker pulse generator would seem irrational, so unless a clear indication of need exists, this appears to be unwise. One important indication for placing prophylactic epicardial leads is if the cardiac repair involves use of a bidirectional cavopulmonary anastomosis, because transvenous access is not possible.

REFERENCES

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W

Y
Double Inlet Ventricle and Atretic Atrioventricular Valve

**Definition**
Double inlet ventricle is a congenital cardiac malformation in which both atria connect to only one ventricular chamber by either two separate atrioventricular (AV) valves or a common AV valve. Closely related to double inlet ventricle are cardiac malformations in which both atria connect to only one ventricular chamber because of atresia of one AV valve that is imperforate or absent. As a group, double inlet ventricles and those with an atretic AV valve are appropriately considered as having a single ventricle or univentricular AV connection, although these phrases are not appropriate for describing morphology of an individual heart.\(^4\)

The ventricular mass in these settings rarely consists only of a solitary ventricle. When, as is usual, there are two ventricles, one is usually incomplete (rudimentary) and hypoplastic. Often the incomplete ventricle is connected to an atrium by overriding of an AV valve. Such arrangements are termed double inlet ventricle only if more than 50% of the overriding valve lies over the main (dominant) ventricle.

Classic tricuspid atresia (univentricular AV connection with atrial situs solitus, ventricular D-loop, single inlet left ventricular main chamber, right-sided AV valve [tricuspid] atresia, and ventriculoarterial [VA] concordant or discordant connection)^7,8,4^ is separately discussed in Chapter 41.\(^1\) Most

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^1^The adjectives left and right used to modify atrium or ventricle mean morphologically left or right. Position of a chamber or valve is referred to as right sided or left sided.
morphologic variants of left-sided AV valve (mitral) atresia with patent aortic outlet are included in this chapter. Mitral atresia in association with either aortic atresia or aortic stenosis, intact ventricular septum, and concordant AV and VA connections represent two of the four classic morphologic forms of hypoplastic left heart physiology and are discussed in Chapter 49.

HISTORICAL NOTE

One of the earliest descriptions of a variety of this congenital anomaly was by Holmes, who in 1824 noted that it was intermediate between a normal heart and one with a solitary ventricular chamber.1 He is believed that Peacock described a heart with “both auricles opening into the left ventricle” in 1854. Rokitansky described and illustrated a case of double inlet left ventricle in 1875, as did Mann in 1907, describing the heart as cor triloculare biaatriatum.2,3 Taussig described “single ventricle with a diminutive outlet chamber” in 1939.4 Lev and colleagues have listed a number of other descriptions of “single (primitive) ventricle” that were published more than 100 years ago.5,6

An important contribution by Van Praagh and colleagues in 1964 at the Mayo Clinic was clear definition of the entity as one in which both AV valves empty into the same ventricle.7 About the same time, Elliott and colleagues expressed the view, now accepted, that hearts with atresia of one AV valve (and thus a single AV valve) have much in common with hearts with double inlet ventricle.8,9 Anderson and colleagues introduced the phrase univentricular AV connection to collate this group of malformations.10,11,12

Lev clearly established as a different entity hearts with a huge ventricular septal defect (VSD) or common ventricle, in which one side of the common chamber was morphologically right ventricle and the other left ventricle; he thereby excluded them from the single-ventricle category.13,14

Surgical palliation of double inlet ventricle without pulmonary stenosis began with the original description of pulmonary trunk banding by Muller and Damman in 1952.15,16 Palliation of double inlet ventricle with pulmonary stenosis has as its basis the original Blalock-Taussig shunt; its application to patients with double inlet ventricle and pulmonary stenosis was only a matter of time.17,18 Redo and colleagues may have been the first to show the favorable effect of a Blalock-Hanlon atrial septectomy in patients with left-sided (mitral) valve atresia.19

Septating the main chamber to establish two circulations in series emerged from the Mayo Clinic experience of unexpectedly encountering a patient with double inlet ventricle in 1956.20 Preoperative diagnosis was corrected transposition with VSD, but correct diagnosis was made after opening the ventricle. Septation was accomplished, but the patient died about 6 months after operation, probably during a Stokes-Adams episode. This concept lay dormant for some years, but in 1972 it was further developed by Sakakibara and colleagues and in 1973 by Edie, Malm, and colleagues, who reported four successful septation repairs.21,22 Three long-term survivors of septation were reported in 1973 by Arai, Sakakibara, and colleagues, and one was reported by Ionescu and colleagues.23,24 McGoone, Danielson, and colleagues began to report successful results from the Mayo Clinic about this same time.25 The right atrial approach to septation was suggested and applied by Doty and colleagues in 1979.26

A different surgical concept—using the main (dominant) ventricular chamber for generating systemic blood flow and allowing the via a to the systemic venous system to generate pulmonary blood flow—was stimulated by the work of Fontan and Baudet (published in 1971 and known as the Fontan operation, Table 1)27 and by the work of Kreutzer and colleagues.28 Application of this concept to surgical treatment of double inlet ventricle was reported by Yacoub and Radley-Smith in 1976.29

Subaortic stenosis became apparent as a major problem when experience with the Fontan operation increased during the early 1970s.30,31 In 1973, Neches and colleagues applied the concept of placing the main chamber in direct communication with the aorta by performing an anastomosis of pulmonary trunk to aorta.32 Others have accomplished this by an anastomosis of the proximal segment of the divided pulmonary trunk to the side of the ascending aorta, a part of a Damus-Kaye-Stansel (DKS) operation.33,34,35 This concept has been revitalized more recently by extensive augmentation of the usually hypoplastic aortic arch in conjunction with the DKS operation in the Norwood I operation and by using the arterial switch operation for this purpose, first by Freedom, Williams, Trusler, and colleagues in 1980 and in neonates by Karl and colleagues in 1991.36,37,38 Penkoske and colleagues approached the problem directly by enlarging the VSD in 1984.39

Application of cardiac transplantation to this group of patients was a natural evolution in managing patients with univentricular AV connections and myocardial failure.

MORPHOLOGY

Generalizations

Ventricular Mass

The main (dominant) chamber making up the ventricular mass in double inlet ventricle with two ventricles may have a left ventricular internal architecture, a right ventricular internal architecture, or an indeterminate architecture. Main chamber volume is largest when there is no pulmonary stenosis but considerably smaller when pulmonary stenosis is present.41 This is related to the fact that main chamber volume is positively correlated with pulmonary-to-systemic flow ratio (Qp/Qs).42 The nondominant, incomplete (rudimentary) hypoplastic chamber, when present, is always opposite architecture to the main chamber. Ventricular topology in double inlet ventricles may be either right-handed (D-loop), left-handed (L-loop), or indeterminate (Tables 56-1 and 56-2). (See “Symbolic Convention of Van Praagh” under Terminology and Classification of Heart Disease in Chapter 1.)43

The nondominant chamber is called incomplete (or rudimentary) because it lacks one or more of its component parts, usually the inlet portion but occasionally also the outlet, leaving only the apical trabeculated part. The incomplete chamber is always smaller than the dominant chamber and is connected to the dominant chamber by a VSD. The VSD is sometimes called a bulboventricular foramen, but this term applies only when the incomplete chamber is of right ventricular morphology. Rarely, such as when there is double inlet to one chamber and double outlet from the other, both chambers are incomplete. The ventricular septum is malaligned


Table 56-1 Ventricular Architectural Pattern and Atrial Situs in Double Inlet Ventricles

<table>
<thead>
<tr>
<th>Atrial Situs</th>
<th>Solitary Ventricle</th>
<th>Two Ventricles</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Indeterminate</td>
<td>Right-Handed (D-Loop)</td>
<td>Left-Handed (L-Loop)</td>
<td>Undetermined Loop</td>
<td></td>
</tr>
<tr>
<td>Solitus</td>
<td>101 (87) + 89</td>
<td>32 + 89</td>
<td>50</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Inversus</td>
<td>2 (2)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ambiguus:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral right-sidedness</td>
<td>8 (7)</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Bilateral left-sidedness</td>
<td>4 (3)</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (1)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>116 + 89 = 205</td>
<td>23 (20)</td>
<td>39 (34) + 89</td>
<td>50 (43)</td>
<td>4</td>
</tr>
</tbody>
</table>

Data from Stefanelli and colleagues.114 Cases of classic tricuspid atresia (n = 89) are included and underlined.

Key: ( ), Percentage of 116.

Table 56-2 Morphologic Findings in 189 Patients with Double Inlet or Common Inlet Ventricle

<table>
<thead>
<tr>
<th></th>
<th>DIRV (n = 31)</th>
<th>DILV (n = 45)</th>
<th>CIRV (n = 93)</th>
<th>CILV (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atrial Arrangement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual</td>
<td>19 (61%)</td>
<td>40 (89%)</td>
<td>—</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Mirror image</td>
<td>1 (3%)</td>
<td>1 (2%)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Right isomerism</td>
<td>8 (26%)</td>
<td>4 (9%)</td>
<td>89 (96%)</td>
<td>16 (80%)</td>
</tr>
<tr>
<td>Left isomerism</td>
<td>3 (10%)</td>
<td>—</td>
<td>4 (4%)</td>
<td>2 (10%)</td>
</tr>
<tr>
<td><strong>Ventricular Loop</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D-loop</td>
<td>21 (68%)</td>
<td>18 (40%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L-loop</td>
<td>10 (32%)</td>
<td>27 (60%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ventriculoarterial Connections</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SORV</td>
<td>18 (58%)</td>
<td>5 (11%)</td>
<td>42 (45%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>DORV</td>
<td>12 (39%)</td>
<td>1 (2%)</td>
<td>39 (42%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>DOLV</td>
<td>—</td>
<td>2 (4%)</td>
<td>—</td>
<td>2 (10%)</td>
</tr>
<tr>
<td>Discordant</td>
<td>1 (3%)</td>
<td>30 (67%)</td>
<td>8 (9%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Concordant</td>
<td>—</td>
<td>7 (16%)</td>
<td>4 (4%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td><strong>Pulmonary Pathway</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary atresia with nonconfluent PA</td>
<td>5 (16%)</td>
<td>—</td>
<td>3 (3%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Pulmonary atresia with confluent PA</td>
<td>13 (42%)</td>
<td>5 (11%)</td>
<td>39 (42%)</td>
<td>6 (30%)</td>
</tr>
<tr>
<td>Pulmonary stenosis</td>
<td>6 (19%)</td>
<td>16 (36%)</td>
<td>43 (46%)</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>No obstruction</td>
<td>7 (23%)</td>
<td>24 (53%)</td>
<td>8 (9%)</td>
<td>4 (20%)</td>
</tr>
<tr>
<td><strong>Aortic Pathway</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coarctation/interruption</td>
<td>2 (6%)</td>
<td>4 (9%)</td>
<td>1 (1%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>No obstruction</td>
<td>29 (94%)</td>
<td>41 (91%)</td>
<td>92 (99%)</td>
<td>19 (95%)</td>
</tr>
</tbody>
</table>

Modified from Kitamura and colleagues.55 Key: CILV, common inlet left ventricle; CIRV, common inlet right ventricle; DIRV, double inlet right ventricle; DILV, double inlet left ventricle; DOLV, double outlet left ventricle; DORV, double outlet right ventricle; PA, pulmonary arteries; SORV, aorta arising from right ventricle with pulmonary atresia.

and incomplete in nearly all hearts with double inlet ventricle, or is completely absent.

Some consider a solitary ventricle with double inlet to be an indeterminate ventricle, and some consider it to be a right ventricle.53,54

Atria

Any type of atrial situs can be present. However, with double inlet left ventricle, there is usually atrial situs solitus, and with double inlet right and indeterminate ventricles, about half have situs solitus and half have a heterotaxy pattern, right atrial isomerism predominating (see Chapter 58).58 Situs inversus (mirror image) is unusual (see Tables 56-1 and 56-2).

Atrioventricular Connection

There are usually two perforate AV valves positioned entirely in the dominant ventricle. Their morphologic characteristics are frequently indeterminate, neither tricuspid nor mitral, and it is therefore best to call them left-sided (draining the
Coronary Arteries
Terminology of the coronary artery branches is arguable. Left and right coronary arteries usually arise from the two aortic sinuses facing the pulmonary trunk. There are usually prominent descending branches (encircling coronary arteries) that indicate points of attachment of septum to free ventricular wall, and therefore the boundaries of the incomplete ventricle.

Ventriculoarterial Connections
VA connections can be of any type, except in the case of a solitary ventricle, where there can only be a single or double outlet. In double inlet left ventricle, the most frequent connection is discordant, with aorta and subaortic incomplete right ventricle (outlet chamber) to the left, but sometimes to the right, of the pulmonary trunk; concordant, double outlet, and single outlet connections occur (Table 56-3).

Conduction Tissue
Morphology of the AV node and conduction system is abnormal. Position of the AV node is determined primarily by whether the ventricular septal remnant reaches the crux (see “Atrophicventricular Node” under Conduction System in Chapter 1). From the surgeon’s standpoint, it is important to know that the AV node can be anywhere around the perimeter of the right-sided AV valve.

Types
Double Inlet Left Ventricle
In double inlet left ventricle, the most common double inlet connection, the dominant ventricle is of left ventricular morphology. Apical trabeculations beyond insertions of the papillary muscles display a delicate criss-cross pattern. The septal surface is typically smooth in its superior half, and the crescentic margin bounding the VSD is smooth (Fig. 56-3). VSD morphology, however, can be variable. Of 46 patients with double inlet left ventricle carefully evaluated by Bevilacqua and colleagues, 24 had VSDs separated from the semilunar valves and completely surrounded by muscle (muscular defects), 19 had VSDs adjacent to the anterior semilunar valve (subaortic defect) in association with malalignment or...
Table 56-3  Summary of Morphologic Features of the Ventriculoarterial Connections in 97 Specimens of Double Inlet Left Ventricle

<table>
<thead>
<tr>
<th>Feature</th>
<th>Right Ventricle Leftward</th>
<th>Right Ventricle Rightward</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventriculoarterial Connection(^a)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concordant</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Discordant</td>
<td>51</td>
<td>16</td>
</tr>
<tr>
<td>Double outlet RV</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Aorta from RV/pulmonary atresia</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Double outlet LV</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Aorta from LV/pulmonary atresia</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td>Infundibular Morphology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subpulmonary</td>
<td>2</td>
<td>13</td>
</tr>
<tr>
<td>Subaortic</td>
<td>58</td>
<td>17</td>
</tr>
<tr>
<td>Subpulmonary and subaortic</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Markedly attenuated</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Aortic Valve in Relation to Pulmonary Valve</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right posterior</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>Right anterior</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>Right side-by-side</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Left anterior</td>
<td>54</td>
<td>—</td>
</tr>
<tr>
<td>Left side-by-side</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Arterial Trunks</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spiraling</td>
<td>2</td>
<td>14</td>
</tr>
<tr>
<td>Parallel</td>
<td>60</td>
<td>21</td>
</tr>
</tbody>
</table>

Modified from Uemura and colleagues.\(^{U1}\)
\(^a\)For overriding of the aortic or pulmonary valve, the so-called 50% rule was applied.
Key: LV, Left ventricle; RV, right ventricle.

Figure 56-3  Interior view of specimen of double inlet left ventricle. Right-sided atrioventricular valve (RAV) is larger than the left-sided one (not completely visualized). The large ventricle has left ventricular morphology, with fine trabeculations near the apex and a smooth surface to the superior half of the ventricular septum (VS). There is a smooth crescentic lower margin bounding the ventricular septal defect. The incomplete right ventricle (RV) lies superiorly and leftward (L-loop). Key: LAV, Left-sided atrioventricular valve; LV, left ventricle.

Figure 56-4  Specimen of double inlet left ventricle with L-loop. Incomplete right ventricle (RV) has been opened, showing coarse trabeculations present in its inferior part and a restrictive ventricular septal defect (VSD). The aorta (Ao) arises from this chamber. Key: LAA, Left atrial appendage; LV, left ventricle.

hypoplasia of the infundibular septum, and 3 had multiple muscular defects.\(^{B3}\)

The small incomplete (rudimentary) ventricle is of right ventricular morphology, with coarse apical trabeculations and frequently a recognizable trabeacula septomarginalis (septal band) bounding the VSD anteriorly. A smooth-walled infundibulum is present when one or both great arteries arise from this chamber (Fig. 56-4). Otherwise, and rarely, the chamber exists as a blind pouch. It is always positioned on the anterosuperior shoulder of the dominant left ventricle (Fig. 56-5), usually to the left but sometimes to the right. The septum thus lies obliquely and never extends to the crux.

The typical morphology of double inlet left ventricle, with ventricular L-looping, left-sided incomplete right ventricle, and VA discordant connections, occurs in about half of all cases, with a wide variety of VA connections in the remainder\(^{U1}\) (see Table 56-3). The relatively uniform internal cardiac architecture of the AV valves and myocardium in typical double inlet left ventricle may be more variable when double outlet right ventricle occurs with it.\(^{A3}\) Atrial situs is usually solitus, occasionally ambiguous, but rarely situs inversus.

Two variants of double inlet left ventricle warrant further description: (1) double inlet left ventricle with ventricular L-loop, left-sided incomplete right ventricle, and VA discordant connection and (2) double inlet left ventricle with ventricular D-loop, right-sided incomplete right ventricle, and VA concordant connection.

With Ventricular L-Loop, Left-Sided Incomplete Right Ventricle, and Ventriculoarterial Discordant Connection This is the largest subset of hearts with double inlet ventricle, comprising half the cases (see Figs. 56-3 through 56-5). The large left ventricular main chamber lies to the right and receives left-sided and right-sided AV valves, which usually are of tricuspid and mitral morphology, respectively, although both may be bicuspid. There may be some straddling and overriding (but <50%) of the AV valves. The majority of AV valves function normally, but the most common abnormality is stenosis of the left-sided “tricuspid” valve.\(^{B3}\) A heavy trabecula often separates insertion of the papillary muscles into the diaphragmatic free wall of the left
ventricle. The left-sided tricuspid valve commonly has attachments of the subvalvar tension apparatus to the ventricular septum.\textsuperscript{D1}

The aorta arises above the short infundibulum of the incomplete left-sided right ventricle (see Fig. 56-4). The pulmonary trunk arises from the base of the left ventricle, anterior and superior to the right-sided AV (“mitral”) valve, usually with pulmonary-mitral fibrous continuity. Subvalvar and valvar pulmonary stenoses occur but are not common, and pulmonary atresia occurs only occasionally.

The VSD is usually large and lies beneath the infundibular septum, but it may be restrictive, producing subaortic stenosis (see “Subaortic Stenosis” later under Natural History). As noted, the VSD may be in an atypical position within the apical septal trabeculations, and occasionally it is multiple. Muscular defects are more likely than subarterial defects to be restrictive.\textsuperscript{B5}

The AV node is anterior and away from the atrial septum, lying in the right atrial wall adjacent to the superior comissural tissue between anterior and posterior leaflets of the right-sided AV valve.\textsuperscript{A3,B4,B5} This arrangement also pertains to ventricular D-loop when the left ventricle is the main chamber, because again there is no ventricular septum extending to the crux. The bundle of His passes anterior to the pulmonary valve to reach the ventricular septum (see later Figs. 56-19 and 56-21).\textsuperscript{A3,B2,B4}

Configuration of coronary arteries is similar to that in congenitally corrected transposition of the great arteries (see “Atrioventricular Node and Bundle of His” and “Coronary Arteries” under Morphology in Section I of Chapter 55).

With Ventricular D-Loop, Right-Sided Incomplete Right Ventricle, and Ventriculoarterial Concordant Connection

This occurs in about 10% of cases and most resembles the normal heart. The large left ventricle lies to the left and posteriorly, and the small right ventricle lies to the right, anteriorly and superiorly. It was first described by Holmes and is often called the Holmes heart.\textsuperscript{A6,H1}

There are usually two AV valves (often with the right-sided one straddling but with less than 50% override) or a common valve. The incomplete right ventricle is similar to that present in classic tricuspid atresia, with an extensive infundibulum leading to a pulmonary valve that is normally related to the aortic valve. Pulmonary stenosis is common, and the VSD may be restrictive.

The AV node is again anterior at about the 11-o’clock position relative to the right AV valve, as seen by the surgeon from the right atrium. The bundle of His descends from the anteriorly positioned AV node directly onto the ventricular septum without coming into relation with the ventricular outflow tract.\textsuperscript{B8,W3} Rarely the AV node and bundle encircles the anterior aspect of the right AV orifice.\textsuperscript{A6}

Double Inlet Right Ventricle

In double inlet right ventricle, both atria connect to a morphologically right ventricle. Apical trabeculations are coarse, and the trabecula septomarginalis is recognizable on the septal surface, with the VSD contained between its anterior and posterior limbs. The incomplete left ventricle is always positioned posteriorly and inferiorly (“in the hip pocket”) in relation to the main chamber and usually lies to the left (D-loop; Fig. 56-6) or rarely to the right (L-loop). More often than not, it is very small and slitlike, communicating with the main chamber by a tiny VSD, with no connection to a great artery.\textsuperscript{A2,S11} In other cases, the left ventricle is of reasonable size and the obliquely placed septum is well
formed; in contrast to that in double inlet left ventricle, it extends superiorly to the crux. In these cases, fine apical trabeculations are recognizable, and the superior septal surface beneath the VSD is smooth.

The VA connection is usually double outlet or single outlet (pulmonary atresia) from the right ventricle (Fig. 56-7; see also Fig. 56-1). A concordant connection sometimes occurs, with the aorta arising from the incomplete left ventricle. Pulmonary stenosis can be present.\(^9\)

Two AV valves may enter the large right ventricle, with the left one straddling, or frequently a common AV valve. Atrial situs inversus, and particularly right atrial isomerism, is more common in double inlet right ventricle than in double inlet left ventricle. Double inlet right ventricle associated with right atrial isomerism seems to be particularly prevalent in the Chinese.\(^14\)

In the presence of a D-loop and a ventricular septum reaching the crux, the AV node has its usual posterior position in the atrial septum with its normal relation to the ostium of the coronary sinus.\(^7\) The perforating bundle of His passes through the AV anulus and on to ventricular myocardium, either on the ventricular septum or on a trabecula on the posterior ventricular wall. In rare L-loop, the conduction system is variable, but a conventionally located AV node may be present, as well as a more rudimentary node located more anteriorly and superiorly along the right-sided AV anulus.\(^5\)

The nonbranching bundle then descends onto a free-running trabecula in the main chamber.

**Double Inlet Indeterminate Ventricle**

Double inlet indeterminate ventricle includes hearts in which both atria connect to a solitary ventricle.\(^24\) Prevalence of this subset depends on the care with which a search is made for the possibility that the malformation is actually double inlet right ventricle, because a tiny isolated accessory ventricular chamber may be missed by cardiac imaging and may be found only on careful autopsy examination. Even when the ventricle is truly solitary, it may represent a morphologically right ventricle without a rudimentary left ventricle, because apical trabeculations are always coarse, and there may be a free-standing column posteriorly reminiscent of the trabecula septomarginalis (see Fig. 56-7).\(^3\)

There is a higher prevalence of heterotaxy in double inlet indeterminate ventricle than in the other types of double inlet ventricle. With it, as well as with atrial situs solitus and inversus, two perforate AV valves are usually present. The only VA connection possible is double or single (pulmonary atresia) outlet ventricle. Pulmonary stenosis is common. The great arteries are often more or less normally related.

The AV node is usually posterior when there is a rudimentary ridge in the ventricle and distinct papillary muscles to both AV valves. In this case, the AV node passes down a free-running trabecula.\(^24\) When a ridge is absent, the AV node is usually situated laterally (away from the atrial septum) and anteriorly, and the nonbranching bundle descends into the right parietal wall of the indeterminate ventricle.\(^24\)

**Common Ventricle**

Rarely an apparently common (solitary) ventricle has no ventricular septum or a diminutive apical ridge, but importantly, one side of the ventricular mass is morphologically right ventricle and the other morphologically left. Lev and colleagues consider this to be a heart with a huge VSD rather than double inlet common ventricle.\(^14\)

**Left Atrioventricular (Mitral) Valve Atresia and Patent Aortic Outlet**

Left-sided AV (mitral) valve atresia with patent aortic outlet has a widely varying morphology.\(^5\) All variants are discussed here, with one exception: mitral atresia with patent aortic outlet (aortic stenosis) with intact ventricular septum, atrial situs solitus, levocardia, single inlet right ventricle with D-loop, and hypoplasia of all left cardiac segments, together with VA concordant connection. This variant is considered one of the four classic morphologic variants of hypoplastic left heart physiology, along with mitral atresia–aortic atresia, mitral stenosis–aortic atresia, and mitral stenosis–aortic stenosis (see “Left Ventricle and Mitral Valve” under Morphogenesis and Morphology in Chapter 49).

The atretic valve may be imperforate, in which case there is a hypoplastic membrane, sometimes with a miniature chordal apparatus beneath it; or the AV connection may be absent, with the floor of the atrium being separated from the ventricle by fibrofatty tissue.\(^5\) In a study of 23 patients with patent aortic outlet and atresia of the left AV valve, 15 had absence of the left AV connection, 5 had an imperforate left AV valve, and 3 had atrial isomerism. Those with imperforate left AV valve demonstrated concordant AV connections.\(^1\)

The patent right-sided AV valve may occasionally override the remnant of ventricular septum, but with more than 50% of the anulus committed to the larger right ventricular chamber. The tension apparatus may straddle the septum, which reaches the crux.\(^2\)

In this most common arrangement (“mitral” atresia), there is atrial situs solitus, ventricular D-loop, and a dominant

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**Figure 56-7** Specimen of double inlet right ventricle and double outlet right ventricle. Arguably, the main chamber can be considered of indeterminate type rather than right ventricular. Key: Ao, Aorta; LAV, left-sided atrioventricular valve; PT, pulmonary trunk; RAV, right-sided atrioventricular valve; RV, right ventricle.
right ventricle connected to the right atrium by a patent right-sided (usually tricuspid) AV valve and a small and incomplete left ventricle lying posteriorly and to the left (Figs. 56-8 and 56-9). The left ventricle may be a blind chamber connecting to the right ventricle by a small VSD (in which case the VA connection is either double or single outlet right ventricle), but more commonly it functions as an outlet chamber giving origin to the aorta (concordant VA connection) and rarely to the pulmonary artery. The left ventricle is often smaller than suggested by the position of the left anterior descending coronary artery (see Fig. 56-9). Characteristically, when the aorta arises from the small left ventricle, the VSD is restrictive and the aorta small in association with coarctation or aortic arch hypoplasia. Interatrial obstruction is also common.

Alternatively, and less commonly, the arrangement is atrial situs solitus and ventricular L-loop with single inlet and more or less right-sided left ventricle, in which case the right atrium

Figure 56-8 Specimens of hearts with left-sided mitral atresia but no aortic atresia in hearts with ventricular D-loop. A, Posterior view of the atria, with atrial walls and septum displaced anteriorly and superiorly, except for septum primum. Arrow indicates site of atretic mitral valve. B, External frontal view of another heart. Enlarged right ventricle (RV) is demarcated by anterior descending coronary artery (arrow), although large branches extend over RV. Left ventricle (LV) is underdeveloped. C, View of opened LV in same specimen as in B. Midmuscular ventricular septal defects (VSD) and normally connected aorta (Ao) are seen.
is connected to the dominant left ventricle by a patent AV valve with either mitral or indeterminate morphology. There is an incomplete left-sided right ventricle situated anteriorly and to the left, above which is the atretic left-sided AV valve, and the VSD may be restrictive. The septum does not reach the crux. The usual VA connection is discordant with the right ventricle giving origin to the aorta, but double outlet left ventricle also occurs.

Right Atrioventricular (Tricuspid) Valve Atresia
Excluding cases of classic right-sided (tricuspid) valve atresia (see Chapter 41), right-sided AV valve atresia can occur with single inlet and more or less left-sided right ventricle (ventricular L-loop). Right AV valve atresia has also been reported in association with an indeterminate solitary ventricle. The patent left-sided AV valve may occasionally override the septum and may have multiple leaflets.
Associated Cardiac Anomalies

Associated cardiac anomalies occur in at least one third of patients with double inlet ventricle. AV valve malformations are common and include leaflet dysplasia, leaflet cleft and tags, and anular hypoplasia, in addition to straddling.\(^{31,32}\) These can produce either valvar regurgitation or stenosis. The pulmonary valve may be stenotic from anular hypoplasia and leaflet thickening, or it may be atretic. Subvalvar pulmonary stenosis is common and results from either infundibular narrowing (muscle hypertrophy, hypoplasia, or occasionally a deviated septum) (see Fig. 56-1) or, more commonly, a restrictive VSD leading to an outflow chamber from which the pulmonary trunk arises (see Fig. 56-4). Aortic arch anomalies (coarctation, aortic arch interruption, or arch hypoplasia) also sometimes coexist with single ventricle (see Table 56-2). Multiple VSDs are not rare.

Subaortic stenosis is one of the most important coexisting cardiac anomalies. Because of the variable time of its appearance, it is discussed later under Natural History.

| Figure 56-9 | Relation of left anterior descending coronary artery (LAD) to ventricular septum in hearts with mitral atresia and patent aortic root. Note that in this heart, the clearly visible artery is the LAD, which does not closely relate to the left ventricular (LV) cavity. Key: LA, Left atrial cavity; PT, pulmonary trunk; RV, right ventricle. (From Gittenberger-de Groot and colleagues.\(^\text{30}\)) |

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Clinical manifestations vary with morphology. Patients without pulmonary stenosis or atresia, about one third of the total, present in a manner similar to those with tricuspid atresia and normally related great vessels without pulmonary stenosis or atresia (see Clinical Features and Diagnostic Criteria in Chapter 41).

When mild or moderate pulmonary stenosis coexists, early years of life may be without important symptoms. A \(Q_p/Q_s\) of approximately 2 or less results in only moderate cardiomegaly and mild pulmonary overcirculation on the chest radiograph and good functional status, albeit with mild cyanosis. Presentation in early or middle childhood rather than in infancy is common and is usually precipitated by cyanosis, a cardiac murmur, or typical findings on a chest radiograph. Clinical presentation is similar to that of tricuspid atresia and normally related great arteries with mild to moderate pulmonary stenosis (see Chapter 41).

When pulmonary stenosis is severe or pulmonary atresia is present, important cyanosis usually results in presentation in the early days or weeks of life, similar to that of tricuspid atresia and normally related great vessels with severe pulmonary stenosis or pulmonary atresia.

Atresia of the left-sided AV valve, when combined with a restrictive foramen ovale, results in severe pulmonary venous hypertension with its typical chest radiographic appearance and severe respiratory distress in early life. The presentation can mimic that of classic hypoplastic left heart physiology with restrictive or intact atrial septum (see Chapter 49). This situation may be masked initially by pulmonary stenosis and small pulmonary blood flow, only to become apparent after a systemic-pulmonary artery shunt is created. Severe AV valve regurgitation results in elevated atrial pressure and early appearance of heart failure.

Double inlet single left ventricle with AV and VA discordant connections, restrictive VSD (bulboventricular foramen), and aortic arch hypoplasia typically mimics hypoplastic left heart physiology in its presentation (see Chapter 49).

The electrocardiogram and chest radiograph may raise suspicion of the presence of double inlet ventricle, but echocardiography usually is the first definitive diagnostic procedure. Absence of the posterior (inlet) septum between the AV valves, one of the hallmarks of double inlet ventricle, can usually be diagnosed from the echocardiogram, particularly when associated with apposition of the unsupported septal leaflets of the two AV valves.\(^{31,32,33,34}\) Echocardiography with Doppler color flow imaging can provide all the necessary diagnostic information (Figs. 56-10 and 56-11).\(^{34,35}\)

Cineangiography may be performed (Figs. 56-12 and 56-13) but currently is not necessary for planning therapy in the neonate or infant, and may be disadvantageous to the condition of the patient. It should be recalled that the Holmes heart is easily misdiagnosed as tetralogy of Fallot.\(^35\) Cardiac catheterization and cineangiography can provide important information about the patient presenting in older infancy or later, or about the patient who has previously undergone surgery, primarily by defining pulmonary vascular resistance and morphology of the branch pulmonary arteries.

Magnetic resonance imaging and computed tomography have little diagnostic role in the neonate.
PART VII  Congenital Heart Disease

Figure 56-10  Four-chamber echocardiographic view demonstrating S,L,L double inlet left ventricle (see “Symbolic Convention of Van Praagh” in Chapter 1). Atrial septum is intact, and right-sided atrioventricular valve (RAVV) is smaller than left-sided one (LAVV). The dominant ventricle shows features of a morphologic left ventricle and is positioned to right side and posteriorly. The small outlet ventricular chamber is positioned to the left side and anteriorly. This image views the posterior aspect of the heart, so the great arteries, which are L-transposed with the aorta arising from the incomplete ventricle, are not seen. There is a communication between main and incomplete ventricular chambers (ventricular septal defect, or bulboventricular foramen). Key: AS, Atrial septum; BVF, bulboventricular foramen or ventricular septal defect; LA, left atrium; LV, left ventricle; OC, outlet ventricular chamber, or incomplete right ventricle; RA, right atrium.

Figure 56-11  Echocardiogram from heart with S,L,L double inlet left ventricle. A, Subcostal coronal image demonstrating a somewhat more anterior region (compared with that shown in Fig. 56-10). This image shows pulmonary trunk and aortic connections to heart. Aorta is left sided and anterior in relation to pulmonary trunk and arises from incomplete outlet ventricular chamber. Bulboventricular foramen is visible. Inlets to dominant left ventricle and atrioventricular valves are not visualized because of the anterior image. B, Lateral projection. Note anterior position of aorta arising from the anterior incomplete ventricle, and posterior position of pulmonary trunk arising without obstruction from dominant left ventricle. Bulboventricular foramen is very small, causing severe subaortic obstruction. Key: A, Aorta; BVF, bulboventricular foramen, or ventricular septal defect; LV, left ventricle; OC, outlet ventricular chamber, or incomplete right ventricle; PT, pulmonary trunk.

NATURAL HISTORY

Double Inlet Ventricle

Estimated overall survival without treatment is about 57% at 1 year and 45% at 5 years. The monumental study by Franklin and colleagues documented the relatively favorable prognosis of certain subsets. Specifically, patients with atrial situs solitus and double inlet left ventricle, ventricular L-loop, discordant VA connection without systemic outflow obstruction, Qp/Qs of about 1 to 2 (due to mild to moderate pulmonary stenosis), and presentation between 14 and 60 days of age have about a 90% chance of surviving for at least 10 years without intervention. Although the natural history impact of differing AV connections has not been clearly defined, evidence exists that differences in left ventricular function are present depending on whether the inlet connection has two patent valves or one. Presentation with severe acidosis and low cardiac output has been a particularly severe risk factor for early death without intervention. Systemic outflow obstruction at any level, particularly aortic atresia, is also a strong risk factor for early death.

Mitral Atresia

When atresia of the left AV valve coexists with a restrictive opening in the atrial septum, such as in mitral atresia (atrial situs solitus, ventricular D-loop, right ventricular main...
chamber, and absent or imperforate left AV valve), the situation is rapidly fatal; death usually occurs within the first few months of life. Prognosis is the same in patients with ventricular L-loop and ventriculoarterial discordant connection. Atria are in situs solitus, and small left-sided right ventricle (outlet chamber) gives origin to aorta. The ventricular septal defect is large. (Frontal projection.)

**Figure 56-12** Ventriculograms in double inlet ventricle. **A,** Double inlet left ventricle with ventricular L-loop and ventriculoarterial discordant connection. Atria are in situs solitus, and small left-sided right ventricle (outlet chamber) gives origin to aorta. The ventricular septal defect is large. (Frontal projection.) **B,** Double inlet left ventricle (LV) with ventricular L-loop and ventriculoarterial concordant connection. Atria are in situs solitus, and small left-sided right ventricle (RV) gives origin to pulmonary trunk (PT). (Frontal projection.) **C,** Double inlet LV with ventricular D-loop and ventriculoarterial discordant connection. Atria are in situs solitus, and small right-sided RV gives origin to aorta (Ao). (Long axial view.)

Continued

**Subaortic Stenosis**

The tendency to develop subaortic stenosis when the aorta arises from the incomplete ventricle (outlet chamber) poses a serious threat. This category includes patients with (1) double inlet left ventricle and VA discordant connection, (2) tricuspid atresia and VA discordant connection, and (3) mitral atresia and VA concordant connection. The
**Figure 56-12, cont’d**  
D, Double inlet RV with ventricular L-loop and double outlet RV. Atria are in situs solitus, and rudimentary LV lies “in the hip pocket” posteriorly (arrow) (elongated right anterior oblique view). Other projections demonstrated coarse trabeculations in right ventricle.  
E, Double inlet indeterminate ventricle, with double outlet and severe subpulmonary stenosis. There is an azygos extension of inferior vena cava, which accounts for catheter course. (From Soto and colleagues.)

**Figure 56-13**  
Cineangiogram in mitral (left atrioventricular valve) atresia with ventricular D-loop and double outlet right ventricle.

**Figure 56-14**  
Survival without treatment of patients born with double inlet ventricle. Kaplan-Meier estimates are based on 191 patients, with vertical bars representing 70% confidence limits. Numbers represent patients still being followed. Solid line depicts overall survival, including any definitive repair (septation or Fontan operation). Dashed line represents survival before definitive repair (patients censored at time of definitive surgery; see “Competing Risks” in Section IV of Chapter 6). (From Franklin and colleagues.)
Figure 56-15 Estimated survival without definitive repair (septation or Fontan operation) of patients born with double inlet left ventricle, left-sided subaortic outlet chamber (ventricular L-loop with discordant ventriculoarterial connection) with sufficient pulmonary stenosis that pulmonary-to-systemic flow ratio Qp/Qs was 1 to 2, presenting at 14 to 60 days of age (line A), or with Qp/Qs less than 1 (line B). Line C depicts the same morphology, but with pulmonary atresia. Line D depicts patients with right atrial isomerism, double inlet and double outlet right ventricle, a common atrioventricular orifice, anomalous pulmonary venous connection, and low pulmonary blood flow, presenting at less than 14 days of age. Numbers in parentheses are calculated relative risks with respect to fictitious baseline patient (dotted curve) (see Fig. 56-14). (From Franklin and colleagues.)

Figure 56-16 Estimated survival without definitive repair of patients with double inlet ventricle (format same as Fig. 56-15). Line E represents patients with usual atrial situs solitus, double inlet left ventricle, discordant ventriculoarterial connection, and high pulmonary blood flow, presenting between age 14 and 60 days. Line F represents same form of double inlet left ventricle but with a common atrioventricular valve. Line G represents same form of double inlet left ventricle but with systemic arterial obstruction (a form of hypoplastic left heart physiology; see under Morphology in Section I of Chapter 49) and high pulmonary blood flow. (From Franklin and colleagues.)

Figure 56-17 Left ventricular ejection fraction in tricuspid atresia compared with that in double inlet left ventricle. Ejection fraction is lower in tricuspid atresia. Key: DILV, Double inlet left ventricle; TA, tricuspid atresia. (From Redington and colleagues.)

Technique of Operation

Fontan Operation

Patients are commonly managed clinically as “single ventricle” physiology. This approach usually results in a definitive Fontan operation, but one or more staging operations done before the Fontan procedure are usually required. These include various forms of pulmonary trunk banding (see “Pulmonary Trunk Banding” in Section I of Chapter 35 and in Section II of Chapter 41), systemic-to-pulmonary artery shunting (see “Techniques of Shunting Operations” in Section I of Chapter 38 and in Section II of Chapter 41), and superior cavopulmonary anastomosis (see Chapter 41). Timing, number, and appropriate application of these staging operations, and details of the Fontan operation itself, are described under Technique of Operation in Section IV of Chapter 41. Table 56-4 lists the palliative procedures performed in 225 patients with double inlet left ventricle prior to the Fontan operation.

Closure of Right Atrioventricular Valve

When one AV valve is regurgitant and the other is more or less normal in size and function, the regurgitant valve is closed, either before or as part of the Fontan operation. When both valves are competent and of adequate size, there has been concern that leaving both open will permit flow through each to be only half normal, and that this may encourage thrombosis in and around the valve. There is no strong support for this concern, however, and it appears reasonable at present to leave both open.

If one AV valve is closed surgically, it is usually the right-sided AV valve. Technique of closure must be secure and not produce heart block. Both criteria are met by polyester patch closure of the area occupied by the valve, sewing the patch in place with a continuous whipstitch of 4-0 polypropylene suture in a way that avoids heart block (Fig. 56-18). This can

subaortic obstruction is usually caused by a restrictive VSD; however, sometimes muscle within the incomplete subaortic ventricle is the cause, not a small VSD per se. The three morphologic variants have a similar natural history, which is discussed in detail for tricuspid atresia and VA discordant connection in Chapter 41.
be achieved by sewing the patch as shown in the figure, or by sewing it precisely to the valve anulus itself. Because the underlying AV valve can open and close beneath the patch, and because thrombi might form between patch and valve, a stitch is placed through the midpoint of the free edge of each leaflet and then through the center of the patch and tied on the atrial side. This is most conveniently done after placing the posterior half of the patch suture line. Simpler techniques of suturing together the free edges of the leaflets, or suturing the patch to the leaflets themselves inside the hinge line, have been associated with more dehiscences than the technique described.

Septation

The septation operation can be performed in either one or two stages. Both procedures are performed exactly the same way as described in text that follows, with the exception that in the two-stage procedure, after the main septation patch is placed, a large hole is made in the center of the patch to create a nonrestrictive VSD. A pulmonary artery band is also placed if there is absence of pulmonary stenosis. At the second stage, performed 6 to 12 months later, the created VSD is closed with a second patch sewn to the first one, and the pulmonary artery band is removed and pulmonary artery reconstructed. The two-stage procedure tends to be performed in smaller patients, particularly those with relatively small ventricular chamber size.334

Although septation occasionally can be applied under appropriate circumstances to several types of double inlet left ventricular main chamber and anterior outlet chamber (and possibly a few with double inlet right ventricle), it is most commonly applied to double inlet left ventricle, ventricular L-loop, and small left-sided subaortic right ventricle. Thus, it is described for this situation. In the series of 11 patients reported by Margossian and colleagues, nine had double inlet left ventricle, one double inlet right ventricle, and one double inlet indeterminate ventricle. Of the nine patients, five had L-transposition of the great arteries, three had related great arteries, and one had D-transposition of the great arteries.334

Preparation, draping, incision, and preliminaries to cardiopulmonary bypass (CPB) are the same as for most operations (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2). The aortic purse-string suture may be awkward to place and is most easily done as described for corrected transposition (see Technique of Operation in Section I of Chapter 55).

Cardiac morphology is examined, particularly to identify anomalies of pulmonary or systemic venous return or of AV valve regurgitation. The ventricular mass is frequently enlarged. Interestingly, the right atrium does not usually appear to be as large as it is in patients with isolated VSD, atrial septal defect, or tetralogy of Fallot, but this should not discourage use of the atrial approach.

The approximate size of the septation patch is determined before CPB. This is done by noting the external dimensions of the ventricular mass and subtracting estimated wall thickness.335 An appropriate-sized patch is cut from a polyester tube (see “Grafts for Use in Aortic Surgery” under Special Situations and Controversies in Chapter 24) or alternatively, polytetrafluoroethylene.334 Although the patch usually seems too small, this size is appropriate because if it is made too large, it bulges into the right ventricle with each systole and impairs cardiac function.334 If it is made too small, there is an increased tendency toward dehiscence.

CPB is established by the usual techniques (see “Preparation for Cardiopulmonary Bypass” in Section III of Chapter 2), using direct caval cannulation. Myocardial management is by cold cardioplegia and controlled reperfusion (see “Cold Cardioplegia, Controlled Aortic Root Reperfusion, and [When Needed] Warm Cardioplegic Induction” under Methods of Myocardial Management during Cardiac Surgery in Chapter 3) or by simple single-dose cold crystalloid cardioplegia (see “Single-Dose Cold Cardioplegia in Neonates and Infants” in Chapter 3). The patient is usually cooled to

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**Table 56-4** Palliative Procedures Performed before Fontan Operation in 225 Patients with Double Inlet Left Ventricle

<table>
<thead>
<tr>
<th>Procedure</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary artery band</td>
<td>92</td>
</tr>
<tr>
<td>Blalock-Taussig shunt</td>
<td>77</td>
</tr>
<tr>
<td>Cavopulmonary shunt</td>
<td>24</td>
</tr>
<tr>
<td>Subaortic resection</td>
<td>14</td>
</tr>
<tr>
<td>Waterson shunt</td>
<td>11</td>
</tr>
<tr>
<td>Central shunt</td>
<td>11</td>
</tr>
<tr>
<td>Atrial septectomy</td>
<td>11</td>
</tr>
<tr>
<td>Potts shunt</td>
<td>4</td>
</tr>
<tr>
<td>Coarctation of aorta repair</td>
<td>4</td>
</tr>
<tr>
<td>Placement of permanent pacemaker</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>255</td>
</tr>
</tbody>
</table>

From Earing and colleagues.317

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**Figure 56-18** Right atrioventricular (AV) valve may be closed as part of Fontan-type repair in double inlet left ventricle. Several possible locations of AV node and proximal bundle of His are shown. Because the location in a given patient is not known precisely, suture line for patch closure of right-sided AV valve is 5 mm outside anulus all the way around.
18°C to 20°C so that periods of circulatory arrest can be used when needed to improve exposure. A small right atriotomy is made and a pump-oxygenator sump sucker passed across a natural or surgically created foramen ovale. The atriotomy is extended into the usual long oblique atriotomy, and stay sutures are applied (Fig. 56-19).

The interior of the left ventricular main chamber is examined through the right-sided AV valve. The subpulmonary area is visualized, as are the VSD, left-sided AV valve, and the relation between these structures. A determination is made whether the repair can be made through the intact right AV valve or whether a radial incision needs to be made in its base. Such an incision (see Fig. 55-15, B in Chapter 55) gives a direct approach to the area between the tension apparatus of the left-sided and right-sided AV valves where the sutures for septation must be placed.

A few marking sutures are placed to outline the proposed septation suture line (see Fig. 56-19, A-B). Goals are to (1) partition the two ventricles about equally; (2) provide unobstructed pathways from right atrium through the right-sided AV valve to pulmonary trunk, and from left atrium through the left-sided AV valve to VSD, outlet chamber (right ventricle), and aorta; and (3) avoid damage to coronary arteries by placing all sutures from within the ventricle. As McGoon and colleagues emphasized, position of the suture line is predeterined by anatomy of the tension apparatuses of the AV valves posteriorly and inferiorly and by location of semilunar valves and VSD superiorly. Therefore, only anteriorly can the surgeon select the suture siting in an attempt to partition the ventricle equally.

Pledged 2-0 polyester mattress sutures are placed and held individually by small hemostatic forceps. The most difficult area is the heavily trabeculated diaphragmatic surface. Suturing is begun here, if necessary invaginating the ventricular wall with a finger outside the heart as the stitches are placed. Suture placement is then carried posteriorly and superiority between the tension apparatuses of right-sided and left-sided AV valves. Starting again at the diaphragmatic surface, suture placement is carried to the left and anteriorly and then superiorly along the anterior left ventricular wall along the previously determined line. The suture line passes over the VSD and then swings posteriorly and to the right beneath the subpulmonary area (see Fig. 56-19, A-B). Sutures must be placed close together; 20 to 30 sutures are usually required. As they are individually clamped and set aside, care is taken to maintain their proper order. Alternatively, a running suture can be used.

Size and shape of the previously trimmed patch are inspected and altered if needed. Sutures are passed through the patch, the patch slid into position, and the sutures tied. If a two-stage approach is used, the hole in the patch is made at this time (Fig. 56-20). If the right-sided AV valve has been incised, it is repaired with continuous 6-0 polypropylene sutures (see Fig. 55-15 in Chapter 55).

Cardiac reperfusion is begun, and remainder of procedure is completed as described previously (see “Completing Cardiopulmonary Bypass” in Section III of Chapter 2). A groove or indentation can usually now be seen in the ventricular wall along part of the suture line. Two temporary right atrial and two temporary ventricular epicardial wires are placed, and AV sequential pacing is begun. Usual de-airing procedures are carried out (see “De-airing the Heart” in Section III of Chapter 2).

After hemostasis has been secured, two permanent pacing electrodes are placed on the right atrium and two on the ventricle. Their ends are brought subcutaneously into the right upper quadrant, and in most patients an appropriate pacemaker is inserted a day or two later (see “Permanent Pacing after Intracardiac Surgery” under Technique of Intervention in Section I of Chapter 16).

Cardiac Transplantation

Cardiac transplantation can usually be accomplished, no matter how complex the coexisting venous and arterial anomalies (see Technique of Operation in Chapter 21). Procedures for Subaortic Obstruction

Operations designed to address subaortic stenosis are detailed in Chapter 41. Arguments have been developed both in favor of routinely addressing real or potential subaortic stenosis using the DKS anastomosis, Norwood procedure, or rarely the arterial switch in the neonatal period, and in favor of selective use of neonatal pulmonary artery banding with early follow-up and surgical management of subaortic stenosis, if and when it develops. If subaortic stenosis is to be surgically approached by direct VSD enlargement, an incision is made in the free wall of the incomplete ventricular chamber. This exposes the VSD, aortic valve, and internal dimensions of the incomplete ventricle. From this perspective, the conduction pathway is always posterior and inferior in relation to the VSD (Fig. 56-21), regardless of whether the heart is L-looped or D-looped. Based on this relationship, the VSD is enlarged as depicted in Figs. 56-22 to 56-24. The ventriculotomy is always closed with a patch (see Fig. 56-24).

SPECIAL FEATURES OF POSTOPERATIVE CARE

Fontan Operation

Care after a Fontan-type procedure is discussed under Special Features of Postoperative Care in Section IV of Chapter 41.

Septation Operation

Usual protocols are followed postoperatively (see Chapter 5). Following septation, right atrial pressure is usually a few mmHg higher than left and should be maintained around 12 to 14 mmHg in the early hours after operation.

Other Operations

Special features of postoperative care after pulmonary trunk banding, atrial septectomy, shunting operations, and operations for subaortic stenosis are described in Chapter 41.

RESULTS

Fontan Operation

Results of the Fontan operation are discussed in detail under Results in Section IV of Chapter 41. However, the several studies have examined the effect of ventricular hypertrophy on outcome following the Fontan operation. In those
Figure 56-19  Septation operation for double inlet left ventricle and left-sided, small subaortic right ventricle in a patient with atrial situs solitus. A, Septation operation is performed through a right atrial approach, but it is best illustrated through the alternative fishmouth incision in the ventricular main chamber. Positions of atrioventricular (AV) node and bundle of His are shown by dashed lines. Note that AV node is anterior, in the right atrial wall at the junction of right atrial roof and atrial septum. The bundle of His penetrates the junction of right AV valve and pulmonary valve to pass over subpulmonary area along anterior left ventricular free wall. B, As viewed through right atrium, as it passes along the interventricular septum, it courses anterior to ventricular septal defect (VSD) (or outlet foramen), as seen from this perspective, and divides into left and right bundle branches (see Figs. 56-20 to 56-23 to appreciate the posterior relationship of conduction system to the VSD when viewed from the perspective of an incision in the free wall of the incomplete ventricle). Septation operation usually results in heart block when performed in one stage. Dots indicate suture placement for inserting septation patch. Key: Ao, Aorta; AV, atrioventricular; LA, left atrium; LV, right-sided morphologic left ventricle; PT, pulmonary trunk; RA, right atrium; RV, left-sided morphologic right ventricle; SVC, superior vena cava.
Chapter 56  Double Inlet Ventricle and Atretic Atrioventricular Valve

Figure 56-20  Illustration of septation patch fenestration in two-stage repair of double inlet left ventricle with left-sided small subaortic right ventricle in situs solitus. Hole in septation patch (created “VSD,” fenestration) is placed in a convenient spot in middle of patch for easy access at second-stage procedure. It must be made large enough to create a nonrestrictive communication. (Modified from Margossian and colleagues.\textsuperscript{144})

Figure 56-21  Relationship of course of conduction system to ventricular septal defect in hearts with double inlet left ventricle, as viewed from the incomplete (rudimentary) ventricle, which is the same whether the incomplete subaortic ventricle is left sided (left depiction) or right sided (right depiction). Line of tiny circles illustrates course of conduction system. (Modified from Cheung and colleagues.\textsuperscript{142})

Figure 56-22  Direct relief of subaortic stenosis in double inlet left ventricle with left-sided subaortic incomplete right ventricle. A portion of apical ventricular septum is removed by wedge resection, as illustrated in upper panel. Lower panel shows resection to be clear of conduction tissue (pathway depicted by line of small circles). (From Cheung and colleagues.\textsuperscript{142})
studies, the populations were either predominantly or exclusively patients with double inlet left ventricle with subaortic obstruction. Ventricular hypertrophy was shown to be a risk factor for death and poor outcome at and following the Fontan operation, and attempted relief of subaortic stenosis at the time of, or anytime following, the Fontan operation was attended by an increased risk of death at the time of the procedure.\textsuperscript{1,4,8}

**Fig. 56-23** Autopsy specimen, viewed after opening incomplete right ventricle and aorta, from a patient who died after enlarging ventricular septal defect as described in Fig. 56-22. Sinus rhythm had been present throughout the postoperative period. A large opening has been created that is clear of conduction tissue, the path of which is demonstrated by black dots. (From Cheung and colleagues.\textsuperscript{2})

**Fig. 56-24** Sketches of operative procedure for enlarging ventricular septal defect as described in Figs 56-21 and 56-22. Note enlarging patch that has been used to close ventriculotomy. (From Cheung and colleagues.\textsuperscript{2})

### Septation Operation

#### Early (Hospital) Death

In a 1984 report, overall hospital mortality after septation operation was high, about 30% to 40%\textsuperscript{14} (Table 56-5). However, among patients with moderate enlargement of the left ventricular main chamber without concomitant AV valve replacement or an extracardiac conduit, hospital mortality has been about 5%, but confidence limits are wide (Table 56-6 and Fig. 56-25). In a more recent report (1997), overall hospital mortality was less than 10%.\textsuperscript{1} In the series by Margossian and colleagues, 2 of 11 (18%; CL 6.3%-38%) patients died. One death occurred in a two-stage repair that included an arterial switch, and the other in a one-stage repair. This improvement may reflect general progress in the field but may also be influenced by patient selection.

#### Time-Related Survival

So few patients have survived the early postoperative period after septation operation that estimates of long-term survival have wide CLs, but intermediate survival is reported to be about 60% when all deaths, including those in hospital, are accounted for (see Fig. 56-25).\textsuperscript{M7} Remarkably, the single slowly declining hazard function is low after about 5 years. In a more recent study of a 23-patient experience, midterm follow-up (3-11 years) showed an overall survival of 78%.\textsuperscript{N1} In the 11-patient series of Margossian and colleagues, there was one late death with median follow-up of 2.3 years, with survival documented up to 8 years.\textsuperscript{M4} There are two single-patient case reports of survival of 9 and 12.5 years.\textsuperscript{N2, O3}

#### Modes of Death

Hospital deaths have usually been in acute heart failure, and late deaths sudden or after reoperation (usually for AV valve replacement).\textsuperscript{M7}
Survival after septation operation for double inlet ventricle

Table 56-5 Hospital Mortality after Septation Operation for Double Inlet Ventricle

<table>
<thead>
<tr>
<th>Morphologya</th>
<th>n</th>
<th>No.</th>
<th>%</th>
<th>CL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular L-loop, two ventricles with dominant and double inlet LV and rudimentary and leftward RV, discordant VA connection, L-malposition of aorta</td>
<td>28</td>
<td>10</td>
<td>36</td>
<td>25-47</td>
</tr>
<tr>
<td>Solitary ventricleb</td>
<td>5</td>
<td>2</td>
<td>40</td>
<td>14-71</td>
</tr>
<tr>
<td>Ventricular L-loop, two ventricles with dominant and double inlet and double outlet RV, superior-inferior ventricles, D-malposition of aorta</td>
<td>1</td>
<td>1</td>
<td>100</td>
<td>15-100</td>
</tr>
<tr>
<td>Ventricular D-loop, two ventricles with dominant and double inlet LV, concordant VA connection, more or less normally positioned great arteries</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0-85</td>
</tr>
<tr>
<td>Ventricular D-loop, two ventricles with dominant and double inlet and double outlet LV, more or less normally positioned great arteries</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0-85</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>36</td>
<td>13</td>
<td>36</td>
<td>27-46</td>
</tr>
</tbody>
</table>

Data from Stefanelli and colleagues.114

aNo patients with atrial situs inversus had septation; cases are with or without pulmonary stenoses.

bOne patient, who lived after operation in 1983, had ventricular L-loop, essentially AV and VA discordant connections with essentially two ventricles, an absent septum, right-sided LV morphology, and left-sided RV morphology; another patient, who also lived after operation in 1983, had ventricular D-loop, essentially AV and VA concordant connections with essentially two ventricles, an absent septum, right-sided RV morphology, and left-sided LV morphology (common ventricle); the other three patients had an indeterminate, primitive ventricle.

cSeverely overriding right-sided ventricular AV valve.

dData from patients with main chamber enlarged grade 3 or more without concomitant atrioventricular valve replacement or use of a valved extracardiac conduit.

Key: AV, Atrioventricular; CL, 70% confidence limits; LV, left ventricle; RV, right ventricle; VA, ventriculoarterial.

Table 56-6 Hospital Mortality and Age Distribution in Septation for Single Ventricle

<table>
<thead>
<tr>
<th>≤ Age Years</th>
<th>&lt;</th>
<th>n</th>
<th>No. of Hospital Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>2</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>8</td>
<td>16</td>
<td>7</td>
</tr>
<tr>
<td>16</td>
<td>16</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>16</td>
<td>1</td>
<td>(6%; CL 0.8%-20%)</td>
</tr>
</tbody>
</table>

Data from McKay and colleagues.407

Incremental Risk Factors for Death

Within the group that currently is considered for septation (double inlet left ventricle, ventricular L-loop, left-sided incomplete right ventricle with VA discordant connection, atrial situs solitus), no risk factors have been identified. However, unusual forms of double inlet ventricle, a small ventricular main chamber, concomitant AV valve replacement, and placement of a valved extracardiac conduit have been risk factors.417 Aside from morphologic factors, increasing age and ventricular hypertrophy have been identified as risk factors.431

Functional Status

Functional status is generally good after septation. This might be expected from the experimental study by Seki, Tsakiris, and McGoon, which showed no demonstrable detrimental hemodynamic effect of replacing the dog’s ventricular septum (and tricuspid valve) with a prosthesis.435 It is also supported

Figure 56-25 Survival after septation operation for double inlet ventricle without atrioventricular valve replacement and without valved extracardiac conduit, in patients with main chamber enlargement greater than grade II (patients are described in Table 56-6). Open circles represent deaths and vertical bars 70% confidence limits (CLs). Solid line represents parametrically estimated survival, and dashed lines enclose 70% CLs. Values in the table are from parametrically determined survival. Numbers in parentheses indicate number of patients available for further follow-up at the interval shown. A, Survival. B, Hazard function. There is only a single slowly declining hazard phase, which reaches a low level 5 years after septation. (Data, except for subsequently updated follow-up, from McKay and colleagues.435)
by detailed hemodynamic study of two patients late after septation by Shimazaki and colleagues. In one patient 8 years post-septation, both right and left ventricular ejection fractions were normal, as was hemodynamic response to exercise. Kurosawa and colleagues found cardiac indices to be higher after septation than after a Fontan operation. However, late after a septation or Fontan operation, cardiorespiratory function by objective measurements at rest and during exercise is depressed compared with normal. Evidence is contradictory as to whether septation provides better cardiorespiratory function than the Fontan operation. In one study, objectively measured postoperative exercise tolerance, compared with that preoperatively, was more improved after the Fontan operation than after septation, but in a later study, superior cardiorespiratory function was found after septation. In a more recent study of double inlet left ventricle patients comparing Fontan or septation, septation patients with native AV valves demonstrated superior cardiopulmonary response to exercise compared with either Fontan patients or septation patients with prosthetic AV valves.

Heart Block
Complete heart block is not inevitable after septation. It occurred after most septation operations in one series from 1982. However, in a series from 2002, only 1 of 11 patients (9.1%; CL 1.5%-28%) developed it. The difference may be that a running suture technique was used in the series with a low occurrence of heart block, rather than interrupted pledgeted mattress sutures that penetrate deeper into the myocardium.

Cardiac Transplantation
Results of cardiac transplantation are discussed in detail under Results in Section II of Chapter 21.

Other Operations
Results for systemic–pulmonary artery shunts, pulmonary trunk banding, operations to relieve systemic outflow obstruction, coarctation repair, atrial septectomy, bidirectional superior cavopulmonary anastomosis, and hemi-Fontan are reported in Chapter 41.

Outcome Related to Specific Morphology
In a multicenter analysis of 150 patients with double inlet left ventricle who were younger than 3 months of age at diagnosis, overall survival was 88% at 1 month and 76% at 10 years. By multivariable analysis, the only risk factor for premature death was a neonatal operation of any kind.

Outcome for the Fontan in double inlet left ventricle patients is excellent, with a 3% early mortality in patients operated on after 1989, and 20-year actuarial survival of about 70% in one large series. Pass and colleagues reported a series of bulboventricular foramen (VSD) enlargement for systemic outflow obstruction in eight patients, five with S,L,L double inlet left ventricle and three with left AV valve atresia. Patients ranged in age from 2 months to 27 years. There was one early and one late death. Gradient relief was complete initially in seven, with one persistent gradient. Two patients developed recurrent obstruction following initial complete relief. All three patients with recurrent or persistent gradients underwent reoperation with relief of the gradient. At mean follow-up of 22 months, all patients were unobstructed. One patient in the series developed new-onset heart block; there was no new-onset aortic regurgitation.

Clarke and colleagues reported a 4% early mortality for interval DKS operation in a series of 15 S,L,L double inlet left ventricle patients initially managed as neonates with pulmonary artery banding and arch reconstruction. These excellent results are more expected in a favorable population of patients that did not have severe neonatal obstruction of the bulboventricular foramen. In contrast, Lan and colleagues noted a higher mortality when the DKS operation was performed in neonates, as did Lotto and colleagues for the Norwood operation in neonates.

Kawahira and colleagues reported on a series of 31 double inlet right ventricle patients. Compared with patients having double inlet left ventricle and common inlet ventricle, the prevalence of pulmonary atresia and discontinuous pulmonary arteries was higher in double inlet right ventricle, resulting in more frequent systemic-to-pulmonary artery shunt procedures in this subgroup. Overall outcomes for double inlet right ventricle were similar to those for double inlet left ventricle, however, and were superior to outcomes for common inlet ventricle (Fig. 56-26).

INDICATIONS FOR OPERATION
Primary considerations in managing patients with double inlet ventricle of any type are first and foremost assessment of, and correction of, important neonatal and infant hemodynamic abnormalities, using the palliative operations described in this chapter. Thereafter, considerations become (1) patients’ suitability for septation, Fontan operation, or cardiac transplantation and (2) preventing additional mortality.
complicating conditions such as subaortic stenosis or pulmonary arterial stenoses.

Fontan Operation

All patients suitable for septation are suitable for a Fontan operation (except those with elevated pulmonary vascular resistance). Some 70% to 80% of patients with various types of double inlet ventricle or atretic AV valve appear at birth to be suitable at a later date,^{14} but nearly 50% of those become unsuitable by about age 2 years (Fig. 56-27). Thus, when in early life a Fontan operation is considered feasible and advisable, an appropriate staged surgical management approach as outlined in Chapter 41 is planned.

Septation Operation

In the past, a septation operation was considered the most desirable of the three if intracardiac morphology was suitable. However, outcomes following the Fontan operation have improved markedly; currently, Fontan operation is generally considered the procedure of choice, possibly even in many cases with suitable morphology for septation.

Apparently, 20% to 25% of patients born with double inlet ventricle are suitable at birth for septation.^{14} By 2 years of age, 30% of those with the malformation are either dead or no longer suitable for septation, and this proportion increases as time passes (Fig. 56-28). A common reason for developed lack of suitability is subaortic stenosis.^{14}

To be suitable for septation, the patient must have a somewhat, but not severely, enlarged dominant ventricle (Fig. 56-29) into which enter two reasonably competent and nonstenotic AV valves with little or no overriding or straddling.^{14,7,1,14} Success with a single common AV valve has been reported.^{8} The VA connection must be concordant with the AV valve connections projected for the septated ventricle. There should be little or no pulmonary or systemic outflow obstruction.

Because of the age-related declining proportion of patients suitable for septation, resulting from the adverse effect of increasing hypertrophy of the dominant (main) chamber, and the strong tendency for development of pulmonary vascular disease unless there is natural or produced (by banding) pulmonary stenosis, septation should be performed during the first year or two of life. Consideration should be given to a two-stage approach to minimize the probability of producing complete heart block (see “Staged Septation” under Special Situations and Controversies).

Cardiac Transplantation

At birth, 25% to 30% of patients are already unsuitable for either septation or a Fontan operation.^{15} Only about 30% survive the first year of life (Fig. 56-30). The place of cardiac transplantation is arguable for this group of patients, but if
anything is to be done for them, transplantation would appear to be appropriate. It should be performed in the first month if possible (see “Indications for Cardiac Transplantation” in Section II of Chapter 21).

Therapeutic Plan in Older Patients

Some patients come for decision making and therapy after infancy, frequently after various palliative procedures. Each case represents a special situation, but some guidelines can be followed.

Unless pulmonary trunk banding has been performed, septation is often contraindicated because of pulmonary vascular disease, severe ventricular hypertrophy, or AV valve regurgitation. Fontan operation is possible when AV valve regurgitation has developed in one of two valves, but at Fontan operation, or as a separate preliminary operation, the valve needs to be perfectly repaired or closed (see “Closure of the Right Atrioventricular Valve” under Technique of Operation earlier in this chapter).

If pulmonary trunk banding was performed in early life, probability of subaortic stenosis is considerable. It should be suspected, even if no gradient is demonstrable, if the VSD is small or only moderate sized. If subaortic stenosis is severe, consideration should be given to treating this before undertaking the Fontan operation. In this setting, direct enlargement of the VSD is a better option than in neonates, but the DKS anastomosis or arterial switch operation can still be considered.

SPECIAL SITUATIONS AND CONTROVERSIES

Staged Septation

Ebert reported a two-stage approach to septation in a subset of patients. At the first stage, performed in infancy, a partially septating patch was placed at the apex of the ventricle and a second superiorly between the AV valves, using widely spaced interrupted sutures. A pulmonary trunk band was placed. Septation was completed with a third patch 6 to 18 months later. The other patches were then completely sealed into position. The band was removed. All patients survived, and all were in sinus rhythm. Margossian and colleagues have also reported success with this approach, as have McKay and colleagues.

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B

6. Blalock A, Taussig HB. The surgical treatment of malformations of the heart in which there is pulmonary stenosis or pulmonary atresia. JAMA 1945;128:189.


Anatomically Corrected Malposition of the Great Arteries

**Definition**
Anatomically corrected malposition is an anomaly in the position of the great arteries but not in cardiac connections. Thus, there is atroventricular (AV) and ventriculoarterial (VA) concordant connection as in the normal heart, but the aortic origin lies to the left and usually anterior to the pulmonary trunk origin when there is situs solitus (Van Praagh’s S,D,L; see “Symbolic Convention of Van Praagh” in Chapter 1) and to the right of the pulmonary trunk origin when there is situs inversus (I,L,D). The circulatory pathways remain in series.

**Historical Note**
Anatomically corrected malposition of the great arteries was first reported by Theveanin in 1895 (cited by Van Praagh and Van Praagh\textsuperscript{2}) and was first termed *anatomically corrected transposition of the great arteries* by Harris and Farber in 1939.\textsuperscript{1} It is possible similar cases were described earlier under a variety of names. This confusion is exemplified by the case of Raghib and colleagues, described in 1966 with the phrase *isolated bulbar inversion in corrected transposition.*\textsuperscript{8,1} The Van Praaghs, who had doubted its existence, described three cases in 1967 using the term *anatomically corrected transposition of the great arteries.*\textsuperscript{2} At that time, Abbott’s influential 1927 definition of transposition, according to which any abnormality in the relationship of the great arteries or between the great arteries and the ventricles was called *transposition,* was still accepted.\textsuperscript{1} This confusion was clarified when Van Praagh and colleagues redefined *transposition* in 1971 as the origin of the aorta from the morphologically right ventricle and the pulmonary trunk from the morphologically left ventricle (i.e., VA discordant connection) and proposed that other positional and connection abnormalities be included in the definition of *malposition.*\textsuperscript{2} The present condition was thus renamed *anatomically corrected malposition of the great arteries.*\textsuperscript{1,3}

**Morphology and Morphogenesis**

**Morphology**
When there is situs solitus of the atria, usually the right atrium is connected to the right ventricle\textsuperscript{1} (D-loop), which lies to the right, and the left atrium is connected to the left ventricle, which lies to the left (S,D,L arrangement). Structure of the sinus portions of both ventricles is normal. However, although the aorta arises from the left ventricle and the pulmonary trunk from the right ventricle, there are abnormalities of the outlet, or infundibulum, in both ventricles. The left ventricle probably always exhibits a subaortic conus (infundibulum) with a well-formed conal septum, and muscle exists between aortic and mitral valve anuli.\textsuperscript{1} Aortic origin is accordingly displaced superiorly and anteriorly. The right ventricle may also have an infundibulum, but it may be less well developed than normal and in some cases is absent.\textsuperscript{2} In the latter case, there is pulmonary-tricuspid fibrous continuity. The aorta lies to the left and usually anterior to the pulmonary trunk, and both arteries are parallel. Rarely, there may be situs inversus with an I,L,D arrangement.\textsuperscript{2}

Hearts with similar types of infundibular development but AV discordant connection, although originally included in this category by both the Van Praaghs and Anderson and colleagues, are not called *anatomically corrected malposition* in this text but are included as variants of isolated ventricular inversion (see Section II of Chapter 55).\textsuperscript{2,2}

**Morphogenesis**
Van Praagh argues that all forms of abnormally related great arteries relate to maldevelopment of the subsemilunar conal free walls—an abnormality of what he terms the *embryonic*...
aortic switch procedure. In anatomically corrected malposition of the great arteries, the ventricles have looped in one direction, which the great arteries have twisted in the opposite direction, carrying with them the subsemilunar conal free wall. Although the great arteries are normally related (aligned), Van Praagh notes that the VA connection is very abnormal because of the abnormality in subsemilunar conal resorption.

Associated Anomalies

All reported cases of anatomically corrected malposition have been associated with other congenital cardiac anomalies. A large ventricular septal defect (VSD) is commonly present, usually conoventricular but occasionally elsewhere, as would be anticipated with abnormal subarterial conal connections to the ventricles; VSDs may be multiple. When the VSD is subpulmonary, the pulmonary trunk may override onto the left ventricle such that the condition merges with double outlet left ventricle (see Morphology in Chapter 54). When the VSD is subaortic, the aorta may override onto the right ventricle such that the condition merges with double outlet right ventricle (see Morphology in Chapter 53). In a recent report of six cases from one institution, VSD was absent in three, although a literature review of 53 cases reported absence of VSD in only three.

Pulmonary stenosis is usual, often infundibular in association with the subpulmonary conus, but occasionally valvar. Subaortic stenosis may occur from narrowing of the muscular subaortic conus. Tricuspid atresia or tricuspid valve hypoplasia has been noted in half the reported cases, accompanied by right ventricular hypoplasia. A right aortic arch is common, as is leftward juxtaposition of the atrial appendages and dextrocardia.

Aortic coarctation and arch hypoplasia has been reported in five cases. Two of these have had severe subaortic stenosis and left ventricular hypoplasia, and three had no physiologic left ventricular outflow tract obstruction and a normally developed left ventricle.

CLINICAL FEATURES AND DIAGNOSTIC CRITERIA

Clinical features depend on associated anomalies such as VSD or pulmonary stenosis. Correct diagnosis may first be suspected from the characteristic appearance of L-malposition in the chest radiograph (Fig. 57-1). Two-dimensional echocardiography usually establishes the diagnosis, confirming abnormalities of ventricular outflow tracts, concordant AV and VA connections, situs, positions of cardiac chambers and great vessels, and associated intracardiac defects. Additional studies such as cineangiography (Fig. 57-2), magnetic resonance imaging (Fig. 57-3), or computed tomography (Fig. 57-4) are confirmatory or diagnostic if echocardiography fails to fully characterize the lesion. Occasionally, correct diagnosis is made only at operation. The diagnosis may remain ambiguous when there is a conoventricular VSD and one of the great arteries is overriding.

Possible diagnoses other than anatomically corrected malposition in patients with atrial situs solitus and L-malposition of the aorta include complete transposition with L-malposition (see Chapter 52), AV discordant connection with double outlet right ventricle and L-malposition (see Chapter 53), AV discordant connection with double outlet left ventricle (see Chapter 54), congenitally corrected transposition of the great arteries (see Chapter 55), AV discordant connection with double outlet right or left ventricle (see Chapter 55), and several forms of univentricular AV connection, most commonly those associated with double inlet left ventricle, rudimentary left-sided right ventricle, and VA discordant connection (see Chapter 56).

NATURAL HISTORY

The simple positional anomaly of anatomically corrected malposition per se has no impact on the natural history of patients. Rather, natural history is affected as typical for the associated cardiac anomalies.

TECHNIQUE OF OPERATION

Surgical treatment of anatomically corrected malposition is determined by associated cardiac anomalies. The few special problems imposed on aortic cannulation by L-malposition are discussed under surgical treatment of congenitally corrected transposition of the great arteries (see Technique of Operation in Section I of Chapter 55).

When there is tricuspid atresia or important right ventricular hypoplasia, a Fontan-type procedure is performed (see Technique of Operation in Section IV of Chapter 41). When both ventricles are of adequate size, the VSD (if present) is closed, and pulmonary stenosis is treated. This may be accomplished as simply as possible, preferably by valvotomy, infundibular resection, or both. When necessary, a more complex solution is required, such as a transanular patch, an allograft-valved extracardiac conduit, a Lecompte intraventricular repair (réparation à l’étage ventriculaire [REV]) (see
undergoing biventricular repair can reasonably be expected to have outcomes similar to those of patients with double-outlet right or left ventricle. Those treated as having single-ventricle physiology can reasonably be expected to have outcomes similar to those of patients undergoing various staged procedures leading to and including the Fontan operation (see Chapter 41). In one series, three of four patients survived biventricular repair at midterm follow-up, with one patient dying at reoperation for an obstructed conduit. In another

"Lecompte Intraventricular Repair" under Technique of Operation in Chapter 53), or translocation in continuity of the pulmonary trunk and valve to the right ventricle.

RESULTS

Because the anomaly is rare and the associated anomalies that determine indication for operation are variable, no meaningful statements can be made regarding outcomes. Patients undergoing biventricular repair can reasonably be expected to have outcomes similar to those of patients with double-outlet right or left ventricle. Those treated as having single-ventricle physiology can reasonably be expected to have outcomes similar to those of patients undergoing various staged procedures leading to and including the Fontan operation (see Chapter 41). In one series, three of four patients survived biventricular repair at midterm follow-up, with one patient dying at reoperation for an obstructed conduit. In another

Figure 57-2  Left ventriculograms of anatomically corrected malposition of the great arteries and ventricular septal defect. There is an infundibulum beneath both aorta and pulmonary trunk. The aorta is to the left of the pulmonary trunk, and they are parallel. There is subvalvar pulmonary stenosis. A, Anteroposterior projection. B, Lateral projection. C-D, Later sequences. Key: AO, Aorta; C, infundibulum (conus); LV, left ventricle; PT, pulmonary trunk; RV, right ventricle. (From Kirklin and colleagues.)
report, two patients undergoing VSD closure and right ventricular outflow tract conduit placement survived operation. Kirklin and colleagues reported two patients, both of whom survived following VSD closure and procedures to relieve right ventricular outflow obstruction. In the largest single institution report to date (six cases), two patients underwent surgical correction, both successfully. Beyond these reports, only isolated case reports exist. Two separate cases of associated aortic coarctation with VSD report repair with staged operations. The first had arch repair with pulmonary artery banding followed by VSD closure and debanding. Both patients survived.

Figure 57-3  Cardiac magnetic resonance images (MRI) of a patient with anatomically corrected malposition of the great arteries. Steady-state free precession cardiac MRI. A, Four-chamber view demonstrating mesocardia, atrial situs solitus, and D-looped ventricles. B, Axial view demonstrating an abnormal great artery relationship, with the aorta arising slightly more anterior and to the left of the pulmonary trunk. C-D, Two-chamber views demonstrating left- and right-sided atrioventricular and ventriculoarterial concordant connections, as well as bilateral conal tissue (arrows) resulting in aortic-mitral and pulmonary-tricuspid discontinuity. Key: A, Anterior; Ao, aorta; LA, left atrium; LV, left ventricle; PT, pulmonary trunk; R, right; RA, right atrium; RV, right ventricle; S, superior. (From Clarke and colleagues.)
Figure 57-3, cont’d E, Three-dimensional reconstruction of a gadolinium-enhanced magnetic resonance angiogram demonstrating an abnormal great artery relationship. The aorta arises slightly more anterior and to the left of the pulmonary trunk. Each great artery arises from the appropriate ventricle, resulting in ventriculoarterial concordance.

Figure 57-4 Computed tomography images of anatomically corrected malposition of the great arteries. A-B, Coronal and axial views showing left anterior position of the ascending aorta to the pulmonary trunk; pulmonary valve stenosis was also noted. Key: AA and Ao, ascending aorta; DA, descending aorta; LPA, left pulmonary artery; LV, left ventricle; PA, pulmonary artery; PS, pulmonary valve stenosis; RPA, right pulmonary artery; RV, right ventricle; VSD, ventricular septal defect.

INDICATIONS FOR OPERATION
Anatomically corrected malposition of the great arteries is not an indication for operation. Coexisting cardiac anomalies may present an indication for operation. Most frequently these are VSD and obstruction to right ventricular outflow.

SPECIAL SITUATIONS AND CONTROVERSIES
Several special morphologic concerns warrant emphasis. A transanular patch may be difficult or impossible to place in some cases of right ventricular outflow obstruction, because the right coronary artery passes across the free wall of the
right ventricular infundibulum. Not unexpectedly, coronary artery abnormalities are common, including abnormalities of the origins and surface course along the ventricles. These variations make the coronary arteries unreliable guides when planning ventriculotomy.

REFERENCES

A

C

D

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DEFINITION

Atrial isomerism is a condition in which the right-sided and left-sided atria, normally morphologically different, are morphologically similar.\(^1\) Thus, left atrial isomerism and right atrial isomerism can occur. Atrial isomerism is a specific phenotypic feature highly associated with generalized somatic laterality disorders characterized by abnormal arrangement of thoracic and abdominal viscera, including important structural cardiovascular anomalies. The terms *situs ambiguous* and *heterotaxy* are used to describe these laterality disorders.

Attempts to classify specific constellations of the many clinical and phenotypic features that can occur with heterotaxy have resulted in descriptive terms such as *asplenia syndrome* and *polysplenia syndrome*.\(^2\) Experience shows that although there is some tendency for certain constellations to occur, exceptions are frequent or even the rule. About 3% of all congenital heart anomalies occur in the context of heterotaxy.\(^3\) The various cardiac anomalies found in heterotaxy are shown in Table 58-1.\(^4\)

In this chapter, individual cardiovascular anomalies and commonly recognized constellations of cardiovascular anomalies that occur with heterotaxy are discussed. These complex associations are analyzed from a perspective that uses left atrial isomerism and right atrial isomerism as reference points or starting points for analysis.

HISTORICAL NOTE

Anomalies of right and left sidedness related to asymmetry of the body were recognized at least by the 15th century with Leonardo da Vinci’s drawing of situs inversus. In the early 17th century, Marco Aurelio Severino described this anatomic variant, but it was Matthew Baille, a student of John Hunter, who is credited with scientifically describing anomalies of sidedness and their associated lesions in the latter part of the 18th century.\(^5\) In 1933 Kartagener drew attention to the association of situs inversus with sinusitis (Kartagener syndrome), providing an important clue to the possible morphogenesis of all anomalies of sidedness, although this had been suggested by Siewert in 1904.\(^6\) Biorn Ivemark in 1955 identified the syndrome of right atrial isomerism, asplenia, symmetry of thoracic organs, and conotruncal anomalies during his studies at Children’s Hospital Boston.\(^7\)

Subsequently, general interest in the asymmetry of many bilateral animals, from snails to humans (the science related to chiral [asymmetric] bodies), has led to the hypothesis that left-right patterning is related to genetic factor processes that become reflected in midline left-right ciliary structure and function during embryogenesis.\(^8,9\) In the 1986 first edition of this book, Kirklin presented the UAB surgical experience with heterotaxy patients, consisting of 28 complete repairs and 28 palliative operations (including two Fontan operations).
MORPHOLOGY AND MORPHOGENESIS

Morphology

Atrial Isomerism

In atrial isomerism, both atria have similar internal, external, and appendage configuration. They are considered either morphologically bilaterally right atria or bilaterally left atria.\(^\text{M6,R4,V2}\) Validity of the concept of atrial isomerism, at least from the perspective of the purist, has been questioned.\(^\text{C4,V3}\)

Atrial situs is most usefully determined by morphology of the atrial appendages,\(^\text{Cl,M1,S4}\) because all other studies provide indirect information. Right atrial appendage morphology is present when the appendage is blunt and has a broad junction with a smooth-walled atrium. This type of junction is accompanied by protrusion of the crista terminalis into the atrial cavity.\(^\text{M5}\) Left atrial appendage morphology is present when the appendage is long and thin with constrictions along its length. Such appendages have a rather constricted junction with a smooth atrium, within which a crista terminalis is not identifiable.\(^\text{M1}\) Rarely, atria and their appendages have mixed right and left atrial morphology.

Atrial isomerism (right or left) commonly corresponds to thoracic isomerism; however, disharmony between atrial and thoracic morphology and pulmonary and bronchial morphology occurs.\(^\text{C1,P5,S4,U1}\) Atrial and thoracic isomerism (i.e., bilateral atrial and thoracic right- or left-sidedness) usually corresponds to bilateral right-sidedness (asplenia) or left-sidedness (polysplenia) of the abdominal viscera, but there are exceptions to this correspondence.\(^\text{1,2,U1}\) Abdominal asplenia or polysplenia may occasionally exist without atrial isomerism, so splenic state does not always predict atrial morphology.\(^\text{55}\)

Because of this variability, Anderson prefers the term heterotaxy to denote presence of any of the numerous possible lateralization abnormalities, and then recommends describing the morphologic details for each patient.\(^\text{A2}\)

Among 58 consecutive newborn cases of heterotaxy within a single institution, 25 had asplenia and 20 had polysplenia.\(^\text{1,6}\)

In surgical series, left atrial isomerism is more common than right, in one surgical experience with 41 patients, 23 had left and 18 had right atrial isomerism.\(^\text{57}\) Several heterotaxy studies performed in Asian populations show a strong predilection (80% of cases) for right atrial isomerism, suggesting there may be racial differences in the expression of left and right atrial isomerism.\(^\text{15,31}\)

Conduction System

Right atrial isomerism is usually accompanied by bilateral sinus nodes, one in each atrium.\(^\text{53,D3,V2}\) Two atrioventricular (AV) nodes may be present, with a sling of conduction tissue between them. In left atrial isomerism, the sinus node is absent in the majority of cases, but when present is unusually positioned and often hypoplastic.\(^\text{H8}\)

The AV node may be normally situated when ventricular architecture is right-handed (D-loop); when it is left-handed (L-loop), two AV nodes and a sling may be present.\(^\text{D3}\) Other more severe conduction system abnormalities may also be present, because complete heart block occurs in some neonates with left atrial isomerism.\(^\text{G1,H4,M5}\)

Supraventricular atrial tachycardias occur in right atrial isomerism in up to 25% of patients, whereas abnormal axis P waves with slow atrial or junctional rates are the rule in left atrial isomerism.\(^\text{W3}\)

Anomalies of Systemic Venous Connection

Anomalies of systemic venous connection are common. The inferior vena cava often does not connect directly to the atrium from below, but instead passes superiorly along the right-sided paravertebral gutter (azygos extension of inferior vena cava) or left-sided gutter (hemiazygos extension of inferior vena cava), emptying into a right-sided or left-sided superior vena cava\(^\text{12}\) (Table 58-2). Azygos extension of the inferior vena cava occurs exclusively in patients with left atrial isomerism, in whom it occurs in about 75% of cases (see Table 58-2).

Table 58-1 Prevalence of Major Anatomic Cardiac Variables in 81 Patients with Prenatal and Postnatal Diagnosis of Heterotaxy Syndrome

<table>
<thead>
<tr>
<th>Anatomic Variables</th>
<th>Prenatal Diagnosis ((n = 43)) N (%)</th>
<th>Postnatal Diagnosis ((n = 38)) N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isomerism of left atrial appendages</td>
<td>17 (39.5)</td>
<td>13 (34.2)</td>
</tr>
<tr>
<td>Isomerism of right atrial appendages</td>
<td>26 (60.5)</td>
<td>25 (65.8)</td>
</tr>
<tr>
<td>Right-sided heart</td>
<td>14 (32.5)</td>
<td>14 (36.8)</td>
</tr>
<tr>
<td>Interrupted inferior vena cava</td>
<td>15 (34.9)</td>
<td>8 (21.0)</td>
</tr>
<tr>
<td>Totally anomalous pulmonary venous return ((extracardiac))</td>
<td>14 (43.8)</td>
<td>8 (21.0)</td>
</tr>
<tr>
<td>Common atrioventricular junction/ common atrioventricular canal</td>
<td>31 (72.1)</td>
<td>30 (78.9)</td>
</tr>
<tr>
<td>Hypoplastic left heart syndrome</td>
<td>9 (20.9)</td>
<td>3 (7.9)</td>
</tr>
<tr>
<td>Double outlet right ventricle</td>
<td>13 (30.2)</td>
<td>17 (44.7)</td>
</tr>
<tr>
<td>Double outlet right ventricle with pulmonary atresia</td>
<td>13 (30.2)</td>
<td>13 (34.2)</td>
</tr>
<tr>
<td>Pulmonary outflow obstruction</td>
<td>33 (76.7)</td>
<td>28 (73.7)</td>
</tr>
<tr>
<td>Systemic outflow obstruction</td>
<td>9 (20.9)</td>
<td>6 (15.8)</td>
</tr>
<tr>
<td>Complete heart block</td>
<td>8 (18.6)</td>
<td>3 (7.9)</td>
</tr>
</tbody>
</table>

Modified from Cohen and colleagues.\(^\text{C4}\)

Table 58-2 Patterns of Inferior Vena Cava Drainage \((n = 183)\)

<table>
<thead>
<tr>
<th>Atrial Appendage Isomerism</th>
<th>Atrioventricular Junction Present</th>
<th>Interrupted</th>
<th>Via Right-Sided Azygos Vein (%)</th>
<th>Via Left-Sided Azygos Vein (%)</th>
<th>Other Patterns</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>To Right-Sided Atrium (%)</td>
<td>To Left-Sided Atrium (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>48</td>
<td>52</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left</td>
<td>12</td>
<td>12</td>
<td>34</td>
<td>40</td>
<td>2</td>
</tr>
</tbody>
</table>

Data from Uemura and colleagues.\(^\text{12}\)
Bilateral superior venae cavae occur frequently: in half of patients with right atrial isomerism and in two thirds of patients with left atrial isomerism.\textsuperscript{12} (Table 58-3). When present, each typically connects to the top corner of the corresponding atrium; however, in left atrial isomerism, one may connect to the coronary sinus.\textsuperscript{M1}

When the inferior vena cava connects directly to the atria from below, it may connect to either the left- or right-sided atrium (see Table 58-2). Hepatic veins connect directly to the atria from below, usually to one atrium but sometimes to both or to both sides of a common atrium.\textsuperscript{M1} Such a direct hepatic vein connection is present in all patients with an azygos extension of the inferior vena cava, but it also occurs in patients whose inferior vena cava connects to the atria from below (Table 58-4).

Uemura and colleagues report that the coronary sinus orifice is absent in about 40% of patients with left and in 100% of patients with right atrial isomerism.\textsuperscript{U1} Other series, however, show substantial variation from these percentages.\textsuperscript{P2,P4,V3} Anomalies of systemic venous connection do not occur exclusively in patients with atrial isomerism.\textsuperscript{M4}

### Anomalies of Pulmonary Venous Connection

Extracardiac total anomalous pulmonary venous connection (TAPVC) is usually seen in patients with right atrial isomerism (Table 58-5). When pulmonary veins connect to an atrium, pattern of connection is variable. Importantly, there is usually the normal wide area of posterior atrial wall between the pulmonary veins when the heart is viewed from behind.\textsuperscript{M1} Pulmonary venous obstruction may be present in up to 40% of patients with right atrial isomerism, especially when the connection is extracardiac.\textsuperscript{C3,H2,R3} Pulmonary venous obstruction in left atrial isomerism is much less common.\textsuperscript{P2} Atresia of the common pulmonary vein has been reported in right atrial isomerism.\textsuperscript{M1}

### Atrioventricular Connections

About 75% of patients with left atrial isomerism have biventricular AV connections that are ambiguous.\textsuperscript{C3,D2} However, there is a univentricular AV connection in about 50% to 75% of patients with right atrial isomerism, a considerably higher percentage than in any other type of atrial situs, and most of these patients have a solitary ventricular chamber.\textsuperscript{C3,H3,S7,U1} (Table 58-6).

### Atrioventricular Septal and Other Atrial Septal Defects

The complexities of pulmonary and systemic venous connections, variability in the position and nature of AV valves through which the atria empty, and anomalous muscle bands that sometimes traverse the atria often make it difficult to apply conventional terms describing atrial septal defects (ASDs). However, a common atrium (see “Common Atrium”

---

### Table 58-3 Patterns of Superior Vena Cava Drainage (n = 183)

<table>
<thead>
<tr>
<th>Atrial Appendage Isomerism</th>
<th>Unilaterally Present</th>
<th>Bilaterally Present</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>To Right-Sided Atrial Roof (%)</td>
<td>To Left-Sided Atrial Roof (%)</td>
</tr>
<tr>
<td>Right</td>
<td>29</td>
<td>19</td>
</tr>
<tr>
<td>Left</td>
<td>22</td>
<td>14</td>
</tr>
</tbody>
</table>

Data from Uemura and colleagues.\textsuperscript{U2}

### Table 58-4 Patterns of Hepatic Vein Drainage (n = 183)

<table>
<thead>
<tr>
<th>Atrial Appendage Isomerism</th>
<th>Confluence Present</th>
<th>Via Independent Channels</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Via IVC (%)</td>
<td>Via Common Channel (Interrupted IVC) (%)</td>
</tr>
<tr>
<td>Right</td>
<td>76</td>
<td>0</td>
</tr>
<tr>
<td>Left</td>
<td>14</td>
<td>43</td>
</tr>
</tbody>
</table>

Data from Uemura and colleagues.\textsuperscript{U2}

Key: IVC, Inferior vena cava.

### Table 58-5 Patterns of Drainage of Pulmonary Veins (n = 183)

<table>
<thead>
<tr>
<th>Atrial Appendage Isomerism</th>
<th>Direct Connections of All Pulmonary Veins to Atrial Chambers</th>
<th>Via Sump Outside Heart (Confluence of All Pulmonary Veins Present)</th>
<th>Others (Confluence of Pulmonary Veins Incomplete)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>To Left-Sided Atrium (%)</td>
<td>To Right-Sided Atrium (%)</td>
<td>Bilaterally to Chambers (%)</td>
</tr>
<tr>
<td>Right</td>
<td>19</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>Left</td>
<td>26</td>
<td>14</td>
<td>60</td>
</tr>
</tbody>
</table>

Data from Uemura and colleagues.\textsuperscript{U2}

\textsuperscript{a}Via central confluence.
under Morphology in Chapter 34) is present in nearly half the cases. AV septal defect is present in about 80% of patients, with a higher prevalence in right than in left atrial isomerism (see Table 58-6). Most patients with atrial isomerism and AV septal defects have a common AV orifice (see “Complete Atroventricular Septal Defect” under Morphology in Chapter 34) rather than two AV valve orifices. Rarely the atrial septum is well formed and intact or has only a probe-patent foramen ovale.

**Ventricular Morphology and Ventricular Septal Defects**
Complexities of AV valves and connections and frequent occurrence of solitary ventricular chambers make it difficult to apply conventional terms. Only rarely is the ventricular septum intact; about 80% of patients with a VSD have an AV septal defect, and in the remainder with intact AV septal structures, various types of VSD are present.

**Pulmonary Outflow**
Unobstructed pulmonary outflow is rare in right, but more frequent in left, atrial isomerism. In right atrial isomerism, pulmonary stenosis is present in slightly more than half of patients, and pulmonary atresia in about one third. In left atrial isomerism, pulmonary stenosis is present in about half and pulmonary atresia in less than one tenth (see Table 58-6).

**Ventriculoarterial Connections**
In surgical series, ventriculoarterial connections are most commonly discordant, and an unusually high proportion (33%) of patients have double outlet right ventricle. In autopsy series, about 75% to 90% of specimens with right atrial isomerism have discordant ventriculoarterial connection (transposition) or double outlet right ventricle; in left atrial isomerism, this is true in about 20% to 65% of specimens (see Table 58-6). In some cases, such as double outlet from an indeterminate ventricle, the ventriculoarterial connection cannot be easily characterized.

**Other Coexisting Cardiac Anomalies**
Anomalies other than those inherent in atrial isomerism are infrequent in surgically treated patients. In autopsy series, obstructive lesions on the left side of the heart, excluding left ventricular hypoplasia and mitral stenosis, are common.

**Summary**
In the surgically more common left atrial isomerism, anomalies of systemic venous connection are common, as are abortive forms of cor triatriatum, but extracardiac TAPVCs are not. Common atrium and other types of AV septal defects occur in about half the cases. Univentricular AV connections are uncommon, as are solitary ventricular chambers, but double outlet right ventricle is common. Pulmonary stenosis is present in about half of cases.

In surgical patients with right atrial isomerism, anomalies of systemic venous connection are less common, as are abortive forms of cor triatriatum, but extracardiac forms of TAPVC occur more frequently. Common atrium and other forms of AV septal defect occur in more than 90% of patients, and solitary ventricular chamber occurs in nearly half. The fact that cardiac anomalies are more complex and numerous in hearts with right rather than left atrial isomerism probably explains the higher prevalence of left atrial isomerism in surgical series than in autopsy series.

**Morphogenesis**
The genetic basis of heterotaxy is thought to be related to genetics of ciliary dysfunction on the embryologic midline node.

**CLINICAL FEATURES AND DIAGNOSTIC CRITERIA**
There are no clinical features absolutely specific to atrial isomerism, because there is no specific functional derangement uniformly associated with the atrial morphology. The clinical sign most intimately related to the atrial morphology itself is presence of abnormal P-wave morphology and slow atrial rhythm associated with left atrial isomerism. Asplenia, commonly associated with right atrial isomerism, is associated with an increased number of Howell-Jolly bodies in the routine blood smear in newborns, or persistent Howell-Jolly bodies in older infants. Clinical features depend, therefore, on the specific cardiac anomalies and the many possible noncardiac anomalies and disorders that may be present, including intestinal malrotation, absence of splenic function, primary ciliary dyskinesia, biliary atresia, central nervous system anomalies, craniofacial anomalies, intraabdominal vascular anomalies such as congenital extral hepatic portosystemic shunt, and musculoskeletal anomalies.

Atrial situs is best diagnosed preoperatively by determining thoracic situs, because atrial and thoracic situs are nearly always the same. Thoracic situs is best indicated by bronchial anatomy, which does not always correspond to

### Table 58-6 Summary of Anatomic Findings (n = 93)

<table>
<thead>
<tr>
<th>Right Isomerism (n = 61)</th>
<th>Left Isomerism (n = 32)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>UVH</td>
<td>39</td>
</tr>
<tr>
<td>Two ventricles</td>
<td>22</td>
</tr>
<tr>
<td>CAVV</td>
<td>56</td>
</tr>
<tr>
<td>Two AV valves</td>
<td>2</td>
</tr>
<tr>
<td>MA or TA</td>
<td>3</td>
</tr>
<tr>
<td>VA concordant connection (Ao from LV)</td>
<td>6</td>
</tr>
<tr>
<td>VA discordant connection (Ao from RV)</td>
<td>55</td>
</tr>
<tr>
<td>Pulmonary atresia</td>
<td>20</td>
</tr>
<tr>
<td>Pulmonary stenosis</td>
<td>36</td>
</tr>
<tr>
<td>Bilateral SVC</td>
<td>33</td>
</tr>
<tr>
<td>Right SVC</td>
<td>24</td>
</tr>
<tr>
<td>Left SVC</td>
<td>4</td>
</tr>
<tr>
<td>Right IVC</td>
<td>43</td>
</tr>
<tr>
<td>Left IVC</td>
<td>17</td>
</tr>
<tr>
<td>IVC absence</td>
<td>1</td>
</tr>
<tr>
<td>TAPVC</td>
<td>37</td>
</tr>
<tr>
<td>PAPVC</td>
<td>1</td>
</tr>
</tbody>
</table>

Data from Hirooka and colleagues. Key: Ao, Aorta; AV, atrioventricular; CAVV, common atrioventricular valve; IVC, inferior vena cava; LV, left ventricle; MA, mitral atresia; PAPVC, partial anomalous pulmonary venous connection; RV, right ventricle; SVC, superior vena cava; TA, tricuspid atresia; TAPVC, total anomalous pulmonary venous connection; UVH, univentricular heart; VA, ventriculoarterial.
associated with both left and right atrial isomerism and as a result can strongly suggest the diagnosis \(^{17}\) (Figs. 58-2 and 58-3). Echocardiography, however, is limited in delineating all morphologic details related to atrial isomerism, particularly when complex pulmonary artery and pulmonary venous anomalies are present (e.g., pulmonary atresia with discontinuous branch pulmonary arteries, mixed TAPVC). Specific characteristics of the atrial appendages cannot usually be identified with certainty, and the relationship of bronchi to pulmonary arteries cannot be determined. Complex pulmonary artery and pulmonary vein anomalies, and the extra-cardiac thoracic and abdominal features of left and right atrial isomerism, can best be determined by computed tomography and cineangiography (Figs. 58-4 and 58-5). Specific hemodynamic data can only be obtained by cardiac catheterization.

Almost all children with right atrial isomerism are in sinus rhythm, and most have a normal P-wave axis. \(^{\text{W1}}\) Complete AV block coexists in about 10% of patients with left atrial isomerism but is rare in right atrial isomerism. \(^{\text{W1}}\)

At operation, the surgeon must make direct observations of the atrial appendages and atrial walls to confirm or deny the preoperative diagnosis of right or left atrial isomerism.
Atrial isomerism with asplenia (probably bilateral right-sidedness). Echocardiography can reliably identify most cardiovascular defects associated with the various atrial isomerism (heterotaxy) syndromes. Because the constellation of findings is variable and complex, multiple echocardiographic views are required. This subcostal coronal view demonstrates enlarged atrial chamber. Almost complete absence of atrial septum is evident, with only a central band present. There is a large ostium primum defect and a large ostium secundum defect. The single atrioventricular valve and ventricular mass are also seen. Key: AS, Atrial septum; ASD1, ostium primum defect; ASD2, secundum atrial septal defect; V, ventricle.

Figure 58-2  Atrial isomerism with asplenia (probably bilateral right-sidedness). Echocardiography can reliably identify most cardiovascular defects associated with the various atrial isomerism (heterotaxy) syndromes. Because the constellation of findings is variable and complex, multiple echocardiographic views are required. This subcostal coronal view demonstrates enlarged atrial chamber. Almost complete absence of atrial septum is evident, with only a central band present. There is a large ostium primum defect and a large ostium secundum defect. The single atrioventricular valve and ventricular mass are also seen. Key: AS, Atrial septum; ASD1, ostium primum defect; ASD2, secundum atrial septal defect; V, ventricle.

NATURAL HISTORY

Natural history of patients with atrial isomerism is determined primarily by details of cardiac structures and nature of coexisting cardiac anomalies. However, atrial isomerism itself may contribute to natural history because of its association with neonatal complete heart block and sometimes neonatal death.  

Right atrial isomerism is often accompanied by asplenia, a condition believed to render the patient susceptible to infection, particularly pneumococcal. Left atrial isomerism is often accompanied by polysplenia and a high prevalence of extrhepatic biliary atresia; the polysplenia is also accompanied by splenic incompetence.

TECHNIQUE OF OPERATION

Cardiopulmonary Bypass

In patients with atrial isomerism, cardiopulmonary bypass (CPB) often presents venous cannulation problems because of systemic venous anomalies. Basic venous cannulation techniques are used, as well as those for situations involving three venae cavae (see “Venous Cannulation” under Preparation for Cardiopulmonary Bypass and “Left Superior Vena Cava” under Special Situations and Controversies in Section III of Chapter 2). Direct caval cannulation is particularly advantageous because of complex intraatrial repairs that are often required.

In patients with left atrial isomerism and two superior venae cavae, it must be remembered in selecting venous cannula size that one of the superior cavae is probably returning the entire inferior vena caval flow by way of the azygos continuation as well as its usual flow, and that a larger than usual cannula is required. In such situations, blood returning from hepatic veins connected directly to an atrium is picked up by a pump-oxygenator sump-sucker placed in the depths of the atrium. The hepatic veins, especially if they become confluent before entering the atrium, may also be directly cannulated. Occasionally, patients with right atrial isomerism will have bilateral superior venae cavae as well as hepatic veins that drain to the atrium separate from the inferior vena cava; in this situation, four venous cannulae may be necessary.

In all of these situations, complexity of the cannulation arrangement (and accompanying complexity of the intracardiac repair in many cases) is such that cooling to moderate to deep hypothermia (20°C-24°C) and using aortic clamping and cold cardioplegia are advised to allow maximum visibility and flexibility of the perfusion flow rate. For example, if a complex atrial baffle is required, one or more of the multiple venous cannulae may be temporarily removed and replaced with a cardiotomy suction device to enhance visibility and ensure the baffle is placed without distortion.

One solution to the venous cannulation problem is to use hypothermic circulatory arrest, cooling and rewarming the patient with a single venous cannula through an atrial appendage. (Advantages and disadvantages of this technique are described in Section IV of Chapter 2.) This method is more likely to be chosen for infants.

Intracardiac Repair

A wide variety of intracardiac repairs are required in patients with atrial isomerism, and repair in individual patients may require two or three procedures. These are described under Technique of Operation in chapters on the specific anomaly encountered. Procedures used in repair of AV septal defects, including common atrium (see Technique of Operation in Chapter 54), are particularly important.

Complex Atrial Baffle

In repairing anomalies of pulmonary or systemic venous connections that are frequently part of the cardiac anomaly, a complex atrial baffle is often required. The first step is usually excising remnants of the atrial septum, except for the anterior limbus, which, if present, may contain the AV node or bundle of His. The temptation to retain part of the septum as a flap should generally be resisted because it tends to increase complexity. When a coronary sinus is present, it is usually cut down, as in the Senning or Mustard repair (see Fig. 52-32 in Chapter 52).

Fig. 58-6 shows a complete AV septal defect with bilateral superior vena cavae, interrupted inferior vena cava with azygos continuation to the right superior vena cava, and two separate hepatic venous connections. Spatial arrangements of the orifices of the pulmonary veins, left-sided superior vena cava in the upper left corner of the atrium, right-sided superior vena cava in the upper right atrial corner, and hepatic
After these structures and relationships have been visualized clearly, the proposed suture line of the baffle is marked with four to six interrupted suture markers, and the pericardium that was taken initially and set aside is trimmed to a proper shape and size and sutured into place (Fig. 58-6, B).

This complex atrial baffle is similar to that used for repair of simple unroofed coronary sinus syndrome (see Fig. 33-3 in Chapter 33).

Frequent association of anomalies of venous connection with AV septal defects in patients with atrial isomerism often necessitates combining baffle repair with repair of a complete AV septal defect. In such a procedure, extension of the atrial baffle toward the AV valves is best thought of as simply the intraatrial portion of the two-patch technique used in the repair of complete AV septal defects (see “Two-Patch Technique” under Technique of Operation in Chapter 34).

Techniques have been developed that reduce complexity of the atrial baffle in some circumstances. When bilateral superior venae cavae are present with unroofed coronary sinus, extracardiac connection of the left to the right superior veins lying inferiorly must be visualized in three dimensions and clearly understood (Fig. 58-6, A). Also, the superior vena cava receiving venous drainage from the lower body must be recognized as requiring a larger pathway to the AV valve than usual if flow is to be unimpeded. The relationship of these orifices to left-sided and right-sided AV valves must be clarified, because proper positioning of the atrial baffle depends on this knowledge. Presence of an intact inferior vena cava with separate hepatic venous drainage to the atrium, not shown in this figure, would add further complexity.

In planning the baffle and potential drainage pathways to AV valves, ventriculoarterial connections that will exist at the end of the repair must also be clearly visualized. In this regard, the ventricular situs (handedness or loop) per se is not important, because in what will ultimately be a two-ventricle system, pulmonary venous return must be routed to the ventricle that does (or will) connect to the aorta, regardless of whether it is morphologically right or left. Similarly, systemic venous return must be routed to the ventricle connected to the pulmonary trunk.

After these structures and relationships have been visualized clearly, the proposed suture line of the baffle is marked with four to six interrupted suture markers, and the pericardium that was taken initially and set aside is trimmed to a proper shape and size and sutured into place (Fig. 58-6, B). This complex atrial baffle is similar to that used for repair of simple unroofed coronary sinus syndrome (see Fig. 33-3 in Chapter 33).

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colleagues have identified characteristics of valve repair that increase the likelihood of success. Multiple techniques were used, primarily including direct leaflet apposition at clefts, scallops, or prolapsing leaflet edges and various forms of reduction anuloplasty. Additional techniques used were the Alfieri suture and chordal shortening.

Palliative Operations

Standard techniques are used for shunting procedures (see “Technique of Shunting Operations” under Technique of Operation in Section I of Chapter 38 and “Systemic–Pulmonary Arterial Shunt” under Technique of Operation in Section II of Chapter 41) and pulmonary trunk banding (see “Pulmonary Trunk Banding” under Technique of Operation in Section II of Chapter 41). Coexisting juxtaductal pulmonary arterial stenosis, not uncommon in these patients, should be corrected at the time of the shunting operation. Occasionally, discontinuous branch pulmonary arteries arising from bilateral ductus arteriosus, in association with pulmonary atresia, must be reconstructed at the time of the shunting procedure. In one series, this morphology was present in 7 of 28 patients (25%) having pulmonary atresia with right atrial isomerism.

If a superior cavopulmonary shunt is being considered, careful consideration must be given to presence of bilateral superior vena cavae or of interrupted inferior vena cava. Bilateral bidirectional superior cavopulmonary shunts are discussed in Section III of Chapter 41. The considerations are purely technical, with no physiologic implications different from those of unilateral bidirectional superior cavopulmonary shunt. In contrast, creating a bidirectional cavopulmonary shunt in the setting of interrupted inferior vena cava has important physiologic implications. Because of azygos vein continuation associated with interrupted inferior vena cava,

Fontan Type of Repair

Frequent occurrence of complex cardiac anomalies means that a Fontan type of repair must sometimes be used. Usual techniques of operation as practiced in the current era (see Technique of Operation in Section IV of Chapter 41) serve well. In most instances, some form of extracardiac conduit or lateral tunnel total cavopulmonary shunt operation is useful (see “Persistent Left Superior Vena Cava with Hemiazygos Extension of Inferior Vena Cava” under Special Situations and Controversies in Section IV of Chapter 41). Several variations of these basic techniques can be used when the hepatic veins enter the atria separately.

Atrioventricular Valve Repair

Repair of a common atrioventricular valve is an important consideration in heterotaxy patients with single ventricle physiology. Valve regurgitation is a consistently cited risk factor for poor outcome (see Results section). Ota and
When a bidirectional cavopulmonary shunt is created in the setting of interrupted inferior vena cava, careful mid- and long-term follow-up is critical to monitor development of pulmonary arteriovenous malformations. These pulmonary vascular abnormalities can develop under various conditions of altered pulmonary blood flow, but their development is particularly rapid and aggressive in this setting. The first sign of pulmonary arteriovenous malformations may be decreased \( \text{Sao}_2 \), although contrast echocardiography may document arteriovenous malformations well before that. At catheterization, angiographic evidence of arteriovenous malformations

**SPECIAL FEATURES OF POSTOPERATIVE CARE**

Usual measures of postoperative care are employed after repair of cardiac anomalies in patients with atrial isomerism (see Chapter 5). Special measures used after the Fontan type of procedure are described under Special Features of Postoperative Care in Section IV of Chapter 41.
and desaturated blood in the pulmonary veins confirm the diagnosis. There is evidence that incorporating splanchnic venous blood into the pulmonary circulation along with the remainder of systemic venous return may reverse pulmonary arteriovenous malformations. Lack of splenic function in heterotaxy patients increases the risk of nosocomial infection and demands exquisite attention to preoperative sterile technique. In a series of 29 heterotaxy patients, seven (24%; CI 15%-35%) developed sepsis during treatment. Six of the seven were on appropriate antibiotic therapy when sepsis developed. Underscoring the fact that polysplenia patients as well as asplenia patients have splenic dysfunction, five of the seven patients with sepsis had polysplenia. Bacterial sepsis was associated with a 44% mortality.

RESULTS

Because of wide morphologic variability in patients with atrial isomerism, it is difficult to summarize overall outcomes. However, several general points can be made. First, overall survival is better with left, compared with right, atrial isomerism (94% vs. 79% at 3 years in one series, and 94% vs. 53% at 1 year in another). Second, in most series survival is better when a biventricular repair is undertaken compared with a management plan that leads to a Fontan procedure (Figs. 58-7 and 58-8). In the large series reported by Serraf and colleagues, however, mortality in these two categories was similar (Fig. 58-9). Points one and two above are somewhat related; in all series of heterotaxy, most biventricular repairs are performed in patients with left atrial isomerism morphology. Third, overall results have improved substantially over time, with current-era outcomes suggesting 7% to 15% early mortality, and long-term survival of 75% (Fig. 58-10). In one large series, all mortality beyond that related to initial neonatal management was due to interstage loss in single-ventricle patients.

Left Atrial Isomerism Outcomes

In left atrial isomerism, several large series suggest that about one third of patients received a biventricular repair. The remainder underwent surgical palliation or did not undergo surgical intervention. Of those not undergoing operation, death was almost certain if important cardiac defects were present. In earlier series, even in patients with normal hearts there was 18% mortality within the first few years of life because of important noncardiac abnormalities, and in those patients undergoing some form of surgical intervention, both short- and long-term outcomes were substantially better in those undergoing biventricular repair (Fig. 58-11; see also Fig. 58-7).

In more recent series, patients undergoing surgical palliation have had excellent survival, as have those undergoing biventricular repair, with no differences noted between these two groups. In fact, these recent outcomes in patients

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**Figure 58-7** Flow chart of interventions in 163 patients with left atrial isomerism. *Comprising 9 patients with biventricular hearts, 23 with single ventricle, and 22 with normal hearts. **Four patients had Fontan-type surgery without prior interventions. Fontan-type includes bidirectional cavopulmonary shunt, right atrium to pulmonary artery anastomosis, and hepatic vein to pulmonary artery rerouting. (From Gilljam and colleagues.)
undergoing surgical intervention are substantially better than the 18% mortality in left atrial isomerism patients with normal hearts from older series. Thus, it can be inferred that noncardiac management of heterotaxy patients has also improved. This inference is supported by the fact that noncardiac as well as cardiac risk factors for death were identified in older series (Table 58-7). More recent series show almost no mortality, and understandably: case volumes are small with no identifiable risk factors. One study of 91 biventricular repairs suggests that attempting biventricular repair in the setting of unbalanced AV septal defect is associated with increased mortality.

Right Atrial Isomerism Outcomes

In right atrial isomerism, both short- and long-term outcomes are worse than for left atrial isomerism. Although outcomes have improved in recent series, they still remain worse than in left atrial isomerism. Risk factors in recent series include presence of AV valve regurgitation, obstructed TAPVC, and mixed TAPVC, similar to those identified in earlier series (Table 58-8 and Fig. 58-12). Occurrence of secondary pulmonary vein obstruction after repair of obstructed TAPVC is frequent, adding to the poor prognosis of this association (Table 58-9). Biventricular repair is possible in few patients with right atrial isomerism (see Fig. 58-7). In patients not receiving surgical intervention, death is almost a certainty (Fig. 58-13; see also Fig. 58-8).

In patients undergoing surgical palliation, presence of TAPVC requiring operation creates substantial problems in the setting of single-ventricle physiology. The common occurrence of obstructed outflow into the pulmonary circulation and obstructed pulmonary veins makes management of such infants particularly challenging (see Table 58-8; see also Fig. 58-13).
Figure 58-11  Survival of 163 patients with left atrial isomerism and a normal heart ($n = 22$), a heart suitable for biventricular repair ($n = 71$), and a heart suitable for single-ventricle surgery ($n = 70$). Survivors are denoted by dots. Vertical bars represent 95% confidence limits. Differences between groups were analyzed using the log-rank and Wilcoxon tests. (From Gilljam and colleagues.134)

Table 58-7  Incremental Risk Factors for Time-Related Mortality in Left Atrial Isomerism

<table>
<thead>
<tr>
<th>Variable</th>
<th>Including Birth Weight ($n = 122$)</th>
<th>Excluding Birth Weight ($n = 162^a$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Relative Hazard</td>
<td>$P$</td>
</tr>
<tr>
<td>Lower birth weight</td>
<td>0.40 (0.27-0.58)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Single ventricle</td>
<td>2.31 (1.37-3.89)</td>
<td>.02</td>
</tr>
<tr>
<td>Gastrointestinal malformations$^b$</td>
<td>—</td>
<td>.02</td>
</tr>
<tr>
<td>Biliary atresia</td>
<td>—</td>
<td>.02</td>
</tr>
<tr>
<td>Congenital AV block</td>
<td>—</td>
<td>.02</td>
</tr>
<tr>
<td>Coarctation of aorta</td>
<td>3.40 (1.86-6.22)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Data from Gilljam and colleagues.132

$^a$From Cox’s proportional hazard modeling. Because of the number of patients with missing values for the variable birth weight, the analysis was repeated excluding this variable, with resultant entry of three additional variables.

$^b$Other than biliary atresia.

Key: AV, Atrioventricular; CL, confidence limits.

Table 58-8  Incremental Risk Factors for Time-Related Mortality in Patients with Right Atrial Isomerism (Cox Proportional Hazards Modeling)$^a$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient ± SE</th>
<th>$P$</th>
<th>HR (95% CL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absence of pulmonary outflow obstruction</td>
<td>−0.80 ± 0.37</td>
<td>.03</td>
<td>2.2 (1.08-4.6)</td>
</tr>
<tr>
<td>Presence of major AV valve anomaly</td>
<td>1.65 ± 0.73</td>
<td>.03</td>
<td>5.2 (1.25-22)</td>
</tr>
<tr>
<td>Presence of obstructed pulmonary veins</td>
<td>1.69 ± 0.34</td>
<td>.0001</td>
<td>5.4 (2.8-10.5)</td>
</tr>
</tbody>
</table>

Data from Hashmi and colleagues.111

$^a$Final model based on 84 observations with nonmissing values.

Key: AV, Atrioventricular; CL, confidence limits; HR, hazard ratio; SE, standard error.

Figure 58-12  Kaplan-Meier survival of 102 patients with right atrial isomerism, stratified by presence of total anomalous pulmonary venous connection (TAPVC). (From Foerster and colleagues.11)
Other series support the observation that biventricular repair, when possible, can be performed with low mortality, that surgery in the neonatal period for pulmonary venous obstruction in combination with outflow obstruction to the pulmonary circulation in right atrial isomerism carries a dismal prognosis, and that outcomes following surgical intervention are generally better in left, compared with right, atrial isomerism.\textsuperscript{51,52,53,54}

Fontan Outcomes

In several studies, one multicenter, functional outcome and survival after the Fontan operation were similar in heterotaxy and non-heterotaxy patients.\textsuperscript{4,5,6,7} Heterotaxy patients, however, did undergo their procedure at an older age, were more likely to receive an extracardiac conduit Fontan, had more previous operations, had a higher prevalence of sinus node dysfunction and atrial dysrhythmias, and had more AV valve regurgitation.

Atrioventricular Valve Repair Outcomes

Successful repair can be achieved in two thirds of patients.\textsuperscript{2,3} The technique of leaflet apposition (see "Atrioventricular Valve Repair" under Technique of Operation) was associated with successful repair. Successful repair was associated with improved survival.\textsuperscript{4}

INDICATIONS FOR OPERATION

Need for surgical treatment is dictated by associated cardiac anomalies, not by atrial isomerism. Atrial isomerism, particularly right atrial isomerism and asplenia, strongly suggests the presence of complex cardiac anomalies and a higher-than-usual surgical risk, but coexisting anomalies are usually severe and the natural history unfavorable. Therefore, indications for operation are usually clear.

REFERENCES

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